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Anemia during Pregnancy and Its Prevalence

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Abstract

Anemia is a serious health issue throughout the world affecting both sexes of any age group. This nutritional disease is more common among the pregnant women of developing countries, where it is a major cause of maternal death and negative outcome of pregnancy. Among all anemic types, IDA is most prevalent one and is comprises of about 95% of all anemic cases around the world. In many developing countries it is more common in women of low socio-economic background and with no record of antenatal checkup. There is need for further health educational programs to overcome anemia especially for pregnant females.

Keywords: iron deficiency anemia, pregnancy outcomes, iron supplements

1. Introduction

Anemia is a common nutritional deficiency condition in which the number of healthy red blood cells (the cells which can carry adequate oxygen to all tissues of the body) or the level of hemoglobin within the red blood cells is less than that of normal. Hemoglobin is required to transport oxygen and if a person does not have a normal number of healthy red blood cells, or does not have sufficient hemoglobin then there will be a decreased competence of the blood to take oxygen to all tissues of the body. Some of the ordinary and frequent causes of anemia include nutritional deficiencies including the deficiencies of vitamins and minerals, particularly deficiency of iron, folic acid deficiency, and deficiency of cobalamin or vitamins B12 [1].

Globally Anemia is a deceptive health issue that is especially affecting youngsters and women during pregnancy. World health organization has estimated that about 42% of children with an age less than 5 years and 40% of the women during the 2nd and 3rd trimester of their pregnancy are anemic all over the world. The rate of iron deficiency anemia in pregnant women is very high because of the high demands of iron and blood during pregnancy [2].

It is a worldwide occurring universal problem with more than 2000 million people around the globe of different ages [3]. And it is more customary in pregnant women of economically developed nations and affects both the mother's and fetus's

health [4]. Globally its prevalence is 35% for women who are not pregnant and 51% for women who are pregnant and 3–4 times higher in developed nations [5].

2. Types of anemia

2.1 Iron-deficiency anemia

In case of iron deficiency anemia, the blood lacks an adequate number of normal red blood cells for carrying oxygen to the body tissues. Iron is one of the most plentiful elements on the surface of the earth. It participates in redox reactions which are crucial for numerous elementary organic processes such as cellular respiration and digestion. Therefore, it is not startling that iron contributes an important role in nearly all animal's lives. In *Homo sapien* iron is assimilated into proteins as an important constituent of heme (e.g., globin's, proteins, oxidases, and synthetases). These iron-containing proteins are essential for carrying out vital cellular and organismal functions including oxygen transport, mitochondrial respiration, nucleic acid replication and repair, host defense, and cell signaling. About 4 grams of iron is present in an adult human body. More than 75% of total body iron is correlated with hemoglobin, which is accountable for transporting oxygen (**Figure 1**). Deficiency of iron in the body decreases the production of the iron-containing heme group, which is a prosthetic group of hemoglobin protein that in turn limits the production of hemoglobin and decreases the synthesis of red blood cells (RBCs) from stem cells in the bone marrow which results in anemic conditions [6].

Pregnancy is one of the major reasons for iron-deficiency anemia because during the 2nd and 3rd trimester of pregnancy the iron demands of the body increase incredibly. The other major causes of iron deficiency anemia are heavy menstrual periods, pregnancy, bleeding from the gut, bleeding from the kidney, lack of certain

Figure 1.
Hemoglobin in RBC'S carrying oxygen from lungs.

vitamins, and problems with bone marrow [7]. Apathy, inactiveness, feeling feeble, faded and weak, panting, becoming exhausted and puffed easily, asymmetrical and disorderly heartbeats, fatigue and weariness, taste disturbances, smarting mouth are some common symptoms of iron-deficiency anemia.

Besides this, anemia during pregnancy can increase the risk of premature delivery and premature babies suffering from other health issues including low birth weight and neural tube defects to death. In developing countries, this premature birth is one of the main causes of death of an infant before his or her first birthday and this risk can be reduced by taking iron supplements during pregnancy [8].

2.1.1 Treatment

Due to the astounding effect of iodine deficiency anemia on maternal and fetal wellbeing, iron treatment is emphatically suggested. The adequacy of iron enhancement for the treatment of iron insufficiency is recorded by clinical preliminaries including pregnant ladies. The utilization of liposomal iron may address a promising technique of oral iron treatment in pregnant ladies with IDA. This compound shows high gastrointestinal retention and bioavailability and a low rate of results. Hence, liposomal iron presents great bearableness and favors preferable consistency over iron salts [9].

During pregnancy, a continuous elective treatment to oral iron, when it is not demonstrated, is IV iron. The new details of IV iron treatment advance a higher, just as quicker, increment of Hb focus and SF levels than oral iron supplementation, as was at that point appeared in changed studies in contrast with oral iron, ICM ensures a faster rectification of frailty and an apparent improvement of value existence with a slower pace of side effects like weariness and sorrow. It likewise presents higher bearableness and, thusly, more noteworthy consistency than oral iron. As the carb moiety ties the essential iron all the more firmly, high dosages of FCM (around 1000 mg in a solitary organization with a short implantation time) are permitted, in this way ensuring an improvement in consistency and a decrease of expenses because of rehashed organizations [10].

2.2 Pernicious anemia

Pernicious Anemia is an autoimmune disorder that affects the gastric mucosa of the stomach causing the lower and inadequate absorption of dietary Cobalamin or vitamin B12. It is essential for the proper functioning and forming of red blood cells. Vitamin B12 is also essential for the proper and normal functioning of the central nervous system and peripheral nervous system. The food or products which are enrich with protein such as beef, mutton, chicken, pork, fish, (dried fish, tilapia, halibut, tuna, salmon, carps, and shrimps), cereal, milk, yogurt, cheese, egg white, and other dairy products are major sources of vitamin B12 [11].

Vitamin B12 is separated from the proteins in the stomach through the action of hydrochloric acid. After this separation, vitamin B12 become incorporated with a protein called intrinsic factor in parietal cells of the stomach and is absorbed through villi which is present on the inner wall of the small intestine through which it is either computed into the blood circulation for the formation of red blood cells or stored in the liver (**Figure 2**). In the stomach, the parietal cell synthesizes intrinsic factor (IF) and secretes it, as well as hydrochloric acid into the gastric cavity of the stomach. The inability of parietal cells to secrete the intrinsic factor leads to failure of efficient vitamin B12 absorption into the blood. This inability is due to autoimmune antibody-mediated devastation of parietal cells of the gastric lumen which critically reduces the amount of intrinsic factor secreted in the

Figure 2.
Metabolic pathway for vitamin B12 absorption.

stomach. The antibodies attack and block the active site on intrinsic factors where vitamin B12 binds. This blockage of IF and inhibition of vitamin B12 binding will inhibit the formation of intrinsic factor-vitamin B12 complex. Without the formation of this complex, blood circulation cannot take up vitamin B12 and this will lead to the decrease in the level of red blood cells because vitamin B12 is an essential component in the synthesis of RBC'S. These blocking antibodies have been found in blood-serum or gastrointestinal fluid of 90% of patients suffering from pernicious anemia [12].

The major causes of pernicious Anemia are either the deficiency of vitamin B12 in diet or the inability of the stomach to absorb vitamin B12 from the diet. Vitamin B12 is also stored in the body. This stored vitamin B12 can last for years. When this is eventually depleted, pernicious anemia begins to develop. The amount of vitamin B12 required to fulfill the demands of a body depends on age [13]. The most serious outcome of B12 deficiency is diminished development and function of neurological processes throughout the lifecycle. Low maternal plasma vitamin B12 may result in pregnancies affected by anencephaly that is a type of neural tube defect (NTDs) [14].

Hypotonic muscles, failure to thrive, cerebral atrophy, and developmental regression are general outcomes of deficiency of vitamin B12. Folic acid supplemented pregnant women with negative B12 balance have increased risk for adverse maternal and infant outcomes (e.g., increased cardiometabolic disease risk) while pregnant women with Low B12 and a normal-to-high range of folate have high insulin resistance and adiposity in the offspring at 5 years of age [15].

2.2.1 Treatment

Folate lack is promptly treated with oral folic acid substitution. Folic acid supplementation (≥ 0.4 mg) is prescribed for multi-month before origination

and for the initial 12 weeks of pregnancy as this has been appeared to lessen the danger of fetal neural cylinder defects. High portion (5 mg) folate is suggested for ladies at high danger of neural cylinder surrenders (for example past pregnancy with a neural cylinder deformity) or in danger of malabsorption. To medicate B₁₂ deficiency usually proton pump inhibitor, histamine H₂-receptor antagonists and metformin used [16].

2.3 Hemolytic anemia

Hemolytic anemia is the destruction of red blood cells (RBCs) before their normal 120-day life span. The process of destruction of red blood cells is called hemolysis. There are three types of hemolysis:

i. Intravascular hemolysis

When the RBCs are destroyed in the blood vessel itself, it is called intravascular hemolysis. Intravascular hemolysis is very dramatic because free hemoglobin is released into the plasma leading to hemoglobinuria. In the case of intravascular hemolysis, certain enzymes such as glucose-6-phosphate dehydrogenase (G6PD) or immune-mediated enzymes can be defective.

ii. Extravascular hemolysis

Extravascular hemolysis usually occurs due to more subtle RBC destruction, typically with chronic splenic enlargement and jaundice. In Extravascular hemolysis, RBC membrane disorders such as hereditary spherocytosis can also occur [17].

iii. Antibody-mediated hemolysis

Antibodies are the proteins that are synthesized by the immune system. These proteins normally attach to the surface of any foreign invaders such as bacteria and viruses and destroy them. In the case of antibody-mediated hemolysis, the body makes antibodies against its red blood cells. These antibodies target red blood cells and kill them before completion of their life cycle (**Figure 3**). It depends on the duration and the rate of hemolysis, whether the anemia may or may not occur. If the degree of hemolysis is moderate and the erythropoietic response of the bone marrow is completely compensating for the decreased RBC lifespan, then the hemoglobin concentration may remain normal. If the erythropoietic response is not sufficient to completely compensate for decreased RBCs lifespan, then anemia will occur [18].

Anemia has multi-factorial etiology in pregnancy. There is a rare chance of maternal complication due to Pregnancy-induced hemolytic anemia that occurs during pregnancy and resolves later on delivery. The absence of any identifiable immune mechanism or intracorpuseular or extracorpuseular defects despite the use of specific and sensitive complement-fixation techniques and an assay of all red blood cell (RBC) enzymes are the characteristics of this problem. It is necessary to rule out other causes of non-immune hemolytic anemia including broad etiologies such as congenital, mechanical, toxic agents, medications, infection, lymphoproliferative disorder, etc. to embark on the diagnosis of idiopathic hemolytic anemia. A rare entity called Coomb's negative hemolytic anemia of pregnancy may be life-threatening, and for an optimum maternal-fetal outcome it desires a tireless diagnostic and appropriate treatment approach [19].

Figure 3.
Antibody-mediated hemolysis of red blood cells.

2.3.1 Treatment

They are challenging to treat, given distinct treatments. The basic treatment for TTP and complement-mediated HUS is the exchange of plasma. Delivery is the basic treatment for other pregnancy-related thrombotic microangiopathies (HELLP and preeclampsia) that occur during the third trimester [20].

2.4 Aplastic anemia

Aplastic anemia (AA) is a non-cancerous disorder in which the stem cells in the bone marrow (the cells responsible for making all mature blood cells) are attacked and destroyed by the patient's immune system. Aplastic Anemia can be mild or severe; it can develop suddenly at very early stages of life or slowly at later stages of life [21].

If the parents have defective genes which are constructing antibodies against their stem cells, then this disorder can be inherited into the offspring through parents. The other causes of this disorder can be the usage of some medicines and certain toxins in the environment. An individual who has a record of certain infectious diseases, such as AIDS, HIV, hepatitis, viral diseases, Epstein-Barr, or having a record of consuming several medicines, such as antibiotics and anticonvulsants can also develop aplastic anemia. Subjection to certain toxins and heavy metals such as cadmium, mercury, lead, and thallium can cause aplastic anemia. Exposure to radiation and a history of having an autoimmune disorder, such as lupus are some other major causes of aplastic anemia [22].

Aplastic anemia is a rare disease that occurs due to the destruction of pluripotent stem cells in the bone marrow. Significant factors including extremely low platelet counts, low bone marrow cellularity, and late disease presentation result in severe Aplastic anemia during pregnancy [23]. In pregnancies with Aplastic anemia, Low

hemoglobin concentration and platelet counts may be the primary risk factors for obstetric complications. Premature labor, gestational diabetes, pre-eclampsia, acute heart failure, postpartum hemorrhage, and severe postpartum infection are the major maternal complications [24].

2.4.1 Treatment

The principle of aplastic anemia treatment is to know about the cause and treatment of cytopenias and minimize the side effects of therapy for mother and fetus. Abortion is also preferred in case of severe pancytopenia. It is also treated by the transplantation of hemopoietic stem cells and by using immunosuppressive regimens. Hemopoietic stem cell transplantation (HSCT) is done after the delivery and it may lead to reduced fertility so the patient is asked before the treatment [25].

Antithymocyte globulin (ATG) is also used for the treatment. ATG is a safe medication but it may cause allergic reactions, vein irritation, nausea, vomiting, and diarrhea. It does not cause any drug toxicity but in pregnant women, it may cause low birth weight. Corticosteroids are also used for aplastic anemia treatment. As they cannot cross the placenta so it reduces fetal brain exposure but it also may lead to glucose intolerance, gestational diabetes, and premature rupture of membranes.

Transfusion of blood products is the basic treatment for aplastic anemia. It also causes some complications such as hemochromatosis and HLA alloimmunization. Alloantibodies may cause platelet-transfusion refractoriness (PTR). They are challenging to treat, given distinct treatments. The basic treatment for TTP and complement-mediated HUS is the exchange of plasma. Delivery is the basic treatment for other pregnancy-related thrombotic microangiopathies (HELLP and preeclampsia) that occur during the third trimester.

2.5 Sickle-cell anemia

In normal conditions, the body produces red blood cells which are round and flexible and can flow easily through the blood vessels. But in the case of sickle cell anemia, the body forms sickle-shaped or C-shaped red blood cells which become rigid, sticky and these irregularly sickle-shaped cells become stuck in small blood vessels, which can slow down or inhibit the flow of blood and supply of oxygen to all parts of the body (**Figure 4**). The average life of every red blood cell is 120 days which means that after 120 days red blood cells are replaced with new ones in the circulation. But in the case of sickle cell anemia red blood cells usually die within 10 to 20 days, causing a red blood cell deficiency that leads to Anemia and cannot supply oxygen properly throughout the body [26].

Pregnancy and sickle cell disease have reciprocal impacts on each other and it's a risky situation. The risk of infection becomes significantly higher during pregnancy in sickle cell anemia. The risk of low birth weight increases by 4 times than in the general population in homozygous sickle cell disease. The presence or conjunction of several risk factors including chronic fetal distress, vasculorenal syndrome, acute vaso occlusive crisis, or pelvic dystocia due to bone lesions of the pelvis explains the high cesarean rate in sickle cell women [27].

In the postpartum period, nearly half of women with sickle cell disease experienced a vasoocclusive crisis. Actually, it's a period at high risk of decompensation of sickle cell disease that combines maternal fatigue, intense pain in the absence of epidural analgesia, fasting with dehydration, a state of metabolic acidosis linked to uterine muscle work, and respiratory alkalosis. All of these factors result in a vaso occlusive accident [28].

Figure 4.
Formation of sickle-shaped RBC'S blocking the blood vessels.

2.5.1 Treatment

Enough perinatal care should be given during pregnancy. During severe symptoms, pregnant women should be hospitalized. For pain relief narcotics analgesic and paracetamol should be given. To treat acute chest pain antibiotics, oxygen support, hydration, analgesics should be given. If required blood transfusion should also be done so the risk of stroke and the coronary syndrome is reduced [29].

3. Global prevalence of anemia

Anemia is a universal problem with billions of people around the globe, and it is more common in pregnant women. According to WHO, during pregnancy, less than 110 g/l of Hb level in blood is a sign of anemia and it became severe if Hb level is <70 g/l.

4. Effect on young ones and effect on mother

Anemia is a serious and most common nutritional disorder, the main population who is suffering from anemia are children under 5 years, mostly in the first 24 months of their age. Worldwide 47.4% of patients suffering from anemia are children. Anemia leads to the impairment of physical growth as well as cognitive and motor growth. The consequences of anemia, even if it is treated in later childhood are irreversible. Hence, it is important to recognize and treat anemia, frequently among the young ones because they are more susceptible to it [30]. Anemia also causes a decrease in the performance of school-going children, work productivity in adulthood, personal satisfaction of a person [12].

Anemic children have lower blood concentration than normal and have less motor and cognitive development which affects the output rate of work in adulthood [31]. In developing countries, the frequency of anemia in children of age 5 is 39% and in children from 5 to 9 age the frequency is 48%. The reason for low hemoglobin Hb level in the children are, lack of awareness among the mothers, nutrition and harmful eating habits and other parasitic infections are the factors leading to anemia [32].

In developing countries, anemia is the major cause of maternal death and negative outcomes of pregnancy. There are major nutritional deficiencies (vitamin B12 deficiency, folic acid, or riboflavin deficiency) in developing countries that lead to anemia and other chronic infections, malaria which is a serious parasitic infection, and hemoglobinopathies. Women experience anemia during their maternal periods which increases the risk of low birth weight of the newborn, premature birth of the children, before and after birth mortality of the newborn [33].

Despite the presence of symptoms, patients with Iron deficiency-anemia should be treated as early as possible because they are in danger of organ ischemia, and if not treated further worsening anemia until the fundamental reason for the disease is not revealed and refill the bone marrow with iron [34]. Similarly, children with iron deficiency-anemia alone should be treated because it may lead to sideropenia in children is related to neurocognitive disabilities, affect their learning abilities and capacity, impaired motor function as well. Most frequently, people with anemia may also get Febrile seizures, breath-holding spells, and a restless leg syndrome shown much more in anemic people [22].

During childhood, anemia may be involved in the growth delay of the children such as height, they are more vulnerable to infections, their poor cognitive growth such as mental development and growth from childhood to adulthood, poor motor development which results in low work productivity in the future [35]. Normally 500–800 mg of blood is consumed from a mother during the pregnancy. In pre-menopausal women mostly have less iron stored or iron deficiency ID in them, they may get anemia or are without anemia, they are mostly belonging to less developed areas of the world. Maternal iron deficiency has a huge complex impact on a child. One report stated that the woman was diagnosed with schistosomiasis when she was pregnant, maternal iron deficiency appears in a child at an age of six months. Iron deficiency in the mother results in the abnormal cognitive development of a child [36]. When severe iron deficiency occurs in the mother, placenta hypertrophy occurs and the risk of the premature birth of the child increases. Maternal iron deficiency also causes low-weight birth of the child and death of the newborn. Sometimes in the first trimester, iron deficiency anemia is related to the low birth weight of the child but the development of anemia later is not involved. Maternal anemia or iron deficiency may occur due to less parental care or eating unhealthy food, which may cause similar effects [37].

The newborn may create paleness because of low iron stores in the body [38]. During pregnancy, anemia can cause serious complications maternal as well as in newborn childlike unexpected labor and post-pregnancy anxiety. Anemic mothers, particularly during the early trimester of pregnancy, can be considered as a danger factor for pregnancy results [23].

Iron deficiency in infants leads to serious and major behavior problems. There are uncertain effects of micronutrient deficiency in the middle of childhood. Vitamin B12 deficiency leads to psychological symptoms such as depression, loss of memory, major nervous problems, and structural changes in some parts of the brain that are important in the development of a child in solving behavioral problems that are basal ganglia, hippocampus, the amygdala. Severe anemic conditions may result in brain damage or nerve damage may occur [39].

Anemia with sickle cell disorder is the most common inherited disease, it results in an increased risk of complications and mortality rate. Sickle cell anemia affects pregnancy and increases maternal and perinatal complexities and early labor pain. The most common sign are pale skin, tiredness, vision changes, hand, and feet swelling, and include some bacterial infections [29]. Maternal anemia directly increases perinatal mortality, low weight of the child at the time of birth, stillbirth, and abortion [40]. In pregnancy, anemia lessens the chances of tolerance to blood loss, which results in heart failure or other abnormal functions of the body [41].

5. Preventive measures

In pregnancy, anemia is a major health problem especially in developing countries and it is also a common nutritional deficiency disease globally, approximately affecting two-fifths of pregnant women worldwide. During pregnancy, if anemia becomes severe it can lead to maternal and paternal harmful effects like preterm labor, low birth weight, and intrauterine fetal death. One of the leading causes is maternal mortality due to anemia. In order to prevent anemia during pregnancy preventive measures are required [42].

Multifactorial and nutritional deficiencies of iron, folate, and vitamin B₁₂ are the leading causes of anemia in developing countries. Moreover, malaria and intestinal parasitic infections also contribute to anemia in pregnancy. The causes which contribute to anemia in pregnant women vary greatly by geographical location, season, and dietary practice. Iron deficiency anemia (IDA) is the most common type of anemia all around the world. According to the study, 75% of cases of anemia are due to iron deficiency [43]. Iron deficiency anemia (IDA), often coexists with a deficiency in other important micronutrients, that make it more harmful for fetal growth [44].

5.1 Supplements

Iron intake and folic acid supplements are the keystones for the prevention of anemia in pregnancy. In earlier times these are the initial preventive measures suggested to the women in pregnancy to avoid anemia. The normal level of folic acid in approximately 25% of pregnant women is not sufficient to avert megaloblastic changes in the bone marrow. In developing countries, women in pregnancy should receive 40 mg daily supplementation of folic acid. 100 mg iron and 350 µg folate are present in fefol, women in pregnancy can take this supplement as standard oral preparation for prevention of anemia.

Due to physiological changes in pregnancy iron intakes are several times higher than in nonpregnant women [42]. To maximize iron intake and absorption all women should be given dietary information in pregnancy. 100-200 mg elemental iron should be suggested to women with iron deficiency anemia (IDA) [45].

The amount of iron in the diet, its bioavailability, and physiological requirements in pregnancy are some of the factors that contribute to iron absorption. Pregnant women should eat well-balanced meals that are rich in iron. Heme iron and non-heme iron are the 2 types of iron that are present in our meal or food.

5.2 Dietary advice

Animal flesh like red meat, poultry, and seafood contain dietary heme iron. Non-heme iron absorption is two to three-fold less than that of the heme iron. The meat in which organic compounds like peptides are present promotes the

absorption of iron from non-heme iron sources which are less bioavailable. It is difficult to absorb non-heme iron than heme iron but still non-heme iron forms about 95% of dietary iron intake. Iron absorption from non-heme sources can significantly increase by the use of Ascorbic acid. By the fermentation and germination of cereals and legumes, we can increase the bioavailability of non-heme iron in pregnancy. This results in the decline of phytate content, a component of food that hampers iron absorption. The use of tea and coffee shortly after a meal or with the meal hinders iron absorption because of the presence of tannins. Therefore, Pregnant women should avoid it.

The bioavailability of non-heme iron is enhanced by germination and fermentation of cereals and legumes which results in a decrease in the phytate content, a food constituent that hinders iron absorption. Tannins in tea and coffee hinder iron absorption on consumption with or shortly after a meal [42].

5.3 Oral supplements

In pregnancy, once women are subjected to iron deficiency anemia (IDA), it is very difficult to correct iron deficiency anemia through dietary changes alone. Therefore, oral supplements are necessary to replenish iron deficiency. An effective, inexpensive, and safe way to ensure replenish of iron is oral iron [46]. The inefficiency of absorption of iron ferrous salts show only marginal differences between each other. Ferrous fumarate, ferrous sulphate, and ferrous gluconate are the available ferrous salts. Serum ferritin should be checked in women with known haemoglobinopathy. If the ferritin $<30 \mu\text{g/l}$ then women should offer therapeutic iron [45]. If it is possible women should avoid proton pump inhibitors because they decrease the production of gastric juice. Gastric juice helps with iron absorption by converting the ferric to ferrous salt. But in some cases, oral iron is not tolerated and patients may develop side effects like nausea, abdominal pain, and epigastric discomfort.

5.4 Intravenous iron source (IV)

So, in order to maintain hemoglobin concentration in pregnancy intravenous iron (IV), sources are now recommended. Sodium ferric gluconate (Ferrlecit), iron sucrose (Venofer), iron (III)-hydroxide dextran complex (Cosmofer), ferric carboxymaltose (Ferinject), and iron (III) isomaltoside 1000 (Monofer) are now available forms of IV [47]. In order to combat anemia in pregnancy nutritional education or awareness is the main objective [42].

5.5 Counseling in pregnancy

Proper counseling should be given to pregnant women as to how to take iron supplements correctly. In case of severe anemia, secondary care should be considered. 200 mg elemental iron daily should be starting dose in these types of cases [45]. Moreover, doctors should suggest family planning and control of birth spacing as a preventive measure for anemia [42].

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