Review Article

Risks associated with mild Anemia in apparently healthy individuals: How to combat Anemia in general population

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ABSTRACT

Mild grade anemia in adult population is defined as a blood hemoglobin concentration between 10.00 to 12.9 g/dl in males or between 10.00 to 11.9 g/dl in non-pregnant females. Mildly anemic but apparently healthy subjects are commonly found in general population. Such individuals are at a greater risk of not being sufficiently investigated for the underlying disease and may end up with serious morbidity and health problems such as, diminished cardiovascular responses, compromised physical activity, poor cognitive function and growth retardation in children, and increased risk of falls and fractures and 5-year all cause mortality rates among elderly people. Nutritional deficiencies, chronic diseases, recurrent infections and aging are the major causes of mild anemia. The best approach to combat mild anemia in general population of a developing country would be through initiation of food fortification program, creating more awareness among people about the benefits of dietary diversification, use of fresh fruits and green leafy vegetables and adopting measures such as, frequent hand washing and use of boiled water for drinking to avoid common infections.

KEY WORDS: Anaemia, General population.

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INTRODUCTION

Anemia continues to be a major public health problem worldwide, particularly among growing children, females of reproductive age and elderly people, especially in the developing countries. The World Health Organization (WHO) estimates that anemia affects approximately 1.62 billion people worldwide, corresponding to 24.8% of the human population.[1]

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The causes of anemia are diverse and multifactorial, but among the leading etiologies in the developing countries are: nutritional deficiencies (especially of iron, folate and vitamin B12), chronic or acute blood loss, inherited genetic defects (e.g. thalassemia), chronic diseases and/ or inflammatory disorders, malaria, parasitic infestations (e.g. hookworm), hemolytic disorders, drug-induced hemolysis or marrow suppression or it may be unexplained.[2]

Definitions of anemia and mild-grade anemia:

According to the WHO reference criteria, anemia is said to be present in an adult, if the blood hemoglobin concentration falls below 13.0 g/dl in men or below 12.0 g/dl in non-pregnant women or below 11.0 g/dl in pregnant women.[3,4] However, reference range for normal blood hemoglobin levels may vary in individuals depending on the age, gender, race, geographical location and food habits of the study population.[5]

Anemia is classified according to its severity as: mild, moderate and severe. Mild-grade anemia in an adult population is defined as a blood hemoglobin

concentration between 10.0 to12.9 g/dl in males or between 10.0 to11.9 g/dl in non-pregnant females or between 9.0 to 10.9 g/dl in pregnant females.[6,7]

Anemia and Oxygen delivery:

Under normal circumstances, oxygen consumption in the resting human body is approximately four times less than the oxygen delivery to the tissues. During anemia, reduction in circulating red blood cell mass compromises oxygen delivery to the tissues, thus causing relative tissue hypoxia. The resulting tissue hypoxia obligates the human body to compensate for reduced-oxygen carrying capacity. Both tissue hypoxia and body's compensatory mechanisms together produce the signs and symptoms characteristic of anemic syndrome. A slowly falling level of hemoglobin allows hemodynamic compensation and enhancement of oxygen-carrying capacity of blood.

Mild anemia in apparently healthy people and its clinical features:

Apparently healthy and mildly anemic subjects with borderline hemoglobin levels are reported to be quite common in the general population all over the world. While moderate and severe anemias get immediate attention due to more obvious symptoms, mild anemia is often ignored by the people as well as by the general practitioners. Most of these mildly anemic individuals are not investigated sufficiently to establish the probable cause of their anemia. Many of such individuals consult general practitioners and family physicians for enhancement of their hemoglobin levels and erythropoietic activity even though no other disease or abnormality is clinically detected in them.[8]

Health outcomes of mild anemia in otherwise healthy children and non-pregnant adolescent females:

The WHO estimates that 39% of children younger than five years, 48% of children between 5 and 14 years, 42% of all women and 52% of pregnant women in developing countries are anemic.[9] A growing body of medical literature supports the contention that mild anemia or a 'borderline' hemoglobin level is associated with a broad range of health-related risks for the general population.

Cardiovascular responses are blunted in mild anemia if it persists or remains untreated, mainly because of depleted cardiac reserve. Physiological cardiovascular compensatory response to anemia in adult humans is associated with a progressive increase in heart rate and cardiac output, however these changes are not found in individuals with stable mild or moderate anemia.[10] Mild anemia in apparently healthy adults is often asymptomatic, but during periods of activity or exercise, anemia may manifest itself in the form of unexplained weakness, fatigue, headache, dizziness, tachycardia, palpitations, dyspnoea on exertion, and diminished physical activity.[11]

Millions of relatively healthy infants and children under 5 years of age without serious health problems have undiagnosed mild anemia in many parts of the developing world and receive no treatment.[12,13] Untreated persistent mild anemia has been seen to retard the physical and mental growth in newborns and infants.[14] Mild anemia has been reported to have damaging consequences on the cognitive development, attention span and alertness in the growing children.[15] The physiological response to physical exercise is compromised in children with mild anemia and hence these children may never attain their full potential in various school activities. A previous study reported that the gain in heart rate, systolic blood pressure, total exercise duration and metabolic equivalent (MEV) at peak exercise testing on a treadmill were significantly lower in mildly anemic healthy children, having 7-14 years of age than the age and body mass index (BMI)-matched non-anemic controls.[16]

Apparently healthy young men and women represent a group at high risk of mild to moderate anemia, especially due to iron deficiency both in the developing and industrialized countries of the world.[17] Previous studies have indicated that mild anemia in non-pregnant apparently healthy adolescent women have negative consequences on growth, co-morbidity and reproductive health.[18] Mild grade anemia in the otherwise healthy school-going adolescent females has also been associated with poor school performance.[19]

Negative impact of mild-grade anemia in healthy pregnant women: Iron and micronutrient deficiencies during pregnancy have been shown to have serious implications on the developing fetus. Some of the recent studies have shown that there is a high prevalence of mild anemia in healthy pregnant females all over the world.[20,21] Anemia during pregnancy may have negative consequences on the maternal and perinatal outcomes. Borderline anemia in healthy pregnant women has been associated with easy fatigability, decreased mental concentration and reduced work capacity in these ladies.[22] A recent study suggested that mild iron deficiency anemia in otherwise healthy pregnant women may decrease the iron storage in fetus and may also affect the iron status during early infancy.[23]

Other risks associated with mild maternal anemia include: increased maternal morbidity and mortality, increased perinatal mortality, increased number of preterm births, intrauterine fetal growth retardation and low birth weight in the newborn.[24,25] However, results from multiple studies have revealed that only moderate and severe anemia and not mild-grade anemia in apparently healthy women is associated with risk of still birth.[26]

Risks related to mild anemia in apparently healthy elderly population:

Prevalence of anemia increases with advancing age.[27] Relatively low blood hemoglobin levels are a common laboratory finding in the apparently healthy elderly people which for the most part are judged by physicians as a sign without clinical relevance or as a marker of an underlying chronic disease having no independent influence on health. Recent studies have indicated that aging is associated with dysregulation of cytokines, most notably interleukin-1 (IL-1), interleukin-6 (IL-6) and tumor necrosis factor - alpha (TNF- alpha) which may have a negative impact on hematopoiesis, either by inhibition of erythropoietin (EPO) production or by interaction with EPO receptors.[28]

Anemia has several adverse consequences in the elderly. Recent studies have clearly indicated that mild anemia in these older people is associated with increased risks of poor selective attention performance and decreased quality of life.[29] Mild anemia and even low-normal hemoglobin levels in otherwise healthy elderly women are shown to be linked with weakness, limited mobility, decreased physical performance and decreased muscle strength.[30] Mild anemia has been reported as an independent risk factor for cognitive impairment and worsening of existing dementia in the elderly population.[31,32] It has also been shown that mild-grade anemia in the older people is associated with increased risk of falls and fractures and also with increase in the 5-year all-cause mortality rates.[33-36]

Mild-grade anemia in asymptomatic thalassemia minor cases:

Thalassemias are disorders of hemoglobin synthesis characterized by a reduced rate of synthesis of generally structurally normal globin chains. Their manifestations range from mild anemia with microcytosis (thalassemia minor/ beta-thalassemia trait) to fatal severe anemia (beta-thalassemia major). Previous studies have shown that many of the asymptomatic mildly anemic subjects with unexplained etiology are diagnosed of having thalassemia minor either during routine screening and/ or by hemoglobin electrophoresis.[37,38]

How to combat anemia in the general population?

Deficiency of iron, folate, vitamin B12 and vitamin B6 have been reported to be very common in apparently healthy Pakistani individuals.[39,40] This is suggestive that a significant proportion of the general population could be suffering from mild anemia. It is, therefore, imperative that an effective strategy should be put in place to prevent the development of mild anemia in Pakistani population.

1. Food fortification: Fortification of various food items such as cereals, dairy products, sugar, fats and oils with micronutrients has been carried out for the last several decades in many developed and developing countries with considerable success.[41] However, not much progress has been made in Pakistan regarding fortification of cereals or wheat flour. Many of the micronutrients commonly used in fortification include iron and B-vitamins which have a critical role in combating anemia. Food-based strategy to prevent development of anemia should be preferred over supplementation because of better sustainability of such an approach. Moreover, the risk of overdosing of micronutrient is also minimum in such programs. However, active involvement of Government and public awareness about the importance of essential micronutrients are necessary for a successful outcome. In a recently published community-based study which included iron supplementation, dietary diversification and modification and food fortification, prevalence of anemia in non-pregnant Malawian women has been significantly reduced over a period of 4 years.[42] It is imperative that such large-scale cross sectional surveys are carried out in Pakistan to provide scientific evidence to policy makers to initiate food fortification program in this country.

2. Dietary diversification and food habits: People in South Asia consume food on the basis of what they like and can afford. Cultural habits also play a role in selection of a particular dietary pattern. For example, Muslim communities prefer meat over vegetables. Although meat based food is a rich source of micronutrients, especially iron, yet its consumption could be limited because of high expenses involved in preparing such dishes. However, consumption of certain plant foods such as cereals, legumes, fruits and vegetables can provide the requisite amounts of proteins and micronutrients.[43] They add taste and flavor to diet and considerably improve palatability. Therefore dietary diversification can play a major role

in preventing micronutrient deficiencies, especially those which are involved in erythropoiesis.

3. Cooking habits: South Asian people love overcooked and deep-fried food because it adds to taste and palatability. However, it severely compromises their nutritive value.[44] For example, many of the essential micronutrients such as vitamin C and B-vitamins are unstable to heat. Moreover, washing of rice and pulses with water before or after cooking will also wash away several minerals and water soluble vitamins. These cooking practices deprive the population from getting the required amounts of essential micronutrients involved in erythropoiesis, thereby making many of the subjects vulnerable to developing anemia. It is difficult of change these traditional practices, however, public awareness about the ill-effects of these cooking practices could bring a gradual change. Adequate consumption of fresh fruits and green leafy vegetables would be essential to stay free from anemia.

4. Control of infection: High prevalence of parasitic enteric infestation such as, amoebiasis and giardiasis in Pakistani population could lead to micronutrient deficiency in infected individuals.[45,46] Frequent hand washing and use of boiled water for drinking could be of help in preventing loss of essential micronutrients, especially those which are required for hemoglobin synthesis.[47] Prophylactic use of anthelminthic treatment in children has shown to be beneficial in decreasing prevalence of mild to moderate anemia in Zanzibar.[48] In Pakistan, where helminthic infestations are very common, quarterly anthelminthic treatment in children could be of help in preventing malnutrition and anemia.

CONCLUSION

Anemia is not a disease, but rather a symptom of an underlying illness. Mild grade anemia in apparently healthy population may appear to be innocuous but could lead to significant morbidity and health problems. Failure to identify and investigate mild anemia in apparently healthy people could lead to delayed diagnosis of potentially treatable conditions. Micronutrients deficiencies, frequent infections, chronic diseases and aging are among the major causes. The best approach to prevent the development of anemia in general population would be through food fortification, public awareness about benefits of dietary diversification, consumption of fresh fruits and green leafy vegetables and measures to avoid infections.

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