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A Review on Major Causes of Anemia and its Prevention Mechanism

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Abstract

Anemia is one of the most public health problems that cause serious health difficulty like impaired mental and psychomotor development, reduced work performance, increased susceptibility to parasitic infections, and growth retardation in children. The factors for anemia causation are low socio-economic status, nutritional deficiencies, helminthic infections and other infectious diseases, illiteracy, and blood disorder. The major causes of anemia are iron deficiency, foliate deficiency, hookworm infection and malaria. Out of two billion people suffering from anemia, about 50% cases are related to iron deficiency. The cost-effective interventions against anemia include treatment of the underlying causes, restoration of the hemoglobin concentration to normal levels, and prevention and treatment of complications. Furthermore, the simplest and best way to prevent anemia is to eat the gluten free food made from Ethiopian red teff (*Eragrostis tef*)) which is full in iron and B-complex vitamins.

Keywords: Anemia; Nutritional deficiency; Helminthic infections; Injera; Teff

Introduction

Anemia is one of the most widespread public health problems throughout the world. It is much more common in developing countries where people suffer from malnutrition and helminthic infections. On the other hand, in developed countries iron deficiency in the food is the major cause of anemia [1]. Anemia is the condition resulted when the body has not enough red blood cells to transport oxygen from the lung to each cell [2]. This occurs when hemoglobin (Hb) concentration level is lower than 11g/dl for pregnant women and children six month to five years of age, 12g/dl for children 6-14 age and 13g/dl for men [1]. Anemia causes serious health problems like impaired mental and psychomotor development, reduced work performance, increased susceptibility to parasitic infections (decreased immunity), growth retardation in children and in severe cases increased rate of child and maternal mortality [3]. According to WHO report two billion people are suffering from anemia in the world of which a major proportion is from South Asia. Globally, almost half (47.4%) of all preschool aged children and 41.8% pregnant women suffer from anemia [1]. Now a day, there is not enough compiled information about the major causes of anemia, and its simplest prevention mechanism. Therefore, the aim of this paper is to review the major causes of anemia and to suggest the simplest way of anemia prevention mechanism.

Major Causes of Anemia

Anemia is caused by different factors including low socioeconomic status, nutritional deficiencies, helminthes infections and other infectious diseases, illiteracy, and blood disorder such as sickle cell anemia [4,5]. The major causes in the societies are iron deficiency, hookworm infection, foliate deficiency, and malaria [6]. In the current review the main causes of anemia: nutritional deficiency and parasitic infections are discussed.

Nutritional deficiency

Nutritional deficiency occurs when an individual's daily nutrient intake consistently falls below the recommended requirement. About 1,200 million adolescents suffer from poor nutrition that affects their development and growth [1]. Nutritional deficiencies can lead to anemia, which is the most prevalent health problem in both developed and developing countries. Anemia caused by nutritional deficiency includes iron deficiency anemia, vitamin B12 deficiency anemia and foliate deficiency anemia [7].

Iron deficiency: Iron deficiency is the most widespread condition that mainly causes anemia [1]. WHO estimated that about 50% of anemia is related to iron deficiency [8] It causes reduction in hemoglobin content of red blood cells, the iron containing pigment that carries oxygen from the lungs to the cells [9]. Iron deficiency anemia develops when the amount of iron absorbed

from the diet is lower than the mean daily intakes requirements [10]. The mean daily intake is 0.5mg per day for breast feed infants (0-6 months); 9mg/day for 7-12-month olds; 6-8mg/day for young children and 12-16mg/day for lactating women. Low iron absorption by the body can further be the cause for iron deficiency [11]. Iron deficiency is a major problem affecting health, cognitive development, school achievement and work performance of an individual [12]. Infants, children, adolescents who need additional iron requirements for growth and pregnant women that need additional iron to supply the mother's expanding blood volume and to support the needs of the growing fetus are highly at risk of iron deficiency [1]. Women of childbearing age, who have higher iron loses due to menstrual blood loss also develop iron deficiency [10].

Vitamin B deficiency: Vitamin B-complexes can cause anemia if there is deficiency in the food one eats. Vitamin B_6 deficiency has been associated with anemia because it is important in making hemoglobin that result in increase of oxygen transportation. A form of anemia which results from Vitamin B_6 deficiency is similar to iron deficiency anemia [13]. Riboflavin (Vitamin B_2) deficiency can also cause anemia. It alters iron metabolism by impairing iron absorption, increasing intestinal loss of iron, and/or impairing iron utilization for the synthesis of hemoglobin. In humans, correction of riboflavin deficiency has been known to increase circulating hemoglobin levels thereby improving iron deficiency anemia [1]. Deficiency of vitamin B_{12} most commonly results in megaloblastic anemia which causes neuro-developmental effects and abnormal movements in children due to its role in foliate metabolism. Megaloblastic anemia is a type of anemia characterized by typical morphological changes in red blood cell precursors which are larger than the cells of same stage and maturation [7]. Most common cause of B_{12} deficiency in young children has been particularly related to maternal deficiency which leads to decreased stores at birth [13]. Infants who are exclusively breastfed for prolonged period (3-5 years) tend to develop B_{12} deficiency because of the low content of B_{12} in mother's milk [14]. In developed countries this problem has been reported from infants born to vegetarian mothers as B_{12} is not present in plants [15]. Anemia can also be resulted from impaired absorption of Vitamin B_{12} [1].

Foliate deficiency: Margo et al. [16] described foliate deficiency as a frequent complication of protein-energy malnutrition. Like other nutritional deficiencies, foliate deficiency may also lead to anemia and it occurs when absorbed foliate does not meet requirements level over time [17]. Since it is required for the normal production of red blood cells in bone marrow, foliate deficiency results in anemia by bringing red blood cells deformation and production reduction [18]. During the period of pregnancy and lactation, the problem can be encountered as a result of high demand for foliate. Foliate stored in tissue may be depleted in up to one third of pregnant women worldwide [19].

Vitamin A deficiency: Vitamin A deficiency contributes to anemia by affecting hemoglobin levels as it is involved in iron metabolism and red blood cell production [7]. It brings risk of anemia by influencing tissue storage and release of iron into circulation and having a direct regulatory effect on red blood cell production and development [1].

Parasitic infections

Intestinal parasitic infections, which are more prevalent among poor developing countries of the tropics affect over one quarter of the world's population at any one time [20]. Intestinal helminthes infections bring serious public health problems including causing iron deficiency anemia. Chronic blood loss due to hookworm, schistosomes, *Trichuris trichiura* and iron absorption blockage due to *Ascaris lumbricoides* are a significant cause of anemia [12].

Hookworms: Hookworm is a blood feeding intestinal nematode currently infecting over 740 million people throughout the tropics [21]. The adult hookworm attaches to the intestinal mucosa where it chews and digests tissue within its buccal capsule leading to loss of red blood cells. In other case, up on attachment to the host intestine, hookworms produce numerous proteases which have the ability to degrade hemoglobin for its feeding and survival [22]. The major clinical features of chronic hookworm infection are anemia and malnutrition which resulted from blood sucked by the parasite [22]. In chronic intestinal blood loss, iron deficiency anemia develops when blood loss exceeds the intake and reserves of iron and protein in the host. Depending on the status of the iron in the host, a hookworm burden of 40-160 worms is related with hemoglobin levels below 110g/l [23]. Iron deficiency anemia induced by hookworms depends on the species. The two hookworm species that commonly infect human are *Ancylostoma duodenale* and *Necator americanus*. Infection with *Ancylostoma duodenale* causes greater blood loss up to 0.2ml/day/individual whereas infection with *Necator americanus* brings a loss of 0.03ml/day/individual. On the other hand, the depletion of iron stores in the host has a direct correlation with the intensity of hook worm infection [24]. Women of the reproductive age are considerably affected by hookworm infection with adverse effects on the outcome of pregnancy [23]. Crompton (2000) reported that 44 million pregnant women are infected with hookworm worldwide with 7.5 million women in sub-Saharan African alone. According to WHO report severe iron deficiency anemia during pregnancy has resulted increased maternal mortality, impaired lactation, prematurity, and low birth weight [25].

Schistosomes: Schistosomes infection is one of man kind's oldest parasitic infections currently affecting more than 200 million people worldwide [26]. The disease is affecting many people in most African countries. It also presents in limited areas of South America, the Caribbean, the Middle East, and Asia [27]. The species which cause anemia are *Schistosoma mansoni* and *Schistosoma japonicum* (intestinal parasite), and *Schistosoma haematobium* (urinary schistosomiasis). Severe anemia is more firmly resulted from *Schistosoma haematobium* although all three forms can cause it [28]. As reported by Ezeamama et al. [29], blood loss in the stool as emerging eggs rapture intestinal lining, adult in-

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gestion of host red blood cells, sequestration of red blood cells in an enlarged spleen, and destruction of red blood cells by autoimmune, results in anemia.

Trichuris trichiura: *Trichuris trichiura* which is endemic in tropical and sub-tropical countries is affecting many people especially in developing countries. *T. trichiura* is most prevalent in warm and humid climate and rare or non-existent in arid, very hot or very cold regions. High intensity of *Trichuris* infection which affects iron status through blood loss in the stool has been reported to cause iron deficiency anemia [30]. The adult *T. trichiura* invade the mucosa and produce minor inflammatory changes. Inflammation at the site of attachment caused both from destruction of the normal colonic architecture as well as post inflammation comprised of macrophage and cytokines which leads to mucoid diarrhea and occasional bleeding [31].

Plasmodium parasites: Malaria which is caused by *Plasmodium parasites* is a devastating disease that affects approximately half of the world population. WHO report indicated that 247 million cases of malaria of which most deaths occur among children living in Sub-Saharan Africa [32]. This devastating disease is thought to be the primary cause of severe anemia (Hb<7g/dl) [25]. Even though the mechanisms by which *plasmodium parasites* cause anemia are quite complex, in its simple terms, the parasites cause anemia both by rupturing red blood cells and by suppressing the production of new red blood cells. It also stimulates the activity of macrophages in the spleen which then destroy both parasitized and unparasitized red blood cells [33]. When red blood cells fall down, hemoglobin, the oxygen carrying protein in red blood cells, will also fall to the extent that cell cannot have the ability to carry oxygen. If this is severe enough, it can bring a significant risk of death by profound hypoxia due to the blockage of capillaries by infected red blood cells, and congestive heart failure, or rarely cerebral malaria. Young children are mostly at risk of malaria because they cannot develop protective immunity against the severe forms of the disease which results in anemia [32]. Recently, researchers discovered that a protein produced by immune cells during malaria infection can also trigger severe anemia [34]. The severity of anemia caused by *plasmodium parasites* depends upon many factors including age, nutritional status, host's and parasites' genotype and immunological history. Children under age five do not produce immunity to resist parasitic damaging when they have been repeatedly infected with *plasmodium parasites*. For this reason, young children account for vast majority of deaths due to anemia caused by plasmodium [35]. Factors such as nutrients malnutrition, pregnancy and HIV infection weaken the immune system to increase incidence of plasmodium infection [36]. Individuals with certain genotypes, for example, with sickle-cell hemoglobin allele, have been known to be protected against infection by *plasmodium parasites*. An outcome of the infection also depends upon the genotypes of *plasmodium parasites*. This is obviously illustrated by the existence of localized varieties of *plasmodium falciparum* that show an inherited resistance to anti-malarial drugs [35]. As a result, many children with severe anemia die and others have a depressed reticulocyte response and a significant number of children had abnormalities of erythropoietic cells in the bone marrow [37]. Severe anemia also affects African pregnant woman in malaria endemic areas [38]. As Guyatt, et al. [39] estimated, approximately 400,000 pregnant women develop moderate or severe anemia annually in sub-Saharan Africa as a result of malaria infection.

Anemia Prevention and Control

Since anemia brings serious public health problems its cost-effective prevention and control is in need worldwide. Many cost-effective interventions against anemia that are well documented include treatment of the underlying causes, restoration of the hemoglobin concentration to normal levels, and prevention and treatment of complications [40]. A number of strategies are used to deliver additional iron to humans, but food fortification and dietary diversification with iron has the greatest potential to prevent iron deficiency anemia [41]. On the other hand, in the areas where vitamin A deficiency is found, WHO recommends routine vitamin A supplementation during pregnancy or at any time during lactation [42]. In case of malaria prevention WHO has recommended a combination of integrated vector management, indoor spraying of insecticide and larval control [8]. In areas endemic with parasitic infections, the International Nutritional Anemia Consultative Group (INACG), WHO, and United Nations Children's Fund (UNICEF) recommended certain control measures such as controlling hookworm and other helminthic infections including sanitary disposal of feces and educational campaigns on proper use of latrines All forms of schistosomiasis including intestinal and urinary types can be prevented by eliminating water dwelling snails, which serve as natural reservoirs of schistosomes [42,43]. Since anemia is mainly a condition with iron and vitamin B deficiencies, the other simplest and best strategy to prevent it is to eat the gluten-free food called Injera made from Ethiopian teff (*Eragrostis tef*). Enjera is a major Ethiopian food staple and provides approximately two-thirds of the diet in Ethiopia. Teff is also eaten as porridge and a good thickener for soups, stews, gravies, and puddings and can also be used in stir-fry dishes, and casserole dishes. Furthermore, teff flour is used for making traditional alcoholic drinks like tella (local beer), katikalla (local spirit), kitta (sweet dry unleavened bread), and muk (gruel) [44] Figure 1. Teff is full in iron and B-complex vitamins although many gluten free foods are not enriched with these nutrients. Researchers identified that the iron content of red teff can be up to 150mg/100g and one cup of raw grain teff can provide as high as 82% of the recommended daily intake of iron. As a result, in people living in areas of Ethiopia where consumption of red teff is most prevalent, hemoglobin levels were found to be higher with a decreased risk of anemia [45-47]. In addition to iron, teff contains B-complex vitamins that are used in the formation of red blood cells and facilitate nutrients' metabolism. One cup of uncooked teff contains 47% of the recommended daily intake for vitamin B_6, 50% for vitamin B_1, 31% for vitamin B_2, 32% for vitamin B_3 and 18% for vitamin B_5. Furthermore, teff is full in vitamin C that is used in iron absorp-

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tion but contains small amount of vitamin A [48]. In another study, Gamboa [49] identified different vitamins found in teff as stated on Table 1. Currently, there has been a growing global interest in the use of teff as a food. This interest is mainly attributed to teff being gluten-free and having relatively high nutrient content and thus a candidate ingredient for food products destined for people with celiac disease [50,51].

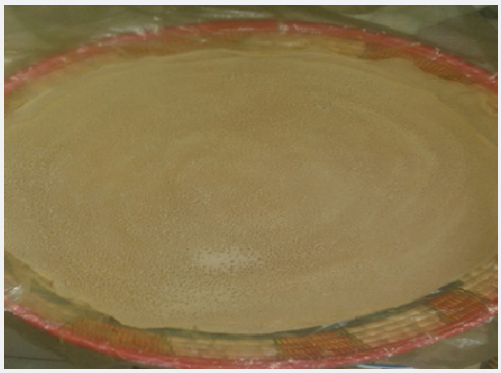

Figure 1: Injera with Mesob (handling material), captured by the author immediately after preparation at home.

Table 1: Amount of vitamins in the flour of teff grain.

Vitamin	mg/100g	Advised daily amount for a 75kg human (mg)
Thiamin (B_1)	0,51	1,0
Riboflavin (B_2)	< 0,1	1,5
Niacin (B_3)	0,80	16
Pyridoxin (B_6)	<0,1	3
Ascorbic acid (C)	0,25	70
Folic acid (M)	<0,02	0,4

Conclusion

Anemia, the most widespread public health problems, causes impaired mental and psychomotor development, reduced work performance, and growth retardation in children. It is mainly caused by nutritional deficiencies and parasitic infections. Nutritional deficiency including iron deficiency anemia, vitamin B_{12} deficiency anemia and foliate deficiency anemia are the major causes of anemia. Blood loss due to hookworm, schistosomes, Trichuris trichiura and iron absorption blockage due to *Ascaris lumbricoides* are a significant cause of anemia. Ethiopian teff (*Eragrostis tef*), which has recently got international acceptance, is recommended as the best remedy to prevent anemia.

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