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EC MICROBIOLOGY
Review Article

Review of Nutritional Anemia in Low and Middle Income Regions

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Received: December 20, 2019; **Published:** December 30, 2019

Abstract

Introduction: It was estimated that nearly one-third of the world's population (32.9%) suffers from anemia in 2010. Due to its substantial consequences for human health, anemia is associated with negative health and development outcomes, such as perinatal mortality, low birth weight, premature birth, and delayed child development. Nutritional anemias is the net effect of decreased nutritional elements involved in RBC production that is insufficient to meet those demands.

Aim of Work: This is an overview of different aspects related to anemia and its nutritional correlates, particularly in low and middle income regions.

Methodology: A comprehensive and systematic search was conducted regarding anemia and nutritional aspects. PubMed and Google Scholar search engine were the mainly used database.

Conclusion: Iron deficiency is yet the most common cause of anemia, though many other nutritional deficiencies can also lead to anemia. Also, significant correlations between Hb and vitamin A status have been reported in many regions and populations including preschool and school-age, adolescents, and adults. Vitamin A supplementation increases Hb concentrations, some iron status indices. Both cobalamin (vitamin B12) and folate deficiency cause macrocytic anemia. These nutrients deficiency impairs DNA synthesis and cell division in the bone marrow. Also, many conditions has been associated with anemia via several mechanisms, including their effects on blood loss, hemolysis or erythropoiesis, and through the effects of inflammation on iron metabolism.

Keywords: *Nutritional Anemia; Vitamin A; Vitamin B12*

Introduction

Inadequate erythropoiesis and reduced hemoglobin concentration are the hallmark of nutritional anemia. This is due to lack of nutritional supply like iron, folic acid and vitamin B12. During intra-uterine life, the source of these nutrients is basically maternally dependent, while postnatally they are found in breast milk and diet. Many other elements are contribute to maintain the hemoglobin level. However, iron deficiency is the main cause of nutritional anemia in the community. Protein, amino acids and calorie malnutrition states are associated with altered erythropoiesis. Protein deficiency compromises erythropoietin response in hypoxia. Thus, decreased amino acids impairs erythropoietin synthesis. In anorexia nervosa, patients may develop moderate anemia, leucopenia and thrombocytopenia; bone marrow is usually hypoplastic [1].

Materials and Methods

A comprehensive and systematic search was conducted regarding anemia and nutritional aspects. PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com) were the mainly used database. All relevant available and accessible articles of all types were reviewed and included. Case reports and case series were used for rarely reported conditions. The terms used in search were: anemia, diet, inflammation, iron deficiency, vitamins, and nutritional micronutrient

Global magnitude of anemia

It was estimated that nearly one-third of the world's population (32.9%) suffers from anemia in 2010 [2]. The most vulnerable population groups to anemia include children under 5 years of age; women in reproductive age; and pregnant women [3,4]. Also, there is an increase of anemia prevalence among adults over 50 years of age [5].

Poverty, for example, has a major influence on health and nutrition. Also, low socioeconomic position is linked to a higher risk of anemia among women and children [6,7]. As reported in global analyses of anemia burden between 1990 and 2010, nutritional deficiencies, disease/infection and genetic Hb disorders were the mos identified risk factors for anemia [8]. The prevalence of anemia also varies by geographic region with the highest anemia prevalence was found in Sub-Saharan Africa, South Asia, the Caribbean in 2010 [2]. The WHO Global Nutrition Target 2025 on anemia aims to cut down anemia in women in reproductive age by 50% by 2025 [9]. However, efforts towards decreasing anemia has been overall slow.

Anemia consequences for development, growth, birth outcomes

Due to its substantial consequences for human health, anemia is associated with negative health and development outcomes, such as perinatal mortality, low birth weight [10], premature birth [11] and delayed child development [12]. This negative effects of anemia arise from the influence of decreased oxygen delivery to tissues (during which multiple organ systems can be affected), as well as effects of the underlying causes of anemia, which are difficult to untie. For instance, in iron deficiency anemia, reduced iron level has potent negative effects on brain development. This effect my even proceed the development of anemia [13].

Nutritional anemias: Iron, vitamins A and B12, folate and riboflavin

Nutritional anemias is the net effect of decreased nutritional elements involved in RBC production that is insufficient to meet those demands [7]. Factors leading to nutritional anemias include inadequate dietary intake, impaired absorption (e.g. *Helicobacter pylori* infection that impair iron absorption), increased nutrient losses (e.g. blood loss from parasites, or heavy menstrual losses), or altered nutrient metabolism.

Iron deficiency is yet the most common cause of anemia, though many other nutritional deficiencies can also lead to anemia. Other causes include deficiencies of vitamins A, B12, B6, C, D and E, folate, riboflavin, copper, and zinc [14]. Many of these nutrients are required for the normal production of RBCs. Also, vitamins C and E, protect RBCs through their antioxidant function [15]. Copper and zinc constitute the structures of enzymes acting on iron metabolism [16]. The extent of each of these deficiencies contribution to the global anemia burden is yet a point of investigation. While some of such nutrient deficiencies are rare, multiple micronutrients deficiencies have a synergistic effect on anemia development [17].

Iron deficiency- ID

Iron deficiency results from decreased dietary intake that fail meet iron needs over a period of time, especially during states of increased physiological demands (e.g. during periods of rapid growth, such as infancy and pregnancy) or when iron losses exceed dietary intake. Iron deficiency progression includes three phases: depletion of iron storage, iron-deficient erythropoiesis, and iron deficiency anemia [18]. Iron status is recommended to be assessed using serum ferritin or soluble transferrin receptor (sTfR) [19,20]. Serum ferritin is elevated during the acute phase response; high sTfR levels indicate tissue iron deficiency. However, sTfR may also be affected by inflammation and other causes of erythropoiesis [19,20]. Thus, acute phase proteins (e.g. C-reactive protein (CRP) and alpha-1-acid glycoprotein (AGP)) should be assessed [19].

The change in Hb concentration from iron supplementation was used by the WHO to estimate the proportion of all anemia adjustable to iron as 42% of anemia in children and 50% of anemia among non-pregnant and pregnant women [21]. Recent report from an analysis of BRINDA project denotes that along with age and malaria, iron deficiency was one of the factors mostly associated with anemia [22,23]. Despite the fact that iron deficiency remains a primary cause in many settings, the proportion of anemic individuals with iron deficiency varies by many factors, and poor iron nutrition cannot be assumed to be the primary cause in all cases. However, iron dietary interventions are yet central to most anemia control programs [24].

Vitamin A deficiency

Vitamin A deficiency is prevalent in many low and middle income countries, especially among pregnant women, and women in reproductive age. It was estimated that 9.1 million pregnant women from regions at risk of vitamin A deficiency were VA deficient, 15% of pregnant women from such countries [25].

Vitamin A deficiency and anemia have been observed to be prevalent in the same populations for decades. Also, significant correlations between Hb and vitamin A status have been reported in many regions and populations including preschool and school-age, adolescents, and adults [26]. Vitamin A supplementation increases Hb concentrations, some iron status indices, regardless of iron supplements administration [15,26]. Deficiency of vitamin A causes anemia through multiple mechanisms, including its role in erythropoiesis, contribution to immune function, as well as its well-established role in metabolism of iron [26]. Unlike iron deficiency anemia, vitamin A deficiency is marked by an elevation in iron stores in the liver and spleen [27]. Vitamin A deficiency anemia is described as hypochromic or microcytic and hypochromic [26]. BRINDA analyses reported that among preschool children, vitamin A deficiency was associated with anemia in approximately half of the surveys (5/12) [23]. Among women in reproductive age, BRINDA project showed that, vitamin A deficiency was associated with anemia in all surveys (5/5 surveys) in both high- and low-infection burden groups [22]. Like iron status indices, vitamin A biomarkers could be affected by inflammation, which in turn, complicate the assessment of anemia attributed to vitamin A deficiency in settings of infection [28].

Deficiencies of B vitamins

Many B vitamins are involved in Hb synthesis and iron metabolism, including cobalamin (B12), pyridoxine (B6), riboflavin (B2), and folic acid. Deficiencies of such vitamins is associated with anemia.

Both cobalamin (vitamin B12) and folate deficiency cause macrocytic anemia. These nutrients deficiency impairs DNA synthesis and cell division in the bone marrow, such as hypersegmented neutrophils on the peripheral blood smear [29]. Also, Folic acid deficiency lead to decreased erythrocyte life span. Vitamin B12 deficiency in low and middle income countries commonly results from low dietary intake. Cobalamin bioavailable forms are only found in animal-source foods. However, its deficiency can also result from malabsorption, particularly among the elderly whom gastric atrophy is common [30] in cases of pernicious anemia, where autoantibodies are formed against intrinsic factor that required for B12 absorption and in parasitic and bacterial infections [7,30]. Folate deficiency is more common in populations that are dependent on unfortified wheat or rice as a staple food and that consume low amounts of green leafy vegetables [30]. Also, pregnant women and preterm infants are at higher risk of folate deficiency [15,31]. During pregnancy, folate demands increase, therefore, starting pregnancy without appropriate folate status may cause megaloblastic anemia. This in turn is augmented by the additional folate need during lactation [7].

There is a lack of data on the prevalence of vitamin B12 and folate deficiencies at the national level [32]. Out of seven countries with national data on B12 status primarily from the Americas and Europe, five had levels of deficiency higher than 5% (above which the authors of the study considered B12 deficiency a major problem of public health) [32]. In the BRINDA project, it was reported that among the 10 surveys of women in reproductive age, four measured vitamin B12 status [22] among these, vitamin B12 deficiency was very low (< 3%) in Mexico and the United States, but higher (nearly 15%) in Colombia [22]. McL and his collogue reported that folate deficiency was estimated to be a public health significance (> 5% deficient) in six out of the eight countries with national data, and particularly affected groups included pregnant women in Costa Rica (48.8%) and Venezuela (25.5%) and the elderly in the United Kingdom (15.0%) [32]. As reported in one review, the high prevalence of B12 or folate deficiency was not necessarily correlated with a high prevalence of anemia except for women consuming vegetarian diets who were B12 deficient [33].

Riboflavin's role is an crucial for iron metabolism, and riboflavin deficiency in animals can decrease iron mobilization from stores, reduced iron absorption, increase losses of iron [34] and impair production of globin [15]. Riboflavin deficiency is noted to be common in many populations and is demonstrated among pregnant and lactating women, infants, school children, adolescent girls, and the elderly in all socioeconomic levels, particularly with decreased consumption of milk/dairy products and meat [34]. Contribution of riboflavin deficiency to anemia in humans remains unclear. Some studies reported that riboflavin supplements provided along with iron supplements is shown to have a higher effect on Hb concentration than iron supplements alone among children and pregnant women [35]. As shown in a Chinese study, reduced riboflavin intake was associated with anemia and increased risk of anemia during a 5-year period of follow-up [36]. However, riboflavin deficiency among schoolchildren in Côte d'Ivoire was not associated with anemia despite a prevalence of riboflavin deficiency of 65%, though it was associated with iron deficiency [35].

Undernutrition and anemia

Stunting and underweight have been associated with anemia as reported in several studies [23,37,38] and opposed in others [39]. Shown in analyses from the BRINDA project, stunting and underweight were linked to anemia in preschool children in more than half of the surveys (9/15, 10/15 and 5/15 respectively) for which these variables were available [23]. These features of poor nutritional status are associated with anemia due to similar factors, including poor maternal nutrition, inadequate complementary feeding habits leading to reduced micronutrient and animal-source food intake. Needles to address the role of contaminated water and poor sanitation, suboptimal breastfeeding practices, and clinical and subclinical infections [40].

Summary and Conclusion

Anemia continues to be a widespread and major global health problem that needs to be adequately addressed, particularly in low and middle income countries where progress has been slow. Although iron deficiency remains the main cause of anemia in most regions, recent report suggests that anemia etiology is yet complex and context specific. Efforts are further needed to understand how the most causes of anemia, including iron deficiency and other nutritional deficiencies, disease, and Hb disorders, contribute to anemia via implementing appropriate interventions in specific settings.

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Volume 16 Issue 1 January 2020