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Review Article

Undernutrition with Special Reference to Iron-deficiency Anemia in Reproductive Age Group Females in Pakistan

Rozina Shahadat Khan[1], Huma Bader Ul Ain[2*], Tabussam Tufail[2], Muhammad Imran[3,4], Sahar Imran[2], Sunair Siddique khan[5], Romaisa Siddique[6], Faiz Rasool[7] , Saira Ahmad[2] and Habib-Ur-Rehman[2]

[1]Specialized Health Care Punjab, Lahore, Pakistan
[2]University Institute of Diet and Nutritional Sciences, Faculty of Allied Health Sciences, The University of Lahore, Lahore, Pakistan
[3]Department of Food Science and Technology, University of Narowal, Narowal, Pakistan
[4] Food, Nutrition and Life style Unit, King Fahad Medical Research Center, Clinial Biochemistry Department, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia
[5]Coventry University, United Kingdom
[6]Lahore School of Economics, Lahore, Pakistan
[7]Global Alliance for Improved Nutrition, GAIN, Pakistan

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***Corresponding Author:**

Huma Bader Ul Ain
University Institute of Diet and Nutritional Sciences,
The University of Lahore, Lahore, Punjab-Pakistan
huma.badar@dnsc.uol.edu.pk

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ABSTRACT

Undernutrition, especially micronutrient deficiency is one of the major but least addressed Global health issues. Wasting, underweight, stunting, and deficiencies of essential minerals and vitamins are results of undernutrition leading to increased mortality and morbidity. The developing countries especially the reproductive age group females are mainly affected by undernutrition. Reproductive age group females' especially pregnant females of the underprivileged rural populations are more prone to develop iron deficiency due to increased physiological requirements or administration of substances acting as inhibitors. Undernutrition is not only responsible for high mortality in women but also impacts their families, especially children and chronically undernourished females likely to give birth to an undernourished child. This pattern runs in generations. But increased usage of substances that act as adjutants can fulfill the physiological requirements of pregnancy. This review aims to explain the roles of different Nutraceuticals in the prevention of iron deficiency anemia, especially in reproductive age group pregnant females.

INTRODUCTION

Undernutrition is a "lack of adequate energy, protein, and micronutrients to meet basic requirements for body maintenance, growth, and development" and is one of the major but least addressed Global health issue [1,2]. Age group and living standards of females are among the significant risk factors but education, cast, religion and cast also influence undernutrition [3,4]. High Parity, lower education, unsafe water, Infectious diseases, lowered immunity, taboos attached to food and its intake, poor dietary intake, food distribution not based on equity within the household, inappropriate preparation and storage of food make the reproductive age females most vulnerable

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to undernutrition, especially rural population. Rural females in the African region are 68% more likely to be undernourished compared to urban [1]. Anemia is a condition in which "the number of red blood cells or the hemoglobin concentration within RBCs is lesser than normal" [4] is a grave public health concern worldwide that predominantly has an effect on children of younger age group and pregnant females. According to World Health Organization (WHO), globally one-third of all women of reproductive age group, 40% of pregnant females and more than 42% of children less than 5 years of age are anemic. Reproductive age group females (15-49 yrs) [5, 6] need high energy and nutrients during pregnancy and while working carrying heavy loads [7] and are more prone to develop iron deficiency due to multiple pregnancies, menstruation, and childbirth [8]. According to a study conducted in Azerbaijan 38.2% of the women were having Anemia, 34.1% had iron deficiency and 23.8% were having iron deficiency anemia (IDA),10.5% of women were having Vitamin A insufficiency 35.0%, Folate and 19.7%, vitamin B12 deficiency with vitamin A insufficiency. Iron deficiency is found as the main risk factor for anemia [9] increases the chances of perinatal mortality, maternal deaths, impaired cognitive development in children and reduced work capability in adults. Undernutrition is the underlying cause of 35% of the pre-school children's disease burden and in poor communities of the developing countries, 50% of children and roughly one-third of reproductive age group females are affected by anemia [5, 6]. IDA is among the principal reasons of disability globally and its effects on the health of adolescent females and women may have consequences affecting generations. As a result of gestational anemia, chances of preterm deliveries and low birth weight babies are high. It can also adversely affect the iron stores of the fetus impacting the motor, social-emotional and neurocognitive development of the child [10]. IDA-affected mothers are more prone to premature deliveries, babies born with low birth weight, newborns that are small for their gestational age, congenital birth defects, and growth impairment. IDA, the major contributor to disability-adjusted life years in women is prevalent in 30-60% of Pakistani women. "Pakistan has a high maternal (276 per 100,000 live births) and perinatal mortality (75 per 1000 pregnancies) and both are associated with acute blood loss in situations of chronic IDA". IDA accounts for 19.3% of births of newborns who are small for their gestational age and 25% of babies born with low birth weight in Pakistan [11]. According to EMRO WHO statistics More than one-fifth of females in Pakistan are suffering from Anemia [12].

Causes of Anemia: Iron, folate, vitamins B12, and vitamin A are all nutritional deficiencies, out of which Iron deficiency is the most frequent cause of anemia. But infectious diseases such as tuberculosis and HIV, malaria hemoglobinopathies, and parasitic infections are other causes of anemia [13-15]. Aging population, nutritional deficiency, chronic disease, and unexplained anemia which might be due to the progressive resistance to erythropoietin, and underlying chronic state are different causes. Anemia can be Aplastic or sickle cell or it can end up in Thalassemia. Nutritional Anemia can be due to Vitamin deficiency or Iron deficiency. Depending upon the deficiency and its duration anemia can be mild to severe, congenital or acquired due to any other condition. Anemia can occur if the blood is not having enough red blood cells or the body cannot synthesize sufficient red blood cells. Red blood cell loss occurs due to Bleeding more quickly than they can be replaced [16]. One of the most common types of nutrient deficiency anemia is due to Iron deficiency in the body [17]. Hematopoiesis requires an adequate amount of iron, folic acid, and vitamin B12. Vitamin deficiency anemia includes Folate and vitamin B-12 which are required for enough healthy red blood cell synthesis. But in the case of pernicious anemia, vitamin B-12 absorption remains the issue [10–13]. Megaloblastic anemia is caused by Folic acid deficiency which is widely distributed in green leafy vegetables [18]. Anemia of inflammation can occur due to acute or chronic inflammatory diseases. Aplastic anemia, leukemia can be life-threatening. Hemolytic anemia can be inherited or due to certain blood diseases which increase red blood cell destruction. Sickle cell anemia is caused by a defective form of hemoglobin resulting in abnormal crescent (sickle) shaped red blood cells which die prematurely, consequential to chronic deficiency of these cells [19, 20].

Risk Factors of Anemia: These are the factors that increase the risk of anemia including a diet lacking in Copper, iron, vitamin B12, and folate, certain Intestinal disorders which can affect the absorption of nutrients in the small intestine, reproductive age group females having menstrual loss, pregnancy which enhances requirement of folic acid and iron, chronic conditions which can cause a shortage or can deplete store of iron from body, causing IDA, age over 65years, autoimmune disorders, certain infectious blood diseases exposure to toxic chemicals and alcoholism, Family history is also significant, such as sickle cell anemia.

Iron deficiency anemia: It is the most common form of anemia globally [21] and is caused by iron deficiency in the body. There are four forms of proteins containing iron but more than half of total-body iron is contained within hemoglobin, the most abundant iron-containing protein. Iron requirement for erythropoiesis is generated by

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changes in oxygenation of tissues, red blood cell turnover, and blood loss. Bone marrow needs iron for hemoglobin synthesis and if sufficient iron is not available then red blood cells cannot have enough hemoglobin. Many pregnant women get affected if not provided with the iron supplementation required to fulfill the increased iron demand during pregnancy. Heavy menstrual bleeding or blood loss due to gastric or small intestinal ulcer or large intestine cancer and extensive consumption of pain-killers especially aspirin likely to cause stomach lining inflammation resulting in blood loss[22].

Signs and symptoms of Iron Deficiency Anemia: It includes fatigue, low physical and mental capacity, headache, vertigo, leg cramps, pagophagia, cold intolerance, koilonychias, mucosal paleness, angular stomatitis[23]. In cases of IDA due to blood loss, the signs or symptoms experienced may be due to the disease-causing blood loss[24]**.** Simple Iron deficiency (ID) can lead to anemia, and immune system problems, and in certain cases can cause a neurological problem like depression. A patient with IDA can show signs and symptoms of behavioral and mood disorders like depression[25].

Common Causes of Iron Deficiency Anemia include: Physiological Anemia can be seen in premature babies, during phases of rapid growth, and during pregnancy. Anemia can be due to Poor intake in situations like Malnutrition, pseudo-bulbar palsy, chronic illness, and poor socioeconomic status. Malabsorption in certain diseases, and in certain disease-causing blood loss[22, 26, 27]. IDA is caused by either blood loss or iron malabsorption. The major cause of bleeding in males and postmenopausal women is gastrointestinal tract lesions[28]. Some dietary practices, such as calcium intake, phytates (found in cereals), and tannins (found in tea and coffee) may induce lower iron absorption due to their inhibitory effect on iron absorption. Helicobacter pylori infection (competition for iron, higher pH, and lower vitamin C), gluten-induced enteropathy in celiac disease, increased pH due to atrophic gastritis, and inflammatory bowel illness are all associated with surgical methods and reduced iron absorption. Hookworm infections, schistosomiasis, and menstruation can cause physiologic and chronic blood loss. Drugs including salicylates, nonsteroidal anti-inflammatory drugs, anticoagulants, and corticosteroids can cause drug-induced blood loss by irritating the stomach mucosa directly or raising the risk of bleeding from other causes. Relative or functional IDA occurs when iron is seldom transferred from storage to circulation [29]. Iron-refractory Hepcidin levels rise and intestinal iron absorption falls in IDA, a rare recessive disorder[30-32].

Iron Deficiency Anemia Risk Factors: Adults 65 years and older, women of reproductive age who are menstruating, and youngsters during their rapid development phase (12-15 yr in boys; 10-13 yr in girls), Lactation and pregnancy Low-wage workers, Underweight, You can get IDA if you don't get enough iron or vitamin C in your diet.[33-35].

Iron deficiency anemia in Reproductive age group females: IDA is one of the key public health issues for low, middle, and high-level countries affecting all age groups inclusive of reproductive age group women[36]. One-third of the world's population is affected by anemia and half the cases are due to iron deficiency. Reproductive age group females, pregnant females, and children under five years of age are particularly at risk[37]. In the developing countries not fulfilled Iron demand increases in pregnancy affects 52% of pregnant females. As a result, babies born with poorer iron stores are more prone to develop iron deficiency anemia subsequently. In premature babies, early stop of breastfeeding also results in a reduction of iron stores and increases the risk for IDA. Poor dietary habits, diets with decreased iron consumption, and growing age heavy blood loss all are causes and risk factors for IDA. It ends up in decreased tissues Oxygen supply develops pallor look, tiredness, weakness, breathing difficulty, lethargy, apathy, headaches, tinnitus, palpitation, and hair loss. In Chronic iron deficiency cases, decreases tolerance to work, efficiency, and the quality of life increasing socio-economic difficulties and more chances to contract infections due to Dysfunction in the immune system. Even cardiac failure can develop in a more severe degree of anemia. IDA during pregnancy may result in "premature labor, intrauterine growth retardation, low birth weight, birth asphyxia, and neonatal anemia"[26]. So Maternal anemia can have effects (short-term and long-term) leading to infantile iron deficiency and compromised physical and cognitive development of the child. Reproductive age group females' having IDA ends up into a significant dual burden on the likely economic expansion and population welfare. Near term, the strength for taking care of the child, household preservation, relaxation time activities, and the labor itself decreases due to fatigue. Longer-term implications include causation of permanent decline in child's cognitive ability and socio-emotional execution having impacts on their creative competence throughout the life[38-40].

Treatment of iron deficiency anemia: Reproductive age group IDA is one of the major Public Health issues in developing countries. Iron stores of reproductive age group women get affected by factors like age, parity, socioeconomic status, and diet ending up in anemia and other adverse outcomes preventable through appropriate cost-effective timely interventions through an integrated

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approach [12, 42]. Diagnosis, effectual treatment through the use of medicines prevention through fortification of food, iron supplementation, and most important with lifestyle management are of grave significance. Although prevalent use for nearly a decade of intravenous iron formulations replenishes the iron stores safely and effectively, recommended first-line treatment of IDA is oral iron. So for preparations with varying iron content that fails due to oral iron intolerance, gastrointestinal side effects, excessive blood losses, or malabsorption of iron, then parenteral iron is recommended which can be given in the form of iron sucrose, iron dextran, and iron gluconate. Management through blood transfusion is also an option if not treated by oral preparations or parenteral iron [40-45, 24]. Microcytic anemia, on the other hand, is characterized by refractoriness to oral iron and a sluggish and partial response to intravenous iron infusions [31]. Children 6–23 months (10–12.5 mg elemental iron daily – drops/syrups, three consecutive months in a year), 24–59 months (30 mg elemental iron daily – drops/syrups/tablets, three consecutive months in a year), 5–12 years (30–60 mg elemental iron daily – tablets/capsules, three consecutive months in a year), 24–59 months (30 mg elemental iron daily – tablets/capsules, three consecutive months Iron supplementation for babies and children in malaria-endemic areas should be done in conjunction with public health interventions to prevent, diagnose, and treat malaria. Iron supplementation with 30–60 mg elemental iron daily tablets for three consecutive months in a year is also recommended by the WHO for menstruation adult women and teenage girls (non-pregnant females in the reproductive age range). Because medicines have negative effects, we should focus on eating, which includes both plant and animal-based meals. Geographic distribution, population, food pattern, diet categories, and study findings [46].

Dietary iron: It exists in heme found in hemoglobin or myoglobin of meat and non-heme form legumes, corn, wheat, barley animal-source foods, iron-fortified foods (bread, rice, pasta, and iron-fortified breakfast cereals), cooked spinach, eggs, and dairy products, nuts, seeds, prune juice, dried beans and peas, and dry fruits. These two forms of iron have different absorption and bioavailability. Heme iron has an absorption of 20%–30% and better bioavailability. Non-heme iron is the most copious in the diet and has absorption at a rate of less than 10%. Ascorbic acid and foods with a substantial content of heme iron maximize this absorption but certain Nutraceuticals like phytates, calcium, and polyphenols inhibit it [47]. Good nutrition during pregnancy can also prevent IDA by meeting the increased physiological demands. To improve the plant sources and supplements iron absorption orange juice, tomato juice, or strawberries high in vitamin C should be consumed, iron supplements Intake with orange juice is recommended but avoid the calcium-fortified variety should as it decreases iron absorption although calcium is an essential nutrient during pregnancy [48].

Lifestyle modification: Life style is equally important as obesity; anemia and diabetes mellitus like chronic diseases are associated with a sedentary lifestyle. An effective strategy for decreasing the magnitude of anemia is through food fortification [49]. The main focus should be lifestyle modifications and the use of herbs instead of medicines [50]. Ascorbic acid enhances iron absorption while calcium, phytates, cereals, and tannins consumption originating from tea and coffee inhibits iron absorption and should be considered when supplying iron-rich meals [51]. Ginger is also found effective [52,53]. The risk of iron oversupply should also be considered through adequate and appropriate iron administration [54-56]. A holistic approach is required as in spite of all the efforts made during the last decade to reduce Anemia, especially in women and children still it remains a public health problem globally. Reduce health interventions should be targeted at pregnant females for reducing anemia prevalence. Children and especially female children should be included in these interventions. Various measures to be taken to cure anemia includes health education regarding nutritious intake, de-worming, iron-rich foods intake, and supplements during pregnancy and breastfeeding, and adolescents' weekly usage of iron-folic supplements. These services provision along with fortified foods, screening, and treatment of non-nutritional causes of anemia especially in concern with Improving women's education and empowerment for making improved dietary choices not only for themselves and also for their families [57]. Anemia among reproductive age females can be reduced using a norms-based intervention project The Reduction in Anemia through Normative Innovations (RANI). Descriptive norms refer to people's perceptions about the prevalence of behavior – what they believe others are doing – and injunctive norms refer to pressures people feel to conform [58]. *Prevention* demands that all screening should be done for IDA amongst pregnant females and should be provided with iron supplementation except with genetic conditions like hemochromatosis. So, the strategy to manage should emphasize on prevention with a conservative approach in non-active bleeding cases and through transfusion in actively bleeding cases. Case-specific treatment plan should be opted before considering the therapy from the options available, oral iron and parenteral, blood transfusion, and recombinant

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human erythropoietin (rHuEPO). Severe anemia during pregnancy can be prevented through iron and another nutritional supplementation[59, 60].

CONCLUSION

Low levels of essential precursors such as iron and folate cause anemia in pregnancy instead of chronic blood loss or hemolysis, the fundamental approaches to IDA prevention are dietary changes and diversification to enhance the intake of iron and supplementation with medical therapy. Food combinations should be planned that have synergistic effects with iron complexes to enhance their absorption and bioavailability. However, the price and social taboos especially regarding the safety of the food can affect the iron-fortified foods' acceptability which is possible through education and awareness campaigns. For dealing with iron deficiency and IDA, food fortification through novel food processing methods can result in the materialization of novel approaches. The main focus should be lifestyle modifications and the use of herbs instead of medicines. To control IDA in reproductive age group females, a multifaceted approach is required targeting food insecurity along with iron supplementation and food fortification.

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