# Can an Anemic Patient Be a Partner to Treatment Decision-Making?

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**ABSTRACT** Cognitive impairment due to different types of anemia is well-known. We reviewed the links between different types of anemia and the mechanism of cognition impairment as well as the direct involvement of micronutrients such as iron, vitamin B12, folic acid, and copper on cognitive function. Anemia can lead to cognitive impairment, yet the current health policy usually requires patient involvement in the treatment decision-making. Therefore, can an anemic patient be a partner to shared decision-making concerning the recommended treatment?

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**KEY WORDS:** anemia, cognitive impairment, hypoxia, shared decision-making, treatment decision-making

Anemia is a disorder characterized by a lower-than-normal red blood cell count and insufficient hemoglobin levels. In 2021, approximately 20% of the population, 1.6 billion people worldwide, were affected [1]. Anemia is a global public health problem.

The World Health Organization (WHO) estimates that 40% of pregnant women worldwide are anemic. WHO defines anemia in pregnant women as a hemoglobin concentration < 110 g/L at sea level, and anemia in non-pregnant women as a hemoglobin concentration < 120 g/L. Anemia in men is defined as hemoglobin level < 130 g/L [1].

Cappellini and colleagues [1] found that 11% of healthy older people (> 65 years old) have lower than normal levels of hemoglobin, but that number rises to 40–50% in hospitalized patients. Anemia can be acute or chronic. Iron-deficiency anemia, the most common type of anemia, develops when the blood lacks adequate healthy red blood cells due to iron insufficiency. Both folate and vitamin B12 prevent megaloblastic anemia, but only vitamin B12 can prevent neurological complications. The common causes of acute anemia are hemolysis or hemorrhage, which result in a sudden reduction in red blood cells. Anemia of chronic disease (ACD) is found in people with certain long-term (chronic) medical conditions that involve inflammation such as chronic kidney disease, diabetes, autoimmune diseases such as rheumatoid arthritis or lupus, cancer, chronic infections such as human immunodeficiency virus and tuberculosis, and inflammatory bowel disease such as Crohn's disease or ulcerative colitis.

Hemoglobin is needed to carry oxygen. Insufficient or abnormal red blood cells or deficient hemoglobin result in a decreased capacity of the blood to carry oxygen to the body's tissues. Hypoxia is a state in which oxygen is not available in sufficient amounts at the tissue level, including the brain, to meet the metabolic needs of the cells. This deficiency can result from inadequate oxygen delivery to the tissue due to low oxygen content in the blood or other problems [2].

## COULD COGNITIVE FUNCTIONS AND ANEMIA BE LINKED?

Cognition is the mental action or process of acquiring knowledge and understanding through thought, experience, and the senses. Hypoxia can impair several cognitive domains such as attention, learning and memory, processing speed, and executive function. The severity of cognitive deficit correlates with the duration and degree of hypoxia [3].

**ANEMIA CAN LEAD TO COGNITIVE IMPAIRMENT.**

Anemia negatively affects not only physical function but also cognition, mood, and quality of life in

adults due to hypoxic condition as per its severity [4]. One disturbance of cognitive function can be dementia, a spectrum of neurological diseases characterized by memory impairment and cognitive decline with pathogenesis and effective management remaining elusive. Dementia is a major cause of disability worldwide and affects approximately 5% of people above 65 years old. Anemia is considered one of the most prevalent co-morbidities in older adults with a prevalence of 11% in those above the age of 65 years [5]. Studies have demonstrated a link between anemia and accelerated decline in cognitive functions [6]. To compensate for chronic anemia, the brain increases cerebral blood flow inversely with hemoglobin levels to try to preserve whole brain oxygen delivery [7]. Hypoxia causes symptoms such as confusion and restlessness. It can be life-threatening. Severe anemia or low hematocrit as a cause of hypoxia, has been associated with cognitive dysfunction or impaired cerebral vascular regulation [8]. Many studies have demonstrated that anemia is a significant risk factor for dementia. Results have shown that low brain hemoglobin associated with low oxygen levels may lead to neuron damage [5]. Although a variety of causes can result in anemia, hypoxia is the final pathophysiologic event of anemia. Hypoxia can be a factor in cognitive function impairment, but other deficiencies in iron, folic acid, and vitamin B12 can also influence cognition directly, regardless of anemia [9].

**PATIENTS MUST REGULARLY BE INVOLVED IN TREATMENT DECISION-MAKING PROCESSES.**

Iron is an essential element in humans. It is required for numerous cellular processes. Most of the iron in the human body (approximately 65%) is contained within the hemoglobin-carrying red blood cells [10].

Brain iron homeostasis is crucial for neurological health, with pathological fluctuations in brain iron levels associated with a variety of neurological disorders. Low levels are linked to cognitive impairment [11].

**PATIENTS WITH ANEMIA CAN EXPERIENCE CONFUSION; THEREFORE, IS THEIR PARTICIPATION IN TREATMENT DECISION-MAKING APPROPRIATE?**

Vitamin B12 is involved in the body's metabolism, including the central nervous system. Deficiency can lead to cognitive disorders or Alzheimer's disease [12].

Deterioration of cognitive function caused by degenerative changes in the brain increases with age. The disease mechanism that leads to cognitive impairment due to vitamin B12 deficiency is unclear [13].

Low folate levels may predict a decline in global cognitive function and are associated with accelerated decline in cognitive function [14].

Another crucial micronutrient for humans is copper. Copper deficiency affects physiological systems such as bone marrow hematopoiesis, optic nerve function, and the nervous system. Dietary copper intake is generally not associated with brain copper levels. The association of higher brain copper levels with slower cognitive decline supports a role for copper dyshomeostasis in Alzheimer's disease pathogenesis and suggests that decreased brain copper levels may exacerbate or indicate disease severity. Dietary and brain copper are unrelated, but dietary copper is associated with slower cognitive decline via an unknown mechanism [15].

Anemia of chronic inflammation could be a risk factor for cognitive disturbances. Studies shown a link between anemia in chronic kidney disease, anemia with type 2 diabetes mellitus, and anemia with cognitive disorders [16,17]. Inflammation is perhaps the most studied element of homeostatic network dysregulation, particularly in the context of anemia.

Atti et al. [18] demonstrated a twofold increase in the incidence of dementia in patients with anemia within 3 years, after adjusting for co-morbidities like inflammation, malnutrition, and chronic disease (hazard ratio 1.6, 95% confidence interval 1.1–2.4). Andreev et al. [19] showed a link between anemia with chronic inflammation and Alzheimer's disease and related dementias [19].

## THE PROCESS OF TREATMENT DECISION-MAKING

Treatment decision-making (TDM) models range from paternalistic decision-making (PDM) to informed decision-making (IDM). Between the two extremes lies the shared decision-making (SDM) option [20]. PDM represents the passive involvement of the patient who leaves the decision to the physician. The concept of SDM, which first appeared in the literature in the 1990s, is based on sharing and negotiation toward decision-making. SDM involves both the physician and the patient so that both are responsible for the final decision. There is a growing interest in SDM in which the provider and patient

go through each phase of the decision-making process together, sharing treatment preferences and reaching an agreement on treatment choice. SDM is thought to be the most logical method of TDM.

In contrast, the PDM model is an autocratic style of decision-making where physicians make healthcare decisions based on what they feel is in the best interest of the patient. In the case of IDM, only the patient makes the final decision after having received the required information.

In an era of growing healthcare consumerism, patients have become important partners in making medical decisions. Patient decision making, in which physicians encourage patients to be involved in treatment decisions and to take responsibility for their care, appears to have a number of important benefits. Correct treatment decision-making by the patient is a fundamental cognitive function that involves a combination of cognitive and emotional processes. Studies have shown that patients take more risks in a mildly hypoxic environment than in a normoxic one. The majority of the decisions people make are made without complete understanding of the consequences. Two laboratory studies have empirically demonstrated that undetected mild hypoxia can influence decision-making [20].

Patients confused due to anemia can easily make unsafe decisions, either in IDM or in SDM.

## CONCLUSIONS

Should we perform a cognitive consultation with every anemic patient before including them in the treatment decision-making process? According to the mental health literature, even a psychiatric patient can be involved in SDM. Does every cognitive impairment permit clinicians to include the patient in a TDM program (e.g., a patient with Alzheimer's disease)? Perhaps physicians feel that they know which patients need a cognitive assessment before involving them in TDM. Of course, the physician is the one to initiate the treatment.

There is a concept, anemia without anemia, which is applied to iron deficiency anemia when iron and ferritin begin to decrease and before the onset of actual anemia. In this case, hypoxia is not the cause of cognitive dysfunction; however, microelements may contribute to anemia and hypoxia, which can lead directly to this kind of dysfunction. Iron, vitamin B12, folic acid, and copper can produce anemia and implicit hypoxia, and may cause cognitive impairment before hypoxia appears.

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