

Anemia in the Long-Term Care Setting



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KEYWORDS

• Anemia • Long-term care • Nursing home • Geriatric • Elderly • Iron deficiency

KEY POINTS

- The prevalence of anemia is high among residents living in long-term care setting.
- Anemia is associated with increased risk for falls, decline in physical performance as well as in quality of life.
- Evaluation and treatment of anemia should be based on patient's and caregiver's wishes, goals of care, and whether it will improve quality of life.

INTRODUCTION

Institutionalized elderly have multiple morbidities that are commonly associated with anemia. These conditions include cognitive impairment, frailty, renal disease, heart failure, bleeding and nutritional issues, and, like anemia, associate with a risk of falls. Recognizing the consequences of anemia can be confounded by signs and symptoms associated with comorbid conditions in older people and age-related reduction in organ functional capacity and physiologic reserve. However, the literature on anemia in long-term care settings is quite limited. Considering the potential importance of anemia on quality of life, it may be appropriate to evaluate and treat it. But which long-term care adult should be formally evaluated, and how does the decision to treat differ from other populations? This chapter reviews the prevalence, diagnosis, association with adverse events, and treatment options for anemia in individuals living in long-term care settings.

PREVALENCE IN LONG-TERM CARE SETTING

People older than 65 years are projected to double in number from 46 million in 2014 to 98 million in 2060, or to roughly 1 out of 4 people, whereas those older than 85 years

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are projected to triple from 6 million to 20 million.¹ The number of individuals requiring long-term care services numbered 12 million in 2015 and 63% are older than 65 years of age. That number is also expected to increase to 27 million by 2050.²⁻⁴

Because the population requiring long-term care has multiple morbidities, the prevalence of anemia is expected to be much higher. A systematic review of anemia in older people found prevalence of anemia is highest among nursing home residents with weighted mean of 47%, compared with 12% in community dwellers.⁵ The prevalence in another study of 900 nursing home residents reported anemia in 48%.^{5,6} Robinson and colleagues⁷ examined records of more than 6000 nursing home residents and found 60% with anemia and 43% with chronic kidney disease; more residents with chronic kidney disease had anemia (65%) than those who did not have chronic kidney disease. In 2014, the Centers for Disease Control and Prevention reported that long-term service users totaled 9 million, out of which around 1.4 million people reside in some 15,000 nursing homes in the United States and about two-thirds of these live there permanently.⁸

The high prevalence and nonspecific symptoms of anemia can be attributable to a plethora of other conditions common in nursing home residents; when such symptoms are attributed to other conditions, anemia may not be considered etiologically high enough in the differential diagnosis and accordingly may go undiagnosed. The notion that anemia is an inevitable consequence of aging can be refuted by data that show that most older people have a normal hemoglobin and hematocrit and those who meet the criteria for anemia (Hgb <12 g per dL) have an identifiable cause in most of the cases.⁹ It is also not entirely clear what the clinical significance of anemia is in older people when the cause is not found.

ASSOCIATION WITH CHRONIC DISEASE, DELIRIUM, DEMENTIA, AND DECREASED QUALITY OF LIFE

In older adults, anemia has been associated with worsening delirium, dementia, and a declining quality of life. Investigators have suggested anemia is associated with worse outcomes in people with specific comorbid conditions such as heart failure. A study involving heart failure patients showed that anemia was present in 17% of patients, the most of whom (58%) were found to have anemia of chronic disease.¹⁰ The 5-year mortality rate in this large cohort of people with heart failure is 10% higher in those with anemia.¹⁰

A prospective study of 190 elderly subjects aged older than 70 years with an anemia prevalence of 50% found anemia to be an independent risk factor for delirium. Even after adjusting for age, sex, and diagnosis of dementia, the odds ratio for delirium was found to be significantly associated with anemia.¹¹ Another study found the degree of anemia correlated with the severity of delirium and length of stay in intensive care unit.¹²

Presence of anemia is also associated with new dementia onset and accelerated cognitive decline.^{13,14} A 3-year prospective study involving more than 1400 subjects with normal baseline cognitive function found that those with anemia were twice as likely to develop dementia even after adjusting for age, gender, educational level, comorbid conditions, and nutritional status.¹⁵

ASSOCIATION WITH FALLS, DECLINE IN PHYSICAL PERFORMANCE, HAZARDS OF HOSPITALIZATIONS, AND INCREASE IN MORTALITY

Several studies linked lower hemoglobin levels to the occurrence of those who fall while hospitalized. Dharmarajan and colleagues¹⁶ compared the risk of falls in

hospitalized elderly patients both from the community and from the nursing homes who met WHO defined criteria for anemia. They found that more than half of the patients had a fall during hospital stay and those who experienced a fall had a higher prevalence of anemia (56% vs 38%, $P = .001$). It also revealed a 1.9-fold increased likelihood of falls in those with anemia and a risk independent of age, race, or place of residence, such as the nursing home.¹⁶

Studies also indicate an association between anemia and functional decline.^{17,18} A prospective study following 1146 patients over a period of 4 years found a significant association between anemia and functional decline even after adjusting for anemia-associated laboratory abnormalities (serum iron, albumin, and lipid) and diseases (malignancy, renal insufficiency, and infectious disease).¹⁸

Dhamarajan¹⁹ also compared the number of hospitalizations with the severity of anemia in older nursing home and community elderly. The author reported that 60% of nonanemic individuals were hospitalized during the prior 18 months compared with 80% of anemic individuals. Men, African American race, and chronicity of anemia were linked with higher likelihood of hospitalization.¹⁹ It is not clear whether the anemia itself contributes to the hospitalization risk, or the underlying cause of anemia, or both serve as drivers of that risk.

Several studies have shown an association between anemia and increased mortality.^{20,21} A study examining the association between hemoglobin and all-cause mortality in 17,000 older adults found increased mortality risk associated with both extremes of hemoglobin.²²

In each of these outcomes that associates with anemia, there remains work to be done to determine how anemia figures into the risk in terms of causality or as a proxy for some other problem that directly confers risk. In addition, this work does not answer the question of whether treating the anemia or its cause modifies the risk for these outcomes in general, or specifically in the nursing home setting.

CLINICAL PRESENTATION

Anemia is most commonly found incidentally on abnormal screening tests rather than in the evaluation of signs and symptoms associated with acute blood loss or hemolysis.²³ Slowly progressive or chronic anemia is typically less symptomatic, especially in a sedentary nursing home patient, and gradual compensatory mechanisms can allow it to remain clinically silent. Thus, signs and symptoms may not appear until the hemoglobin drops to where the body's mechanisms (increase in blood volume and cardiac output) for homeostasis can no longer adequately compensate. With acute blood loss anemia, laboratory values can lag until after postural hypotension, tachycardia, and dyspnea become evident.²³

Acute blood loss, such as from a gastrointestinal bleed, can produce an acute, overtly symptomatic presentation. However, most anemic older patients present with milder, more easily missed symptoms such as fatigue, lethargy, weakness, or shortness of breath, which might be easily ascribed to old age.⁹ Symptoms of anemia may be inconspicuous in elderly due to reduction in mobility and physical activity secondary to joint pain, muscle atrophy, and other medical conditions and social expectations, such as for those living in the nursing home setting. Furthermore, many institutionalized elderly have cognitive impairment or frank dementia and may not reliably be able to report symptoms or their chronology. Because the symptoms may be attributed to other comorbid conditions such as heart failure, anemia can go unnoticed without a sufficiently detailed history and physical examination and laboratory evaluation.

Anemia evaluation should seek to assess nutritional history, often best acquired from nursing home staff, who also can provide a longitudinal weight record. The nursing home social worker may also know of any alcohol or illicit drug use. The resident or their family may know of a family history of anemia. Certain inherited disorders are common in certain geographic areas and ethnic backgrounds such as thalassemia and G6PD deficiency. Review of systems and physical examination should include blood in the stool or urine, bleeding from gums or mucosal surfaces, splenomegaly, lymphadenopathy, or other signs of infection.²³

Common red flags that can preclude the onset of symptoms of anemia and prevent an adverse event include a thorough review of comorbid diseases and recent events including hospitalization, procedures, or new medications. Common comorbid diseases that can predispose to anemia are listed in **Table 1**.

Several medications are implicated with anemia (listed in **Table 2**), and therefore, a thorough and regular review of medication should be conducted on every medical encounter and especially after a recent hospitalization.

Common physical signs in the diagnosis of anemia useful in any race because of independence from skin pigmentation include pallor of the conjunctiva, hands, and nailbed.²⁴ Conjunctival pallor had a likelihood ratio of 4.49 for anemia. Thus, conjunctival pallor is independently sufficient to suspect anemia and trigger a hemoglobin measurement to rule out severe anemia.²⁵ Other physical examination findings can include strong peripheral pulses, strong and forceful heartbeat, and rarely a compensatory high-output heart failure from tissue hypoxia.²⁴ Note that severe atherosclerosis, as can be found in older nursing home residents, may attenuate peripheral pulses.

EVALUATION OF ANEMIA

A detailed history and physical examination are followed by laboratory testing with a complete blood count including peripheral blood smear. The results of the initial blood work can further refine the differential diagnosis and may point toward a certain cause or need for further testing. According to NHANES III data collected between 1991 and 1994 and related to the cause of anemia in persons older than 65 years old, the causes of anemia can be roughly classified into 3 categories. Nutritional deficiency occurs in one-third of those with anemia (iron, folate, and vitamin B12), of which half are attributable to iron deficiency anemia. Chronic inflammation (20%) or chronic renal failure (8%) makes up another third of elderly with anemia. The remaining one-third of anemic elderly has an undetermined cause.²⁶

The proportion of those with anemia of unknown cause increases with age, and the average age of nursing home residents in the United States is 80 years and older.^{26–30} A study involving nursing home residents found that in 45% of those with anemia, the workup of anemia did not yield any identifiable cause.⁵

Types of Anemia	Medical Predispositions
Microcytic anemia	Low dietary intake of iron Recent blood loss (surgical or trauma) Acute or chronic gastrointestinal bleeding
Macrocytic anemia	Low dietary intake of vitamin B12 or folate
Anemia of chronic disease	Chronic inflammation, cancer, chronic kidney disease
Endocrine disorders	Diabetes mellitus, thyroid disease

Table 2 Common medications that contribute to anemia	
Drugs associated with gastrointestinal bleeding	Anticoagulants (eg, Coumadin, heparin, novel oral anticoagulants) Antiplatelets (eg, aspirin, clopidogrel, abciximab) Corticosteroids (eg, hydrocortisone) Bisphosphonates (eg, alendronate) Nonsteroidal antiinflammatory drugs (eg, ibuprofen)
Drugs that affect folate levels and utilization	Alcohol, phenytoin
Drugs that interfere with folate metabolism	Methotrexate, pentamidine, triamterene, lamotrigine, trimethoprim-sulfamethoxazole, primidone
Drugs that affect folate utilization & metabolism	Phenobarbital, sulfasalazine
Drugs that decrease vitamin B12 absorption	Metformin, colchicine, proton pump inhibitor, histamine blockers
Drugs associated with myelosuppression	Azathioprine, 6-mercaptopurine, cyclophosphamide, busulfan, doxorubicin, zidovudine, methotrexate, hydroxyurea, thioguanine
Alternate therapies linked with anemia	Ginkgo (bleeding), yohimbe (renal failure), black cohosh, and green tea

Data from Saffel D. Putting it into practice: strategizing a successful anemia management protocol in the long-term care setting. *Consult Pharm* 2008;23 Suppl A:18–23.

The evaluation of nursing home residents should consider factors not typically germane for younger and healthier patients. Before ordering a barrage of tests, consider whether the test and treatment for the diagnosis the patient is being tested for is warranted and would be tolerated by the patient. For example, would it make sense to do a bone marrow transplant in an elderly patient with advanced dementia? If the patient is bed-bound would the patient achieve meaningful clinical or quality of life gains with an improvement in their hemoglobin concentration? In some cases it may be prudent to test for a cause by evaluating a response to empirical treatment such as giving iron replacement therapy and monitoring hemoglobin and reticulocyte count for a few months. In such cases it would be appropriate to set a target response, which determines failure (stop treatment) or success (diagnosis is made; continue or stop treatment). It is important to weigh the risks and benefits of testing and treatment in due consideration of patient's expected longevity and whether doing more would add meaningful quality of life. Therefore, as in the management of any other serious illness, evaluation of anemia should be done considering expected quality of life and feeling of well-being and patient's goals of care (Fig. 1). If patient is unable to participate, then the patient's family and/or health care proxy should use substituted judgment in deciding management in accordance with patient's values.

Lastly, cost of care should be aligned with benefit to the patient. It is often difficult to choose which way to proceed. For example, should one consider long-term transfusions for an elderly nursing home patient if the tests indicated a myelodysplastic syndrome that is otherwise unresponsive to other interventions?

As discussed earlier, anemia is associated with many adverse outcomes in long-term care residents, so further testing for a treatable cause may be warranted.

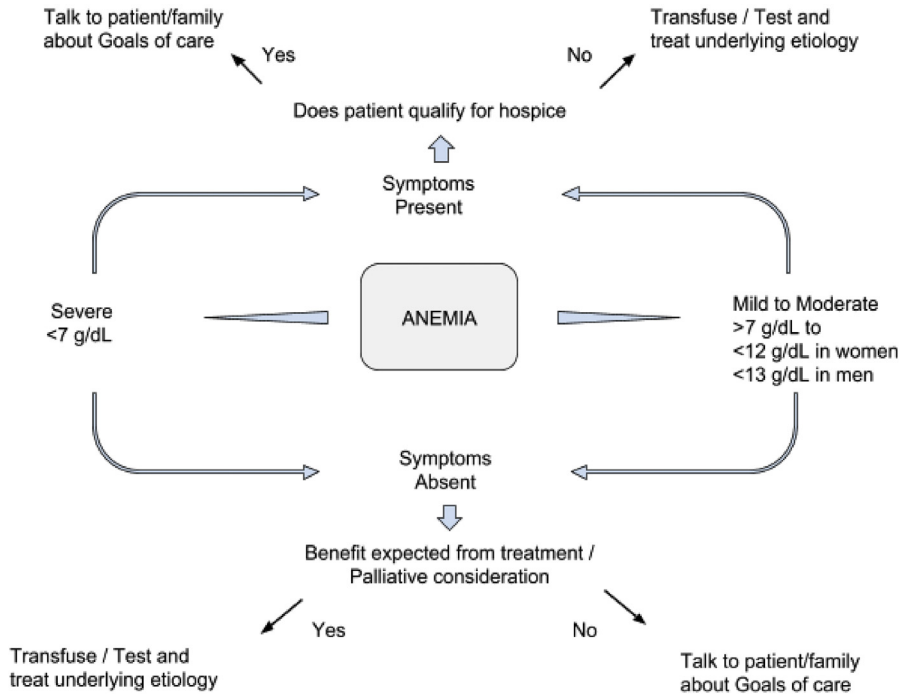


Fig. 1. Evaluating anemia in the long-term care setting.

However, the authors of this chapter have divergent opinions on where to draw the line on both formal anemia evaluation and treatment. Which tests to order to evaluate anemia is dealt with in detail elsewhere in this book.

TREATMENT

Treatment decisions will take into account the subjective considerations of patient wishes, goals of care, and whether it will improve the quality of life. Treatment of anemia found on routine laboratory testing of apparently asymptomatic long-term care residents should be tailored and different clinicians may not be equally aggressive. Aside from acute blood loss such as from a gastrointestinal bleed or following a large bone fracture, when present, signs and symptoms from more insidious causes of anemia that may also suggest anemia are typically nonspecific. When this is the case, a low blood count may be coincident with a decline in cognitive status or change in activities of daily living, intentional or unintentional dietary changes, new onset or an increase in falls, or frequent infections, so who should be evaluated depends on clinical suspicion and anticipated benefit from intervention.³¹ So when these symptoms are due to anemia, they should factor into the decision on whether to treat the anemia.

Specific treatment of anemia depends on the cause. Anemia due to acute blood loss may require volume resuscitation or blood transfusions. Iron deficiency anemia responds well to ferrous sulfate, 325 mg, once daily and increase in daily intake of iron-rich foods (meat, fish, spinach, kale, beans, or iron-fortified cereal). It is recommended to take iron supplements 2 hours after calcium supplements and is better absorbed if taken together with vitamin C. A common side effect of iron therapy is constipation, which should be monitored and treated appropriately. Patients should be

made aware that supplemental iron can make the stool appear dark, so they may not get alarmed and concerned that they may be bleeding per rectum. Conversely, iron supplement can mask upper gastrointestinal bleed, so hemoglobin should be monitored routinely.

Animal protein is the main source of vitamin B12, hence, vegetarians or vegans and elderly who do not consume enough protein can be or become deficient. Vitamin B12 deficiency can be treated with high doses of cyanocobalamin orally (as is common in Europe) or with intramuscular administration of 1000 mg/mL of vitamin B12. It is also available as deep subcutaneous injection and can be given weekly until normal and then once a month.³¹ Folate deficiency can be easily treated with 1 mg of folate daily and levels can be rechecked in 2 to 3 weeks. Dietary folate levels can be replenished by eating green leafy vegetables, whole grains, and nuts. Nutritional management of anemias is more straightforward in the long-term care setting as diet and weight are monitored and can be tracked over time, so there is greater certainty about the adherence to specific interventions than in the outpatient settings.

Anemia associated with chronic kidney disease may require erythropoiesis-stimulating agents (ESA); however, such agents are typically expensive and should be used judiciously and reserved for patients who are expected to have a meaningful benefit in quality of life and physical function from the treatment. Iron deficiency should be excluded by serum ferritin of greater than 100 µg/L and total saturation of greater than 20%, before starting ESA, and the dose of ESA should be titrated to hemoglobin levels between 11 and 12 g/dL.³² These agents are costly and come with a “black box” warning on the label for recommended treatment targets and safety risks by Food and Drug Administration. When anemia is caused by other chronic diseases, the appropriate way will be to treat the underlying condition, if possible. Overall, the treatment should be based on evaluation of individual patient as well as the discussion between the clinician, patient, and/or family.

SUMMARY

Anemia is prevalent among the elderly; however, the signs and symptoms of anemia are often nonspecific and especially in frail elderly such as those living in nursing homes may be attributed to physical decline associated with increasing age. Anemia is often underdiagnosed. As it can be an insidious sign of an underlying disorder with a discernible cause, it may be easily remedied and may warrant formal workup. Anemia is a disease and although the symptoms may be clandestine due to multimorbidity among the elderly, undiagnosed anemia has tangible and perceptible consequences including poor quality of life and early death. Because of the high prevalence of concomitant chronic diseases, the detection of anemia in the elderly poses a diagnostic challenge. A viable approach in diagnosing and treating anemia includes a consideration of the diagnostic burden and potential benefit to the overall functioning and quality of life of the patient.

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