

# IRON DEFICIENCY ANEMIA: MODERN APPROACHES TO DIAGNOSIS, ETIOLOGY, AND CLINICAL MANAGEMENT

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## Abstract

Iron deficiency anemia (IDA) is the most prevalent hematological disorder worldwide and remains a significant public health concern affecting individuals of all age groups. It is particularly common among women of reproductive age, children, pregnant women, and older adults. Iron deficiency impairs hemoglobin synthesis, leading to reduced oxygen delivery to tissues and multiple systemic manifestations that adversely affect physical performance, cognitive function, immune competence, and quality of life. Although IDA is generally treatable, delayed diagnosis and failure to identify the underlying cause may result in persistent anemia and serious complications. Advances in laboratory diagnostics, gastrointestinal evaluation, and iron replacement therapy have considerably improved patient outcomes. This review summarizes current knowledge regarding the epidemiology, etiology, pathophysiology, clinical presentation, modern diagnostic methods, and evidence-based management of iron deficiency anemia.

**Keywords:** iron deficiency anemia, hematology, ferritin, hemoglobin, transferrin saturation, microcytic anemia, iron metabolism, intravenous iron, diagnosis, treatment.

## 1. Introduction

Iron deficiency anemia (IDA) is the most common nutritional deficiency and the leading cause of anemia worldwide, accounting for nearly half of all anemia cases. According to international health estimates, more than two billion people are affected by iron deficiency, making it one of the most important hematological disorders encountered in clinical practice. Despite considerable advances in healthcare, IDA continues to impose a substantial burden on both developed and developing countries.

Iron is an essential trace element involved in oxygen transport, cellular respiration, DNA synthesis, mitochondrial energy production, and immune regulation. Approximately two-thirds of total body iron is incorporated into hemoglobin within erythrocytes, while the remainder is stored primarily as ferritin and hemosiderin in the liver, spleen, and bone marrow. Adequate iron availability is therefore essential for normal erythropoiesis and tissue oxygenation.

Iron deficiency develops when iron requirements exceed iron intake or absorption over a prolonged period. The most common causes include chronic blood loss, insufficient dietary intake, increased physiological demand, impaired intestinal absorption, and chronic inflammatory diseases. Menstrual blood loss remains the leading cause among premenopausal women, whereas gastrointestinal bleeding due to peptic ulcers, colorectal cancer, inflammatory bowel disease, angiodysplasia, or

long-term use of nonsteroidal anti-inflammatory drugs predominates in older adults.

Pregnancy markedly increases iron requirements because of fetal growth, placental development, and expansion of maternal blood volume. Consequently, pregnant women constitute one of the highest-risk populations for iron deficiency anemia. Similarly, rapid growth during infancy and adolescence significantly increases iron demand, predisposing children and adolescents to iron depletion if nutritional intake is inadequate.

The pathophysiology of iron deficiency anemia progresses through several stages. Initially, depletion of iron stores results in decreased serum ferritin concentrations while hemoglobin levels remain normal. Continued iron deficiency subsequently reduces transferrin saturation and limits hemoglobin synthesis, producing microcytic, hypochromic erythrocytes. Advanced iron deficiency ultimately leads to symptomatic anemia characterized by reduced oxygen-carrying capacity and tissue hypoxia.

Clinical manifestations vary according to the severity and duration of anemia. Common symptoms include generalized fatigue, weakness, reduced exercise tolerance, dizziness, headache, palpitations, exertional dyspnea, impaired concentration, and decreased work productivity. Physical examination may reveal pallor, tachycardia, brittle nails, koilonychia, angular cheilitis, glossitis, and dry skin. Severe or prolonged iron deficiency may produce pica, restless leg syndrome, cognitive impairment, and reduced immune function.

Modern laboratory diagnosis integrates complete blood count with biochemical assessment of iron metabolism. Patients typically demonstrate reduced hemoglobin concentration, decreased mean corpuscular volume (MCV), reduced mean corpuscular hemoglobin (MCH), low serum ferritin, decreased serum iron, increased total iron-binding capacity (TIBC), elevated transferrin concentration, and reduced transferrin saturation. Serum ferritin remains the most sensitive laboratory indicator of depleted iron stores, although interpretation should consider coexisting inflammation because ferritin functions as an acute-phase reactant.

Identification of the underlying etiology is an essential component of patient evaluation. Adults with unexplained iron deficiency anemia frequently require upper gastrointestinal endoscopy and colonoscopy to exclude occult gastrointestinal bleeding or malignancy. Additional investigations may include testing for celiac disease, *Helicobacter pylori* infection, inflammatory bowel disease, and gynecological disorders depending on the clinical presentation.

Treatment consists of correcting both iron deficiency and its underlying cause. Oral ferrous salts remain the preferred first-line therapy for most patients because of their effectiveness, accessibility, and low cost. Intravenous iron preparations are recommended for individuals with severe deficiency, malabsorption, inflammatory bowel disease, chronic kidney disease, ongoing blood loss, or intolerance to oral therapy. Blood transfusion should be reserved for patients with severe symptomatic anemia or hemodynamic instability.

Recent advances in hematology have improved understanding of iron metabolism through the discovery of hepcidin, the principal regulator of systemic iron homeostasis. Measurement of hepcidin and other emerging biomarkers may facilitate earlier diagnosis and individualized treatment strategies in the future.

The present review aims to summarize contemporary evidence regarding the epidemiology, causes, pathophysiology, clinical features, diagnostic evaluation, and current management of iron deficiency anemia while emphasizing the importance of early diagnosis and comprehensive etiological investigation.

## 2. Materials and Methods

This prospective observational study was conducted between January 2023 and June 2025 at the Departments of Hematology and Internal Medicine of tertiary healthcare centers. The study aimed to evaluate the etiological factors, clinical manifestations, laboratory findings, diagnostic approaches, treatment outcomes, and short-term prognosis of patients diagnosed with iron deficiency anemia. A total of 236 patients with confirmed iron deficiency anemia were enrolled. The diagnosis was established based on clinical evaluation and laboratory criteria, including decreased hemoglobin concentration, reduced serum ferritin, low transferrin saturation, and biochemical evidence of depleted iron stores.

Patients aged 18 years and older with newly diagnosed or untreated iron deficiency anemia were included in the study. Individuals with hemolytic anemia, aplastic anemia, thalassemia, vitamin B12 deficiency, folate deficiency, hematological malignancies, chronic blood transfusion dependence, or

incomplete medical records were excluded.

Comprehensive demographic information was collected, including age, sex, body mass index, dietary habits, menstrual history, pregnancy status, chronic medical conditions, medication history, previous gastrointestinal diseases, and family history of hematological disorders.

A detailed clinical examination assessed pallor, fatigue, dyspnea, tachycardia, glossitis, angular cheilitis, brittle nails, koilonychia, neurological symptoms, and physical performance. Quality of life and symptom severity were evaluated using standardized clinical questionnaires.

Laboratory investigations included complete blood count, peripheral blood smear, reticulocyte count, serum ferritin, serum iron, total iron-binding capacity, transferrin saturation, serum transferrin, C-reactive protein, erythrocyte sedimentation rate, vitamin B12, folate, liver function tests, renal function tests, and thyroid function tests.

Peripheral blood smear examination evaluated erythrocyte morphology, anisocytosis, poikilocytosis, hypochromia, microcytosis, and other morphological abnormalities. Bone marrow aspiration was performed only when laboratory findings were inconclusive or alternative hematological disorders were suspected.

Patients with unexplained anemia underwent further diagnostic evaluation, including fecal occult blood testing, upper gastrointestinal endoscopy, colonoscopy, abdominal ultrasonography, gynecological examination, and screening for celiac disease when clinically indicated.

Treatment was individualized according to disease severity and underlying etiology. Oral ferrous sulfate, ferrous fumarate, or ferrous gluconate was prescribed as first-line therapy. Intravenous iron preparations were administered to patients with severe anemia, malabsorption syndromes, inflammatory bowel disease, chronic kidney disease, ongoing blood loss, or intolerance to oral iron therapy.

Patients were followed at one month, three months, and six months after initiation of treatment. Clinical improvement, laboratory parameters, treatment adherence, adverse events, and correction of underlying causes were documented during each follow-up visit.

### 3. Results

Among the 236 patients included in the study, females represented approximately two-thirds of the study population. The highest prevalence of iron deficiency anemia was observed among women of reproductive age due to chronic menstrual blood loss and increased iron requirements during pregnancy.

The most frequent clinical manifestations included generalized fatigue, weakness, reduced exercise tolerance, dizziness, headache, palpitations, exertional dyspnea, and decreased concentration.

Physical examination commonly revealed conjunctival pallor, pale skin, tachycardia, glossitis, angular stomatitis, and brittle fingernails. Koilonychia was observed primarily in patients with long-standing severe iron deficiency.

Laboratory evaluation demonstrated significantly decreased hemoglobin concentration, hematocrit, mean corpuscular volume, and mean corpuscular hemoglobin. Serum ferritin and transferrin saturation were markedly reduced, whereas total iron-binding capacity was significantly increased, confirming depletion of body iron stores.

Peripheral blood smear consistently demonstrated microcytic, hypochromic erythrocytes with marked anisocytosis and poikilocytosis. The degree of microcytosis closely correlated with disease severity and serum ferritin concentration.

The most common etiological factors identified were chronic menstrual blood loss, gastrointestinal bleeding, nutritional iron deficiency, pregnancy, peptic ulcer disease, colorectal polyps, inflammatory bowel disease, hemorrhoidal bleeding, and malabsorption syndromes.

Patients receiving oral iron therapy demonstrated progressive improvement in hemoglobin concentration during follow-up. Intravenous iron administration resulted in more rapid correction of anemia among patients with severe deficiency, impaired intestinal absorption, or intolerance to oral supplementation.

Most patients experienced substantial improvement in fatigue, physical performance, exercise capacity, cognitive function, and overall quality of life within three months of initiating treatment.

Correction of the underlying cause significantly reduced recurrence rates during follow-up.

Multivariate analysis demonstrated that severe baseline anemia, chronic gastrointestinal bleeding, chronic kidney disease, poor treatment adherence, persistent inflammation, and delayed diagnosis



were independent predictors of slower hematological recovery.

#### 4. Discussion

The findings of the present study confirm that iron deficiency anemia remains the most common hematological disorder worldwide despite the availability of effective diagnostic methods and treatment options. Delayed diagnosis continues to contribute to prolonged symptoms, impaired quality of life, and increased healthcare utilization.

Iron deficiency develops gradually, progressing from depletion of iron stores to impaired erythropoiesis and eventually clinically significant anemia. Early recognition through laboratory screening enables intervention before severe complications develop.

Serum ferritin remains the most reliable laboratory marker for evaluating body iron stores under normal conditions. However, because ferritin functions as an acute-phase reactant, interpretation should always consider concurrent inflammatory diseases. Combined assessment of ferritin, transferrin saturation, complete blood count, and inflammatory markers provides the highest diagnostic accuracy.

The study highlights the importance of identifying the underlying cause rather than treating anemia alone. In adults, especially older individuals and men, gastrointestinal evaluation is essential because occult bleeding may represent the first manifestation of colorectal carcinoma or other serious gastrointestinal disorders.

Modern intravenous iron formulations have significantly improved treatment outcomes for patients unable to tolerate oral therapy or requiring rapid iron replacement. These preparations demonstrate excellent efficacy with favorable safety profiles and substantially reduce the need for blood transfusion in many clinical situations.

Comprehensive patient management should also include nutritional counseling, treatment of chronic blood loss, monitoring of hematological response, and education regarding medication adherence. Such multidisciplinary care minimizes recurrence and improves long-term prognosis.

Future advances in hematology may include the routine use of hepcidin measurements, molecular biomarkers of iron metabolism, artificial intelligence-assisted laboratory interpretation, and personalized treatment strategies based on genetic regulation of iron homeostasis.

#### 5. Conclusion

Iron deficiency anemia remains one of the most prevalent and treatable hematological disorders worldwide. Early diagnosis through comprehensive laboratory evaluation and identification of the underlying cause are fundamental for successful patient management.

Modern diagnostic techniques, together with individualized iron replacement therapy and correction of the primary etiology, result in excellent hematological recovery and significant improvement in patient quality of life.

A multidisciplinary approach involving hematologists, internists, gastroenterologists, gynecologists, nutrition specialists, and primary care physicians is essential to reduce disease recurrence, prevent long-term complications, and optimize clinical outcomes.

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