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Review

Common Causes and Diagnostic Approaches to Anemia in Hospitalized Adults

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Abstract

Anemia remains a frequent and clinically significant finding among hospitalized adults, often complicating medical and surgical conditions and contributing to longer hospital stays, increased morbidity, and delayed recovery. The etiologies are broad, including anemia of chronic disease, iron deficiency, acute blood loss, nutritional deficiencies, renal dysfunction, bone marrow suppression, and hemolysis. Patients admitted for various reasons often present with overlapping causes, making diagnosis and management complex. Inflammation and infection can obscure typical laboratory patterns, while hospital-related factors such as phlebotomy, poor nutrition, and medication effects can exacerbate pre-existing anemia or create new deficits. Accurate diagnosis begins with a structured evaluation of red blood cell indices and classification by mean corpuscular volume, followed by targeted testing such as reticulocyte counts, iron studies, vitamin B12 and folate levels, and markers of hemolysis. The interpretation of results must consider acute illness and coexisting conditions. Underdiagnosis of reversible forms of anemia, particularly nutritional deficiencies, remains common and may affect functional outcomes after discharge. Clinical judgment is essential in decisions around red blood cell transfusion, iron replacement, or the use of erythropoiesis-stimulating agents. Management strategies vary by etiology and patient context. Restrictive transfusion thresholds have been shown to be safe in stable patients, while intravenous iron and vitamin supplementation can be effective in hospitalized populations when used appropriately. Integration of diagnostic algorithms into hospital workflows and increased awareness of the multifactorial nature of anemia can improve outcomes and resource utilization. Attention to anemia during hospitalization provides an opportunity to address reversible causes, reduce readmissions, and support overall recovery.

Keywords: *anemia, hospitalized adults, diagnostic evaluation, iron deficiency, patient management*

Introduction

Anemia is one of the most frequently encountered hematologic abnormalities in hospitalized adults, with significant implications for morbidity, length of stay, and mortality. Defined by the World Health Organization as a hemoglobin concentration of less than 13 g/dL in men and less than 12 g/dL in women, anemia affects a wide spectrum of patients across medical and surgical services. Its presence in hospitalized individuals often signals an underlying pathology that may be chronic, acute, or multifactorial in nature. A study of inpatient records found that up to 40 percent of hospitalized adults exhibit some degree of anemia during their stay, underscoring the condition's clinical relevance and the need for timely recognition and appropriate workup (1).

The etiologies of anemia in hospitalized patients vary depending on demographics, comorbid conditions, and the reason for admission. Common causes include anemia of chronic disease, iron deficiency, acute blood loss, renal insufficiency, bone marrow suppression, and nutritional deficiencies. Inflammation plays a major role in anemia of chronic disease, where cytokine-mediated changes reduce erythropoiesis and iron availability. Additionally, frequent phlebotomy, poor nutritional intake, and medication effects may contribute to the development or worsening of anemia during hospitalization. Identifying the predominant cause can be challenging in complex patients, as overlapping mechanisms are often present and confounding factors, such as fluid shifts, can distort laboratory interpretations (2).

Laboratory evaluation remains central to the diagnosis and classification of anemia in the hospital setting. Initial testing often includes a complete blood count, reticulocyte count, iron studies, vitamin B12 and folate levels, renal function tests, and markers of inflammation. The mean corpuscular volume (MCV) offers a useful starting point for morphologic classification into microcytic, normocytic, or macrocytic categories, which then guides further evaluation. For instance, microcytic anemia often prompts iron studies to assess for iron deficiency or chronic disease, while macrocytic anemia raises concerns for B12 or folate deficiency, or myelodysplastic syndromes (3). The rapid turnaround of laboratory data allows clinicians to initiate appropriate interventions early in the hospitalization, which may influence outcomes such as transfusion needs and discharge planning.

Despite the availability of diagnostic tools, gaps remain in the consistent and evidence-based evaluation of anemia in hospitalized adults. Studies have highlighted variability in workup patterns and underuse of confirmatory testing, especially for treatable forms such as iron deficiency anemia. In some cases, empiric iron therapy is started without confirmation, leading to suboptimal management or missed diagnoses. Furthermore, disparities in anemia recognition and treatment may exist across different patient populations, complicating care delivery and widening health inequities. Strengthening diagnostic algorithms and integrating them into hospital workflows may improve both diagnostic accuracy and patient outcomes (4).

Review

Anemia in hospitalized adults represents a multifactorial condition that often requires individualized diagnostic strategies. While anemia of chronic disease remains prevalent, iron deficiency continues to be underdiagnosed despite its potential for effective treatment. Hospitalized patients frequently present with overlapping causes, complicating the diagnostic process. For example, an elderly patient with chronic kidney disease may simultaneously experience functional iron deficiency and anemia related to inflammation, making it difficult to determine the primary etiology without a comprehensive workup (5). Delayed or insufficient diagnostic evaluation may lead to missed treatment opportunities, especially in cases where anemia contributes to functional decline or prolonged recovery.

Recent evaluations of inpatient anemia management suggest that routine testing is often inconsistent, with gaps in ordering iron studies or assessing for nutritional deficiencies. As a result, patients may be discharged without a clear understanding of the

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cause of their anemia, which may have implications for follow-up and long-term outcomes. Incorporating standardized diagnostic algorithms into hospital care could help address these inconsistencies and reduce unnecessary variation in practice. Moreover, increased awareness of common reversible causes, such as iron or B12 deficiency, may prompt earlier intervention, ultimately improving patient outcomes and reducing healthcare costs (6).

Etiologies of Anemia in Inpatient Settings

The causes of anemia in hospitalized adults are diverse, frequently multifactorial, and often influenced by the underlying reason for admission. Medical, surgical, and critical care patients each present with distinct patterns that require tailored diagnostic attention. In general, medical wards, anemia of chronic inflammation is highly prevalent. It results from impaired iron metabolism, reduced erythropoietin response, and limited red cell survival, typically in patients with infections, malignancies, or autoimmune diseases. This form of anemia often presents with normocytic indices and low serum iron despite adequate or elevated ferritin levels, reflecting iron sequestration rather than depletion (7).

Surgical inpatients, particularly those undergoing orthopedic, cardiac, or gastrointestinal procedures, frequently develop anemia due to acute blood loss and perioperative hemodilution. Intraoperative bleeding and the effects of intravenous fluids on hemoglobin concentration contribute to postoperative declines in red cell mass. Moreover, repetitive blood draws and poor nutritional intake during recovery may worsen pre-existing deficiencies. In a multicenter surgical cohort, hemoglobin levels on discharge were significantly lower than admission values, often without corresponding transfusion or supplementation, highlighting the need for greater perioperative management of iron and hemoglobin levels (8).

In critically ill patients, the prevalence of anemia is nearly universal by the end of the first week of intensive care. The mechanisms are complex and include inflammation-induced suppression of erythropoiesis, ongoing blood loss, hemolysis, and iatrogenic factors. Medications such as antibiotics, antithrombotics, and chemotherapeutic agents can contribute to bone marrow suppression or hemolytic processes. Furthermore, patients receiving renal replacement therapy or extracorporeal membrane oxygenation face additional risks due to circuit-related hemolysis and blood volume losses. An observational study across several ICUs found that daily phlebotomy volumes exceeded physiologic red cell production in a substantial proportion of patients, making anemia an almost inevitable complication of prolonged critical care (9).

Beyond acute illness and procedural factors, nutritional deficiencies also play a substantial role in hospital-associated anemia. Iron, vitamin B12, and folate deficiencies may go unrecognized, especially in elderly or malnourished patients. Gastrointestinal malabsorption, chronic alcohol use, and long-term use of medications such as proton pump inhibitors or metformin can further exacerbate these deficiencies. Another study found that more than 20 percent had laboratory evidence of nutritional anemia, yet only a minority received targeted treatment during admission (10).

Current Diagnostic Approaches and Laboratory Evaluation

Diagnosing anemia in hospitalized adults involves a structured yet flexible approach that integrates clinical judgment with laboratory data. The initial step often includes a CBC, which provides red cell indices such as hemoglobin concentration, hematocrit, and MCV. These parameters help narrow the differential diagnosis by classifying anemia into microcytic, normocytic, or macrocytic types. MCV-guided classification, though not definitive, offers a useful framework for early workup. Normocytic anemia is frequently encountered in hospitalized settings and often reflects multifactorial causes like chronic kidney disease, inflammation, or early nutritional deficiencies (11).

The reticulocyte count is equally critical, as it indicates the bone marrow's response to anemia. A low reticulocyte index suggests underproduction,

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often pointing toward bone marrow suppression, chronic disease, or nutritional deficiencies. In contrast, an elevated reticulocyte count may reflect hemolysis or acute blood loss. Clinicians must interpret this value in context, accounting for confounders such as recent transfusions or medications that affect erythropoiesis. Serum ferritin, transferrin saturation, and total iron-binding capacity (TIBC) help distinguish between absolute and functional iron deficiency. Ferritin, as an acute-phase reactant, may be falsely elevated in inflammatory states, masking iron deficiency if used in isolation (12). Therefore, combinations of iron studies are often more informative than single parameters.

Vitamin B12 and folate levels should be measured when macrocytic indices or neurologic symptoms raise suspicion. These tests are particularly useful in elderly patients, those with gastrointestinal disorders, or individuals taking long-term medications like metformin or anticonvulsants. A low-normal vitamin B12 level may not exclude functional deficiency, prompting the use of methylmalonic acid or homocysteine testing in selected cases. Folate deficiency, though less common due to food fortification, remains relevant in hospitalized populations with poor nutritional intake or alcohol use. Testing for both vitamins can prevent misattribution of macrocytosis to other etiologies such as liver disease or myelodysplastic syndromes (13).

Hemolysis panels are often overlooked unless anemia presents acutely or with rapid progression. Tests including lactate dehydrogenase (LDH), haptoglobin, indirect bilirubin, and peripheral blood smear help identify intravascular destruction of red cells. A smear can reveal schistocytes in microangiopathic processes, spherocytes in hereditary spherocytosis or immune hemolysis, or hypersegmented neutrophils in megaloblastic anemia. Bone marrow evaluation, although rarely the first step, may be warranted when pancytopenia, unexplained reticulocytopenia, or suspected marrow infiltration is present. The decision to pursue invasive testing typically follows the exclusion of more common etiologies through noninvasive workup. In certain cases, flow cytometry or genetic panels may supplement the diagnosis, particularly when rare causes like paroxysmal nocturnal hemoglobinuria or inherited bone marrow failure syndromes are in the differential (14).

Clinical Implications and Considerations for Patient Management

Managing anemia in hospitalized adults extends beyond correcting laboratory values. It requires attention to the patient's overall clinical status, the acuity of the anemia, and the broader context of their hospitalization. Decisions related to transfusion, for instance, are often complex and require balancing the potential benefits of improved oxygen delivery against the risks of volume overload, immunologic reactions, and infection. Current guidelines support restrictive transfusion strategies in stable patients, typically using a hemoglobin threshold of 7 to 8 g/dL, though this may be individualized based on symptoms and comorbid conditions such as coronary artery disease or ongoing bleeding (15). Iron repletion is frequently indicated but often delayed or overlooked during hospital stays. Intravenous iron has gained favor in inpatient settings due to its rapid effect, especially in patients with inflammation or poor gastrointestinal absorption. Oral iron is limited by gastrointestinal side effects and slower onset of action, which may not suit acutely ill patients. In surgical patients, proactive iron supplementation prior to elective procedures has shown benefits in reducing perioperative transfusions and improving recovery metrics (16).

Vitamin B12 and folate deficiencies, when present, require prompt correction to prevent irreversible neurologic complications and to support effective erythropoiesis. In acutely ill patients, high-dose parenteral administration may be preferred to bypass potential absorption issues. The subtle presentation of these deficiencies in older adults and those with chronic conditions can lead to delayed diagnosis if not routinely considered. Some hospital systems have integrated automated screening for these nutrients in patients presenting with macrocytic indices, which improves detection without increasing unnecessary testing (17).

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Chronic disease-related anemia poses challenges for management, particularly in patients with renal failure, cancer, or autoimmune disorders. In such cases, treatment is often not curative but focuses on symptom control and stabilization. Erythropoiesis-stimulating agents (ESAs) may be appropriate in selected patients, though concerns about thrombotic risk and tumor progression in oncology populations have led to more cautious use. For patients with kidney disease, ESA therapy combined with intravenous iron is a common approach, with dosing guided by hemoglobin targets and iron parameters. Effective use of these agents requires careful monitoring and coordination across inpatient and outpatient settings (18). Clinicians must also consider the patient's functional goals, prognosis, and quality of life when deciding how aggressively to pursue correction of anemia during the hospital stay. Addressing contributing factors such as ongoing blood loss, medication effects, or untreated infections can often yield improvement without targeted erythropoietic therapy.

Conclusion

Anemia in hospitalized adults demands a multifaceted diagnostic and management approach tailored to diverse clinical scenarios. Timely identification of underlying causes can significantly influence recovery and long-term outcomes. Integrating standardized evaluation protocols may enhance care quality and reduce unnecessary interventions. A patient-centered strategy remains essential in guiding both acute treatment and discharge planning.

Disclosure

Conflict of interest

There is no conflict of interest.

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Ethical consideration

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Data availability

All data are available within the manuscript.

Author contribution

All authors contributed to conceptualizing, data drafting, collection and final writing of the manuscript.

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