Review Article

Multidimensional Impact of Anemia on Wellbeing

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ABSTRACT

A pervasive health concern, Anemia co-occurs with a diverse array of pathologies, encompassing chronic renal dysfunction, hepatic diseases (alcoholic and non-alcoholic), congestive heart failure, and parasitic infestations like schistosomiasis and malaria. Furthermore, infectious agents such as COVID-19, HIV, and tuberculosis, along with autoimmune conditions exemplified by systemic lupus erythematosus, rheumatoid arthritis, and celiac disease, are evidently linked to anemia. The ramifications of this condition extend beyond the physical, as there is a well-established association between anemia and cognitive dysfunction, potentially manifesting as depression, dementia, learning disabilities, attention deficit hyperactivity disorder, and autism spectrum disorder. Chronic ailments like cancer and thyroid hormone dysregulation further compound the issue, contributing to a diminished quality of life and an escalation in healthcare costs. The presence of anemia demonstrably exacerbates morbidity and mortality rates in patients with co-existing medical conditions. Fortunately, therapeutic interventions for anemia hold promise in ameliorating the outcomes associated with these various diseases. The timely diagnosis and initiation of interventions for anemia hold the potential to rectify a multitude of the associated health concerns. This review comprehensively analyses the multifaceted implications of anemia on healthcare delivery, encompassing its association with various diseases, its neurocognitive sequelae, the economic burden it imposes, and its outcomes for optimal patient management.

Keywords: Anemia, Cognitive impairment, COVID-19, Autoimmune conditions, Thyroid disorders, Cancer, quality of life, Length of hospitalization, Economic burden.

INTRODUCTION

Anemia, characterized by low red blood cell (RBC) count or hemoglobin (Hb) concentration, is influenced by factors like age, sex, pregnancy, health, genetics, and environment. Sex disparities in Hb levels manifest during puberty. Menstrual blood loss in females and the stimulatory effect of testosterone on RBC production in males contribute to this divergence, which persists throughout the reproductive years. Pregnancy further complicates the Hb picture, with levels typically declining in the first and second trimesters due to blood volume expansion, followed by a partial recovery in the third trimester. While some studies posit race as a biological determinant impacting Hb distribution and anemia prevalence, others contend that race is a social construct. Disparities in Hb levels observed along racial lines might be rooted in unequal access to healthcare and other social determinants of health, rather than inherent biological differences. This underscores the intricate interplay of genetic, environmental, and socioeconomic factors that collectively shape Hb levels.[1]

PREVALENCE

Globally, an estimated one-third (32.9%) of the population was afflicted with anemia in 2010. Certain demographics exhibit a heightened susceptibility to this condition, particularly children under five years of age (42% anemic in 2016), especially infants and toddlers. Women of reproductive age (39% anemic in 2016) and pregnant women (46% anemic in 2016) are also at substantial risk. A consistent disparity exists, with females across most geographic regions and age groups demonstrating a greater propensity for anemia compared to males. Limited data suggests that the elderly population may also be vulnerable, as the prevalence of anemia appears to escalate with advancing age among adults exceeding fifty years old. In recognition of this public health concern, the WHO established a Global Nutrition Target for 2025, aiming to achieve a 50% reduction in anemia prevalence among women of reproductive age by that year.[2]

SYMPTOMOLOGY

The spectrum of symptoms associated with anemia is contingent upon both the severity and rapidity of its development. These manifestations arise from a diminished capacity to deliver oxygen to vital organs, and can be further exacerbated decreased blood volume. The body attempts to compensate for lower hematocrit levels by augmenting both heart rate and stroke volume, thereby enhancing oxygen extraction and delivery. Individuals with mild or gradually progressive anemia may be asymptomatic, while others may experience a constellation of symptoms including fatigue, diminished exercise tolerance, headaches, dizziness, tinnitus, palpitations, syncope, impaired concentration, and restless legs syndrome. In some cases, blood shunting away from the splanchnic bed can manifest as nausea, irregular bowel movements, and abdominal discomfort. Pediatric anemia

can impede cognitive and psychomotor development. Furthermore, heightened cold sensitivity can be due to diminished blood flow to the skin, particularly in children with pre-existing vascular diseases, can exacerbate symptoms like cerebral ischemia, claudication, or angina. Beyond the telltale pallor manifested in the skin and conjunctiva, anemic individuals may exhibit tachycardia and a widened pulse pressure as a consequence of augmented cardiac output. In severe cases of anemia, retinal hemorrhages may be observed, while jaundice can signal red blood cell destruction or underlying liver pathology. Iron deficiency and vitamin B12 insufficiency can both manifest as glossitis. Swollen lymph nodes may be indicative of infections like HIV or tuberculosis, as well as hematologic malignancies. Additional clinical signs include systolic ejection murmurs, venous hums, and the potential for hepatomegaly and splenomegaly. A deficiency in vitamin B12 can lead to deficits in proprioception and balance.[3]

CONTRIBUTORS TO ANEMIA

Iron deficiency anemia (IDA) represents the most prevalent global etiology of anemia. However, in the elderly population (individuals exceeding 65 years of age), a multifaceted presentation of anemia is more commonplace. This can encompass contributions from chronic kidney disease, nutritional deficiencies, occult blood loss, gastrointestinal disorders, the use of antithrombotic medications, and ineffective red blood cell production. Additionally, anemia of chronic disease (CDA) is frequently observed in this demographic. In some cases, however, the underlying cause of anemia in older adults may remain elusive. It is crucial to acknowledge that the primary factors responsible for mild to moderate anemia often diverge from those that precipitate severe anemia.

Severe anemia exhibits a well-established association with malaria, particularly among children residing in Africa. The BRINDA project identified consistent risk factors for severe anemia in population-based surveys of pre-schoolers in African nations. These factors included malaria exposure, inadequate sanitation, underweight status, and inflammation. Additionally, stunting and vitamin A deficiency were found to be contributory. Dietary choices and the consumption of processed, nutrient-deficient foods can also lead to the development of anemia. Irregular meal patterns, limited intake of fruits and vegetables, and excessive consumption of sugary beverages are all contributing factors. Certain food items, such as burgers, pasta, bread, and pizza, contain phytates which can impede iron absorption. The concerning trend of increasing junk food consumption parallels the growing prevalence of unhealthy lifestyles and dietary habits.[4]

IMPACT OF ANEMIA

Anemia and Sars-Cov-2

A complex interplay exists between COVID-19 and anemia, potentially involving irregularities within the immune system and co-occurring autoimmune conditions. Both diseases trigger inflammatory cascades that disrupt iron homeostasis in the body. This disruption manifests in two primary ways: an increase in iron sequestration by macrophages and a concomitant decrease in intestinal iron absorption. Furthermore, COVID-19 itself may precipitate hemolytic anemia, possibly through a virus-induced alteration in red blood cell function. Conversely, the inflammatory response mounted in defense against COVID-19 can contribute to a reduction in hemoglobin levels Emerging evidence suggests a potential link between COVID-19-induced hypoxemia, erythropoiesis, and iron homeostasis within the body. Research has yielded a robust correlation between iron levels, interleukin-6 (IL-6, a well-established inflammatory marker), and hepcidin during COVID-19 infection.

The reported prevalence of anemia in COVID-19 patients exhibits heterogeneity across various studies. Zhou et al. identified anemia in 15% of a hospitalized COVID-19 patient cohort, with a higher incidence observed among individuals with pre-existing comorbidities such as cardiovascular disease, hypertension, or chronic kidney disease; all established risk factors for severe COVID-19 outcomes. Other studies have documented a wider range of anemia prevalence, with figures varying from 35.5% to 61% within hospitalized COVID-19 patient populations. Critically, the presence of anemia in these patients appears to be correlated with poorer clinical outcomes, including extended hospital stays and elevated mortality rates.

COVID-19 patients with co-existing anemia exhibit an intensified susceptibility to severe inflammatory reactions, dysregulated blood coagulation, and organ dysfunction. The presence of anemia may act as a potentiating factor, exacerbating the clinical course of COVID-19 and introducing additional complexities to both treatment strategies and patient prognoses.[5]

Anemia and Cognitive Competence

Anemia, particularly among older adults (over 65) with end-stage renal disease, has been linked to an increased risk of cognitive decline and dementia. Research suggests a concerning association, with anemia potentially elevating the risk of dementia by 34% and Alzheimer's disease by 41%. However, further investigation is necessary to fully elucidate the underlying mechanisms of this relationship. Proposed theories states that reduced hemoglobin levels contribute to a cascade of detrimental effects, including beta-amyloid deposition, oxygen deprivation, neuronal inflammation, and ultimately, impaired brain function. Furthermore, anemia can disrupt the process of brain vasodilation, thereby compromising cerebral blood flow and exacerbating existing neurological impairments. Deficiencies in erythropoietin, vitamin B12, and folate may also act as contributory factors in the development of cognitive decline.[6] Anemia has emerged as a significant risk factor for overall cognitive decline, encompassing a broad spectrum of dementias, in individuals compared to their counterparts with normal hemoglobin levels. Furthermore, a well-established correlation exists between anemia and

an elevated risk of Alzheimer's disease, with a demonstrably increased risk of 1.59-fold in anemic patients.[7]

Individuals with a history of stroke, particularly ischemic stroke precipitated by excessive fluid resuscitation, frequently exhibit low hemoglobin levels. This condition has been associated with an increased risk of cognitive decline in patients experiencing acute ischemic stroke. However, upon adjustment for potential confounding factors, the initial correlation between higher hemoglobin levels and improved post-stroke cognitive performance becomes statistically insignificant. This finding suggests that hemoglobin may play a complex role in the pathophysiology of cognitive impairment following stroke. Brain hypoxia induced by anemia can potentially exacerbate oxidative stress, inflammation, and mitochondrial dysfunction, ultimately worsening cognitive decline. Furthermore, low hemoglobin levels following stroke may aggravate the ischemic state of penumbral lesions by compromising blood oxygen delivery capacity.[8]

Anemia can lead to neurodevelopmental disorders in children within the United States, including learning disabilities (LD), attention deficit hyperactivity disorder (ADHD), and autism spectrum disorder (ASD). Research proposes a potential link between iron deficiency anemia (IDA) diagnosed in new-borns and aberrant electroencephalogram (EEG) activity during development, delayed response times, and compromised accuracy in executive function tasks. Furthermore, children diagnosed with ASD exhibit demonstrably lower levels of ferritin, hemoglobin, and serum iron compared to healthy control groups. The co-occurrence of anemia with prenatal exposure has been associated with an increased risk of developmental behavioural problems, including ADHD, ASD, and LD. These findings suggest a compelling link between anemia and neurodevelopmental disorders, potentially indicating the presence of shared underlying biological processes across these three conditions.[9]

Low Hemoglobin and Depression

A growing body of research has investigated the potential association between anemia and depression in elderly populations. Several studies have demonstrated that older adults with co-existing anemia and baseline cognitive impairment exhibit a fivefold increase in their risk of developing depression over a four-year follow-up period. These findings indicates a link between anemia and an elevated risk of depression, with this association, impacting both men and women in later life. Interestingly, the prevalence of depression appears to be lowest among individuals receiving treatment for anemia compared to those who remain untreated. Study participants with untreated anemia display a raised propensity for experiencing depression compared to those without a history of the condition. For individuals struggling with depression, anemia presents a significant public health concern due to its multifaceted symptomatology, including weakness, fatigue, and an increased risk of falls. Anemia can potentially exacerbate depressive symptoms through several mechanisms: first, by inducing fatigue and cognitive decline; and second, by contributing to the development or progression of cardiovascular diseases. Additionally, certain underlying medical conditions, such as inflammatory diseases or renal failure, may contribute to the co-occurrence of both depression and anemia. Depression itself can also lead to the adoption of unhealthy lifestyle habits, such as excessive alcohol consumption or poor dietary choices, which can worsen anemia by promoting vitamin deficiencies.[10] Work of Vilser et al., has demonstrably established an independent association between depression and anemia, persisting even after controlling for a variety of sociodemographic and health-related factors. This compelling evidence underscores the importance of incorporating anemia screening into the clinical assessment of patients with depression, and conversely, screening for depression in patients diagnosed with anemia. Such a comprehensive approach to patient care necessitates acknowledging and addressing the potential for a bidirectional relationship between these two conditions. By implementing a holistic approach that identifies and manages both depression and anemia concurrently, healthcare providers can deliver more effective care that caters to the multifaceted needs of their patients and ultimately optimizes overall health outcomes.[11]

Several factors contribute to the risk of maternal depression, encompassing a complex interplay of biological, psychosocial, and nutritional elements. Hormonal fluctuations, such as variations in estradiol levels and sustained elevations in glucocorticoids, represent a significant biological component. Psychosocial stressors, including stress and inadequate social support systems, also play a prominent role. Nutritional deficiencies, particularly low serum levels of vitamin D, magnesium, and zinc, further contribute to the risk profile. Epidemiological research shows that anemia may be an additional risk factor, with one study demonstrating a fourfold increase in the likelihood of postpartum depression among women with anemia. These findings highlight the diverse nature of maternal depression and emphasize the importance of recognizing anemia as a potentially significant factor in mitigating postpartum depression risk.[12] For women experiencing postpartum depression, anemia poses a significant concern due to the shared symptoms including fatigue, dizziness, and irritability.[13] A recent meta-analysis revealed that experiencing anemia during and after pregnancy substantially heightened the likelihood of developing postpartum depression.[14]

Evidence suggests a potential bidirectional relationship between iron deficiency and depression. Studies have hinted at a connection between iron deficiency and the development of depressive symptoms, while also suggesting that iron supplementation may alleviate such symptoms. However, a critical gap exists in our understanding of the correlation between antenatal iron deficiency and depression. A significant proportion of

pregnant women, approximately 22%, experience iron deficiency during later stages of pregnancy. Given the potential influence of iron levels on depression onset, progression, and management during pregnancy, elucidating this link is crucial. Considering that nearly one-third of postpartum depression cases manifest prenatally, the presence of antenatal iron deficiency warrants clinical consideration for identifying and addressing depression in pregnant women.[15] Past studies have explored the potential relationships between anemia and postpartum depression, but the results have been varied.[13]

Anemia and Autoimmune Disease

Rheumatoid arthritis (RA) can manifest with anemia, often flowing from iron deficiency induced by chronic nonsteroidal anti-inflammatory drug use (GI bleed), a phenomenon classified as chronic disease-related anemia. RA patients with co-existing anemia frequently exhibit a higher prevalence of swollen joints. This association may be linked to elevated production of inflammatory cytokines, such as tumor necrosis factor-alpha. These cytokines can impair the bone marrow's responsiveness to erythropoietin, resulting in insufficient red blood cell production despite adequate iron stores. Research signifies that successful resolution of anemia in RA patients is associated with improvements in energy levels and overall quality of life, with increased hemoglobin levels correlating with positive changes in patient well-being. Anemia in RA may not only mirror disease activity and symptoms, but also potentially serve as an indicator of impending structural damage.[16, 17]

Systemic lupus erythematosus (SLE) frequently manifests with hematological abnormalities, potentially including anemia, thrombocytopenia, splenomegaly, leukopenia, lymphadenopathy, and lymphopenia. These aberrations may be attributed to either the underlying disease process itself or the administration of immunosuppressive medications. Approximately one-third of SLE patient's exhibit anemia, primarily of the chronic disease type. This form of anemia is associated with hepcidin overexpression, impeding iron incorporation into red blood cells. Additionally, blood loss, such as that associated with menstruation or gastrointestinal bleeding, can contribute to the development of iron deficiency anemia in this patient population. Common manifestations of anemia in SLE include low ferritin and/or transferrin saturation levels, hypochromic normocytic red blood cells, elevated iron binding capacity, and a regenerative pattern. Identifying the source of bleeding is crucial, particularly for individuals with risk factors such as chronic NSAID use and oral glucocorticoid therapy.

Approximately 10% of SLE patients develop autoimmune hemolytic anemia (AIHA). This form of anemia typically presents with normochromic, normocytic indices, indicative of normal red blood cell size and hemoglobin content. Elevated reticulocyte and lactate dehydrogenase (LDH) levels are frequently observed, along with predominantly indirect hyperbilirubinemia. Conversely, peripheral blood smear analysis typically reveals diminished haptoglobin levels and a reduction in spherocytes.[18]

Anemia and Thyroid Malfunction

The thyroid gland plays a vital role in erythropoiesis, and hematological abnormalities are frequently encountered in patients with thyroid disorders, particularly hypothyroidism. In patients with thyroid dysfunction, anemia can arise from both inadequate nutrient stores and diminished thyroid hormone levels. The latter mechanism disrupts red blood cell production in the bone marrow, ultimately leading to compromised oxygen delivery and a reduction in erythropoietin levels. While some studies have yielded inconclusive results regarding a definitive association between anemia and thyroid dysfunction, the current body of evidence suggests a potential, yet inconsistent, correlation.[19]

Research has established that thyroid dysfunction, especially hypothyroidism, exerts a significant influence on various hematological parameters, with this effect manifesting more prominently in females. The most frequently encountered forms of anemia associated with thyroid dysfunction include microcytic hypochromic anemia and normocytic normochromic anemia. A compelling correlation exists between thyroid stimulating hormone (TSH), free thyroxine (FT4), age, sex, and a variety of hematological parameters, with this association achieving statistical significance.[20] Alterations in iron metabolism and increased oxidative stress are hypothesized to contribute to the development of anemia in hyperthyroidism. Iron deficiency anemia in hypothyroidism is frequently associated with impaired iron absorption and blood loss from conditions such as menorrhagia. Banday et al. identified iron deficiency in approximately 20% of individuals diagnosed with hypothyroidism.[21]

Anemia and Cancer

Cancer-related anemia (CRA) is characterized by a presentation of mild microcytic anemia, with normal-sized red blood cells and hemoglobin levels typically falling within a range of 8 to 10 g/dL. Paradoxically, despite possessing adequate iron stores, individuals with CRA exhibit a reduction in serum iron levels and transferrin saturation. Chronic immune system activation triggered by the underlying malignancy is believed to be a key contributor to the development of CRA. In this context, cytokines exert a suppressive effect on erythropoiesis through both direct and indirect mechanisms. Furthermore, increased production of reactive oxygen species exacerbates impairment of red blood cell production. A concerning finding is that over 30% of cancer patients already experience anemia prior to commencing anti-cancer treatment, with the prevalence of this condition increasing post-treatment initiation. For example, studies have shown that the incidence of anemia among initially non-anemic patients rises to 63%, 40%, and 20% following

chemotherapy, chemo-radiotherapy, and radiotherapy, respectively. Anemia exerts a significant negative impact on the efficacy of anti-neoplastic therapy and overall patient survival. Both intravascular and oral iron administration strategies effectively augment iron availability and ferritin levels, and these approaches frequently constitute the primary treatment modalities for CRA.[22] The selection of the iron replenishment method, whether oral or intravenous, is contingent upon several factors including the severity and timing of cancer-related anemia, the extent of iron deficiency, the probability of oral iron absorption, the existence of gastrointestinal issues, and the potential for interactions with other medications.[23]

The management of cancer-related anemia presents a versatile challenge. Oral iron therapy, a mainstay treatment, often suffers from limitations due to poor patient adherence and the occurrence of adverse effects. Intravenous iron administration offers a more efficacious and expeditious alternative, improving both hemoglobin levels and iron stores. Erythropoiesis-stimulating agents (ESAs), while effective in enhancing anemia correction and promoting improved quality of life, carry a concerning risk of thromboembolic events. A comprehensive therapeutic approach for CRA encompasses ESAs, iron supplementation, blood transfusions, targeted nutritional support, and anti-inflammatory interventions. Dietary modifications with anti-inflammatory properties may potentially address underlying causative factors. However, a meticulous evaluation of treatment options remains paramount, necessitating a careful consideration of the trade-off between symptom alleviation and potential risks, particularly the heightened risk of ESA-induced thromboembolic events in the context of cancer-induced anemia.[22]

Anemia poses a clinical hurdle in the application of novel antineoplastic therapies (ANTs), including tyrosine kinase inhibitors and monoclonal antibody conjugates, impacting more than 90% of patients in certain instances beyond compromising quality of life, anemia can significantly restrict patient's daily activities and work productivity. Anemia can emerge as a dose-limiting factor, hindering the ability of patients to receive the maximum therapeutic benefit from ANTs.[23]

Radiotherapy and chemotherapy are known to trigger anemia in cancer patients, albeit to varying degrees. A significant proportion of these individuals experience a form of anemia categorized as chronic disease-related anemia, lacking a readily identifiable specific cause. The prevailing hypothesis regarding this type of anemia centers on cytokine activation, particularly Interferon-γ, Interleukin-1, and tumor necrosis factor. These cytokines are believed to disrupt the production of endogenous erythropoietin, impede iron utilization, and suppress the proliferation of erythroid precursors.[24] Cancer therapies, encompassing surgery, radiation, chemotherapy, targeted drugs, and immunotherapy, significantly disrupt bone marrow function, leading to anemia. Radiation can inflict enduring damage on the bone marrow, particularly when it encompasses a sizable area, hampering the production of red blood cells. Chemotherapy can either temporarily or permanently suppress marrow function. Infections stemming from treatment, such as parvovirus B19, further hinder marrow function. Targeted drugs may inadvertently impede RBC production, while immunotherapy can incite autoimmune hemolytic anemia. These therapy-related effects contribute to anemia rates surpassing 90% in certain cases, detrimentally impacting quality of life and treatment efficacy.[25] Chemotherapeutic agents directly hinder hematopoiesis, particularly the synthesis of red blood cell precursors. Certain drugs, such as platinum-containing agents, exert an additional suppressive effect on erythropoietin production. Patients undergoing treatment for lung and gynecological cancers exhibit increased susceptibility to chemotherapy-induced anemia. Platinum-based regimens, commonly employed in the treatment of lung, ovarian, and head and neck cancers, are particularly likely to exacerbate anemia due to their dual cytotoxic effects on bone marrow and renal function.[26]

Impact of Anemia on Duration of Hospital Stay

Multiple research studies indicate that hemoglobin levels have an independent impact on the duration of hospital stays among patients with heart failure and end-stage renal disease. Specifically, one study revealed that heart failure patients with anemia tended to spend approximately 1.8 days longer in the hospital compared to non-anemic patients. Another investigation involving end-stage renal disease patients undergoing hemodialysis demonstrated that addressing anemia with erythropoietin-stimulating agents resulted in decreased hospital admissions and shorter durations of hospitalization.[27] Individuals with chronic kidney disease had a 50% increase in 1-year mortality, a 20% higher 30-day readmission risk, and an average hospital length of stay of three days longer than those without CKD. In addition, among patients in stages 3-5 of chronic kidney disease, severe anemia is associated with longer hospital stays.[28] A rise of one unit in hemoglobin level or albumin level resulted in a decrease of 0.5 in the median length of stay (LOS).[29] Prolonged hospital stay following birth is linked to severe third trimester anemia. Treatment of postpartum anemia, either by transfusion or intravenous iron supplementation, is the primary cause of prolonged hospital stays.[30]

Effects of Anemia on Quality of Life

Anemia in the elderly is linked to functional impairment, frailty, problems with movement, and a higher chance of falls. Compared to women with hemoglobin levels below 120 g/L, those with levels between 130 and 140 g/L have reduced death rates and improved mobility. Fatigue is a common result of anemia, which lowers quality of life. Anemia treatment has been demonstrated to improve some elements of patients' quality of life in both cancer and renal failure patients.[31]

A twelve-week course of treatment with recombinant human erythropoietin demonstrably improved quality of life and yielded notable gains in energy and physical function in chronic kidney disease patients suffering from anemia. In stark contrast, the untreated control group exhibited a decline in physical function over the same period. This states positive linear correlation between the duration of anemia therapy and the degree of improvement in quality of life.[32] Independent of treatment, the presence of anemia is associated with an elevated risk of mortality over a five-year timeframe.[33]

Anemia in individuals over 60 is linked to poorer Health-Related Quality of Life (HRQoL) and lower overall survival rates. It particularly affects those with age-related chronic illnesses (ACI) like cancer, HIV/AIDS, and chronic renal disease. Erythropoiesis-stimulating drugs can improve HRQoL, especially in older patients with chronic renal disease or chemotherapy-induced anemia. Additionally, maintaining physical activity is emphasized for preserving quality of life in older individuals.[34] Fatigue is associated with a diminished health-related quality of life and impaired physical functioning in individuals with HIV infection. Several factors, including social functioning, emotional well-being, functional abilities, treatment-related adverse effects, and the presence of illness symptoms, all contribute to the overall HRQoL of HIV-positive patients. Epoetin alfa, a medication classified as a recombinant human erythropoietin, has shown promise in enhancing HRQoL specifically in the context of anemia associated with HIV infection. Researches linked improvements in hemoglobin levels to significant positive changes in health-related QOL, particularly with regard to physical well-being. On average, patients experience a perceptible improvement in their quality of life following an increase in hemoglobin levels of approximately 2.5 g/dL.[35]

Numerous investigations have shown that women of childbearing age with iron deficiency experience deterioration not only in physical performance but also in cognitive function, mood, and HRQoL. Previous studies have also demonstrated a decline in HRQoL among anemic or iron-deficient women in this age group. For example, Ando et al. observed diminished vitality and general health scores in 92 anemic premenopausal women compared to national norms, with enhancements observed in all areas following iron therapy.[36]

Untreated anemia in the postpartum period presents a significant challenge to the well-being of both mother and child. Maternal iron deficiency or anemia-related complications can reduce physical capacity and performance, thereby exerting a detrimental effect on the mother's overall HRQoL. Association of Postpartum anemia to adverse effects on various facets of HRQoL, encompassing both physical and mental well-being is reported. Indeed, iron supplementation has been shown to yield significant improvements in symptoms of fatigue and depression. However, the impact of untreated postpartum anemia on the crucial mother-child interaction remains an area of ongoing research.[37]

Economic Burden due to Anemia

Unresolved anemia elevates the chances of increased illness and death rates, extended hospitalization periods, and inferior patient results. It frequently requires allogeneic blood transfusions, which are associated with worse outcomes among specific patient demographics. Anemia significantly raises healthcare delivery expenses, and decreasing unnecessary transfusions can result in fewer postoperative infections and complications. Hospitalization expenses are notably greater for patients experiencing severe infections ($14,000) compared to those without, highlighting the financial advantages of managing these issues.[38]

Anemia in patients diagnosed with congestive heart failure (CHF) correlates with a significant increase in the volume of red blood cell transfusions administered. This translates to a substantial escalation in healthcare expenditures attributable solely to transfusion requirements. Furthermore, the cost of treating anemia itself is higher in the anemic CHF population compared to their non-anemic counterparts. Research states that red blood cell transfusions are the primary driver of these increased costs.[39] The average total annualised expenses per patient for anaemic patients are greater than those of non-anemic patients, averaging $14,535 against $9,450. Patients with anemia incur around twice as much in outpatient and inpatient charges as non-anemic patients.[40]

Anemia in cancer patients undergoing chemotherapy translates to a significant increase in the utilization of healthcare resources. The annual cost attributable solely to anemia is estimated to be $3,775, with 36% of this expenditure dedicated to diagnostic and treatment measures. Furthermore, compared to their non-anemic individuals, anemic patients exhibit a higher rate of healthcare service utilization, including a two-fold increase in hospital admissions, emergency room visits, outpatient service days, and prescription medication claims. Moreover, the average hospital stay duration for anemic patients is longer (10.9 days) compared to non-anemic patients (6.4 days).[41]

The omission of erythropoiesis-stimulating agent (ESA) therapy in chronic kidney disease (CKD) patients with anemia contributes to increased healthcare costs. A study by Moyneur et al. revealed a substantial disparity in total direct costs within a six-month period following the initiation of dialysis. Patients who did not receive ESAs incurred an average monthly cost of $13,199 per patient, while those receiving ESA therapy had an average monthly cost of $11,312 per patient. Although ESAs themselves represent a significant cost factor, research suggests that neglecting to address CKD-related anemia ultimately results in a greater economic burden due to higher healthcare resource utilization. These findings underscore

the economic importance of managing this prevalent condition.[42]

These results highlight the enormous global burden of anemia in older adults. As the population size of older adult's increases within Low and middle income countries, the health burden and economic impact of anemia in older adults in these countries will also increase.[43]

COMPLICATIONS OF ANEMIA

Untreated anemia presents a significant health threat, potentially culminating in multiple organ failure and even mortality. Pregnant women with anemia exhibit a more risk of premature labor and delivering low birth weight infants. Older adults are particularly susceptible to a multitude of complications associated with chronic anemia, including cardiovascular issues such as arrhythmias, cardiac hypertrophy, myocardial infarction, angina, and high-output heart failure. In severe cases of iron deficiency, esophageal webs and restless legs syndrome can manifest. Early-onset severe anemia may impede neurological development, potentially leading to permanent deficits in mental, cognitive, and developmental functions.[44]

PATIENT COUNSELING

Nutritional education is a crucial component of managing iron deficiency anemia. Patients should be instructed on incorporating iron-rich foods into their diets while simultaneously avoiding excessive consumption of tea or coffee, which can impede iron absorption. Additionally, individuals taking oral iron supplements should be informed about the potential for black, tarry stools and an increased risk of constipation. For patients experiencing significant iron intolerance, referral to a physician is warranted to explore the possibility of intravenous iron supplementation. Vegetarians and vegans, at risk for vitamin B_{12} deficiency, should be encouraged to consume fortified plant-based products or discuss alternative supplementation with their healthcare provider. Patients who have undergone gastric sleeve surgery, due to a diminished absorptive surface area, require close monitoring for potential folate and vitamin B_{12} deficiencies.[44]

Anemia poses a significant health threat, negatively impacting overall well-being. A balanced diet rich in iron sources like red meat, tofu, fish, eggs, and dark leafy vegetables is crucial. Additionally, incorporating vitamin-rich foods such as legumes, nuts, and citrus fruits is essential. These dietary choices should supplant unhealthy processed foods, which are detrimental to health. Regular medical check-ups facilitate early detection of anemia, and adopting healthy dietary patterns can mitigate the risk of developing the condition. Food fortification programs are particularly important for individuals facing socio-economic challenges. Prenatal care plays a vital role in safeguarding the health of both mother and child, emphasizing the importance of nutrient-dense diets for expectant mothers. Girls should prioritize a nutritious diet to optimize iron absorption during critical developmental stages, while men also benefit from consuming wholesome foods to support bodily functions and prevent illness.[45]

CONCLUSION

Anemia is a diverse condition stemming from various diseases. It's crucial to identify the underlying cause and treat it appropriately, necessitating teamwork among the patient, primary care provider, and consultant physician. Taking prescribed medications, making lifestyle changes, and regularly following up with the medical team are vital to prevent complications. Collaborative interprofessional care can lead to optimal outcomes in anemia cases. Anemia is not a standalone disease but rather a disease process, and controlling it can prevent the onset of many fatal conditions. Maintaining adequate blood hemoglobin levels can help prevent numerous clinical health issues.

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