



International Journal of Medical Sciences and Pharma Research

Open Access to Medical Science and Pharma Research

Copyright © 2025 The Author(s): This is an open-access article distributed under the terms of the CC BY-NC 4.0 which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited



Open Access

Review Article

Anemia in Pregnancy: Exploring Non-Iron Deficiency Causes

Emmanuel Ifeanyi Obeagu ^{1*}, S K Prajapati ², Sheo Datta Maurya ³¹ Department of Biomedical and Laboratory Science, Africa University, Zimbabwe² Professor & Head, Institute of Pharmacy, Bundelkhand University, Jhansi (U.P.), India³ Pharmacist, Health Unit, Sitarampur, Eastern Railway, Asansol, West Bengal, India-713359

Article Info:

Article History:

Received 17 October 2024
Reviewed 23 November 2024
Accepted 18 December 2024
Published 15 March 2025

Cite this article as:

Obeagu EI, Prajapati SK, Maurya SD, Anemia in Pregnancy: Exploring Non-Iron Deficiency Causes, International Journal of Medical Sciences & Pharma Research, 2025; 11(1):1-7
DOI:
<http://dx.doi.org/10.22270/ijmspr.v11i1.130>

*Address for Correspondence:

Emmanuel Ifeanyi Obeagu, Department of Biomedical and Laboratory Science, Africa University, Zimbabwe

Abstract

Anemia in pregnancy is a global health concern, with significant implications for maternal and fetal outcomes. While iron deficiency anemia (IDA) remains the most prevalent form, non-iron deficiency causes of anemia are increasingly recognized and require attention. These include vitamin deficiencies (folate and vitamin B12), hemoglobinopathies such as sickle cell disease and thalassemias, anemia of chronic disease, infectious diseases, and rare bone marrow disorders. These conditions differ in their etiology and management, underscoring the need for tailored diagnostic and therapeutic approaches. The consequences of non-iron deficiency anemia during pregnancy are profound, ranging from maternal fatigue and increased infection susceptibility to adverse pregnancy outcomes such as preterm birth, low birth weight, and developmental impairments in offspring. Misdiagnosis or delayed recognition of these forms of anemia often leads to suboptimal management and worsened health outcomes. A comprehensive understanding of the underlying causes is essential for improving maternal care and mitigating associated risks.

Keywords: anemia, pregnancy, non-iron deficiency, hemoglobinopathies, chronic disease anemia

Introduction

Anemia in pregnancy is a significant public health issue that affects millions of women worldwide, with profound implications for both maternal and fetal health. The World Health Organization (WHO) estimates that approximately 40% of pregnant women globally experience anemia, which is associated with increased risks of maternal mortality, preterm delivery, low birth weight, and long-term developmental challenges in children. While iron deficiency anemia (IDA) is the most common form, non-iron deficiency causes of anemia contribute substantially to the burden, often complicating diagnosis and management. These less recognized etiologies demand a comprehensive understanding to improve maternal and fetal outcomes.¹⁻² Anemia is defined by a reduction in hemoglobin concentration or red blood cell mass, resulting in insufficient oxygen delivery to tissues. During pregnancy, physiological changes such as plasma volume expansion further complicate the interpretation of hemoglobin levels. While IDA arises primarily due to inadequate dietary intake or increased iron requirements, other causes such as vitamin deficiencies, hemoglobinopathies, anemia of chronic disease, infections, and bone marrow disorders also contribute

to the anemia burden. Recognizing these non-iron deficiency etiologies is critical for accurate diagnosis and effective intervention.³ Vitamin deficiencies, particularly those involving folate and vitamin B12, are common contributors to non-iron deficiency anemia during pregnancy. These micronutrients are essential for DNA synthesis and red blood cell production. Their deficiency leads to megaloblastic anemia, which differs from the microcytic anemia typical of IDA. Hemoglobinopathies, including sickle cell disease and thalassemias, are another significant cause, particularly in regions with high genetic prevalence. These genetic disorders impair hemoglobin structure or production, resulting in chronic anemia and pregnancy complications.⁴⁻⁵

Anemia of chronic disease (ACD), another key contributor, arises in the context of underlying systemic conditions such as autoimmune diseases, chronic infections, and malignancies. ACD is characterized by impaired iron metabolism and reduced erythropoiesis, which make it distinct from IDA. Infectious diseases, including malaria and HIV, are major contributors in endemic regions, leading to anemia through mechanisms like hemolysis, chronic inflammation, and nutrient malabsorption. Furthermore, rare conditions

such as aplastic anemia or other bone marrow disorders can cause severe anemia in pregnancy, complicating care and necessitating specialized interventions.⁶⁻⁷ The clinical implications of non-iron deficiency anemia in pregnancy are far-reaching. These conditions can lead to maternal fatigue, compromised immunity, and increased susceptibility to infections, which pose direct threats to maternal health. For the fetus, anemia increases the risks of intrauterine growth restriction, preterm birth, and low birth weight. Despite these consequences, non-iron deficiency causes of anemia are often overlooked, particularly in resource-limited settings where iron supplementation is the default intervention for all anemic pregnant women. Misdiagnosis or inappropriate treatment can exacerbate health risks and undermine maternal and neonatal care.⁸⁻⁹

Causes of Non-Iron Deficiency Anemia in Pregnancy

While iron deficiency anemia (IDA) is the most common cause of anemia in pregnancy, non-iron deficiency causes are increasingly recognized as significant contributors to maternal and fetal health issues. These conditions include vitamin deficiencies, hemoglobinopathies, anemia of chronic disease, infections, and rare bone marrow disorders.

1. Vitamin Deficiencies

- **Folate Deficiency:** Folate is essential for the synthesis of DNA and the maturation of red blood cells. Pregnancy increases the body's folate requirements, and a deficiency can lead to megaloblastic anemia. Folate deficiency is most commonly seen in women with inadequate dietary intake or poor absorption due to conditions such as celiac disease or inflammatory bowel disease. This condition is further exacerbated in pregnant women with poor nutritional status or those taking medications that interfere with folate metabolism (e.g., anticonvulsants).¹⁰⁻¹¹
- **Vitamin B12 Deficiency:** Like folate, vitamin B12 plays a vital role in DNA synthesis and red blood cell production. A deficiency in vitamin B12 results in megaloblastic anemia, which presents with large, immature red blood cells. This deficiency is typically observed in individuals who follow vegetarian or vegan diets, as well as in women with malabsorption disorders or who have undergone gastrointestinal surgeries. Vitamin B12 deficiency during pregnancy can also lead to neurological complications for both the mother and fetus, including developmental delays and neurological impairments in the baby.¹²⁻¹³

2. Hemoglobinopathies

- **Sickle Cell Disease (SCD):** Sickle cell disease is a genetic condition in which abnormal hemoglobin (hemoglobin S) causes red blood cells to become rigid and sickle-shaped, leading to hemolysis and chronic anemia. Pregnant women with sickle cell disease are at increased risk for complications such as vaso-occlusive crises, preterm birth, and fetal

growth restriction. Anemia in sickle cell disease is a result of the ongoing hemolysis, and pregnancy-related changes, including increased blood volume, can further exacerbate this condition.¹⁴

- **Thalassemias:** Thalassemia is a group of inherited blood disorders characterized by reduced or absent production of one of the hemoglobin chains (alpha or beta), leading to microcytic anemia. Pregnant women with thalassemia may experience worsened anemia due to increased iron turnover and ineffective erythropoiesis. Thalassemia minor (trait) may not require treatment, but thalassemia major often necessitates blood transfusions to maintain hemoglobin levels and manage pregnancy-related complications such as preterm labor and poor fetal growth.¹⁵

3. Anemia of Chronic Disease (ACD)

Anemia of chronic disease is a type of anemia that arises as a secondary condition in response to chronic inflammation, infection, or systemic disease. In pregnancy, ACD may occur in women with autoimmune diseases (such as lupus or rheumatoid arthritis), chronic infections (such as tuberculosis or HIV), or malignancies. This form of anemia is characterized by impaired iron utilization and reduced red blood cell production, despite normal or elevated iron stores in the body. The underlying condition that causes the chronic inflammation impairs erythropoiesis, making ACD distinct from iron deficiency anemia.¹⁶

4. Infectious Diseases

- **Malaria:** Malaria is a significant cause of anemia in pregnancy, particularly in regions where it is endemic. The infection leads to the destruction of red blood cells by the malaria parasite, causing hemolytic anemia. Pregnant women are particularly vulnerable to malaria because of the physiological changes that occur during pregnancy, such as increased plasma volume and decreased immune function. Malaria can also increase the risk of pregnancy complications, including preterm birth, low birth weight, and stillbirth.¹⁷
- **HIV/AIDS:** HIV infection can contribute to anemia during pregnancy through multiple mechanisms, including direct effects on the bone marrow, opportunistic infections, and the side effects of antiretroviral therapy (ART). HIV-induced anemia can worsen as pregnancy progresses, further compromising maternal health and increasing the risk of complications like preterm labor and poor fetal growth.¹⁸
- **Parasitic Infections:** Other parasitic infections, such as hookworm and schistosomiasis, lead to anemia through chronic blood loss and nutrient malabsorption. These infections can exacerbate anemia in pregnant women, particularly in areas with inadequate sanitation and nutrition.

5. Bone Marrow Disorders

Rarely, pregnant women may develop bone marrow disorders such as aplastic anemia or myelodysplastic syndromes. Aplastic anemia is a condition in which the bone marrow fails to produce adequate numbers of red blood cells, white blood cells, and platelets, leading to pancytopenia. This condition can present as severe anemia in pregnancy, often with additional symptoms such as bleeding or infection. While aplastic anemia is a rare cause of pregnancy-related anemia, its impact can be life-threatening and requires immediate medical intervention.¹⁹

Clinical Implications

The clinical implications of non-iron deficiency anemia (NID-A) in pregnancy are vast, affecting both maternal and fetal health. While iron deficiency anemia is typically associated with fatigue, weakness, and increased risk of preterm birth and low birth weight, the effects of NID-A can be more varied and, in some cases, more severe. These anemias, which result from conditions such as vitamin deficiencies, hemoglobinopathies, chronic diseases, infections, and rare bone marrow disorders, can lead to unique complications that complicate both maternal well-being and pregnancy outcomes. The recognition and management of NID-A are essential for minimizing risks and improving health outcomes for both mothers and their infants.²⁰⁻²¹

1. Maternal Health Complications

NID-A can significantly impact maternal health, leading to symptoms such as fatigue, weakness, and shortness of breath, which may be more severe than what is seen with iron deficiency anemia. For example, folate and vitamin B12 deficiencies can lead to megaloblastic anemia, characterized by the production of large, ineffective red blood cells that impair oxygen delivery to tissues. In the case of hemoglobinopathies like sickle cell disease or thalassemia, ongoing hemolysis and ineffective erythropoiesis can result in chronic anemia, increasing the risk of infections, fatigue, and cardiovascular complications. Additionally, maternal anemia due to chronic disease can result in worsened immune function, increased susceptibility to infections, and poor wound healing, all of which increase the risk of complications during pregnancy, labor, and postpartum recovery.²² Pregnant women with NID-A may also experience greater difficulty in managing preexisting health conditions. For example, anemia of chronic disease, which is commonly seen in individuals with autoimmune disorders or infections such as HIV, can complicate the management of these conditions. Furthermore, NID-A increases the likelihood of hospitalizations during pregnancy, which further strains healthcare resources and increases the risk of adverse outcomes due to delays in treatment or mismanagement.²³

2. Fetal and Neonatal Outcomes

The implications of NID-A on fetal and neonatal health can be particularly severe. Pregnancy-related anemia,

regardless of its cause, can lead to intrauterine growth restriction (IUGR), preterm birth, and low birth weight (LBW). For instance, sickle cell disease and thalassemia, both forms of hemoglobinopathy, are associated with increased rates of miscarriage, preterm delivery, and perinatal mortality. The effects on fetal development can be profound, with potential for neurological impairment and long-term developmental delays in the child, especially when maternal folate and vitamin B12 deficiencies are present.²⁴ Non-iron deficiency anemias can also increase the likelihood of stillbirth, particularly in women with untreated or poorly controlled chronic conditions like HIV or systemic autoimmune diseases. Malaria, as a leading cause of NID-A in pregnancy in endemic regions, poses significant risks to both the mother and fetus, including maternal death, preterm labor, and fetal death. The fetal risks associated with NID-A are not only confined to the immediate neonatal period but may also influence long-term health outcomes, including neurodevelopmental delays and cognitive impairments.²⁵

3. Diagnostic and Treatment Challenges

One of the most significant clinical implications of NID-A in pregnancy is the challenge of diagnosis. Pregnant women are routinely screened for iron deficiency anemia, but non-iron deficiency anemias often go unrecognized or misdiagnosed, particularly in areas where access to specialized testing and care is limited. The overlap of symptoms between different types of anemia—such as fatigue and pallor—further complicates accurate diagnosis. For instance, the symptoms of vitamin B12 deficiency can mimic those of IDA, and without proper diagnostic testing, women may receive inappropriate treatment, such as iron supplementation, which is ineffective in these cases.²⁶ The management of NID-A during pregnancy requires a more personalized and multifaceted approach. While iron supplementation is effective in treating IDA, non-iron deficiency anemias require targeted treatments. Folate and vitamin B12 deficiencies can be treated with vitamin supplementation, whereas hemoglobinopathies like sickle cell disease and thalassemia require more specialized interventions, including blood transfusions or other supportive therapies. Anemia of chronic disease, often linked with autoimmune or infectious diseases, necessitates addressing the underlying condition, whether through immunosuppressive therapy or the treatment of infections like malaria or HIV. The complexity of these conditions underscores the importance of a multidisciplinary approach, involving obstetricians, hematologists, and other specialists, to optimize both maternal and fetal health outcomes.²⁷

4. Long-Term Health Implications

Beyond the immediate pregnancy outcomes, NID-A can have long-term health implications for both mothers and children. Women with chronic anemia due to underlying conditions may experience long-term cardiovascular strain, resulting in higher risks of hypertension and heart disease later in life. Moreover, untreated or poorly managed NID-A can exacerbate preexisting conditions, such as diabetes or

hypertension, complicating future pregnancies and increasing the risk of adverse outcomes in subsequent pregnancies.²⁸ For the child, the long-term consequences of maternal NID-A are equally concerning. Children born to mothers with untreated NID-A may experience developmental delays, cognitive impairments, and behavioral issues. This is particularly true for deficiencies in folate and vitamin B12, which are critical for fetal brain development. Long-term neurocognitive outcomes, including learning disabilities and lower IQ scores, have been observed in children born to mothers with vitamin B12 deficiency. Additionally, infants born to mothers with hemoglobinopathies may face a higher risk of inherited blood disorders, requiring ongoing medical care and monitoring throughout childhood.²⁹

Diagnostic Approaches

Accurate diagnosis of non-iron deficiency anemia (NID-A) in pregnancy is crucial for appropriate treatment and management. Given that anemia in pregnancy can result from various underlying causes—such as vitamin deficiencies, hemoglobinopathies, chronic diseases, infections, and rare bone marrow disorders—differentiating between these conditions is essential to avoid misdiagnosis and inappropriate treatment. Diagnostic approaches typically involve a combination of clinical assessment, laboratory tests, and sometimes specialized imaging or genetic testing, depending on the suspected underlying cause.

1. Initial Clinical Evaluation

The diagnosis of NID-A in pregnancy often begins with a detailed clinical history and physical examination. Key elements of the clinical history include dietary intake, medical history (such as chronic diseases, autoimmune disorders, or infections), family history of hematologic conditions (like sickle cell disease or thalassemia), and any recent surgeries or gastrointestinal conditions that might affect nutrient absorption. Pregnant women with NID-A may present with symptoms such as fatigue, pallor, weakness, dizziness, and shortness of breath, but these symptoms can overlap with those of iron deficiency anemia (IDA), making clinical suspicion a key factor in guiding further testing.³⁰ Physical examination may reveal signs of anemia, such as conjunctival pallor or tachycardia. In cases of more severe anemia, symptoms of heart failure or hypoxia might also be noted. In addition, certain conditions like sickle cell disease or thalassemia may present with distinctive physical findings, such as splenomegaly or jaundice, which can aid in diagnosing the underlying cause. The next step in diagnosis is laboratory testing, which will help identify the specific type of anemia.

2. Complete Blood Count (CBC) and Reticulocyte Count

The first line of laboratory testing for anemia is a complete blood count (CBC), which provides information on hemoglobin levels, red blood cell (RBC) count, hematocrit, and mean corpuscular volume (MCV). In cases of NID-A, the MCV can be particularly useful. For example, a low MCV (microcytic anemia) may

suggest thalassemia or iron deficiency, while a high MCV (macrocytic anemia) may indicate folate or vitamin B12 deficiency, or bone marrow disorders like aplastic anemia. The reticulocyte count, which reflects bone marrow response to anemia, can help differentiate between anemia caused by blood loss, hemolysis, or ineffective erythropoiesis, which is common in conditions like anemia of chronic disease (ACD).³¹ The CBC can also provide additional clues to the underlying cause. For example, in thalassemia, the RBC count is often normal or elevated, while in folate or vitamin B12 deficiency, the RBC count is typically low, and the cells are large and immature (megaloblastic anemia). In sickle cell disease or hereditary spherocytosis, the CBC may show an elevated reticulocyte count due to ongoing hemolysis. Therefore, while the CBC is a critical part of initial diagnostic workup, it often needs to be supplemented with more specific tests to identify the underlying cause of NID-A.

3. Iron Studies and Vitamin Testing

Although iron deficiency is a common cause of anemia in pregnancy, non-iron deficiency anemias require testing for other deficiencies. Vitamin B12 and folate levels are commonly measured to assess the possibility of megaloblastic anemia. In cases of suspected folate deficiency, serum folate levels are checked, whereas vitamin B12 deficiency is assessed through serum B12 levels or more specific tests such as homocysteine and methylmalonic acid levels, both of which are elevated in B12 deficiency. These vitamin levels can be influenced by dietary intake, malabsorption, or medications, making accurate interpretation of the results essential.³² In addition to vitamin levels, iron studies, including serum ferritin, transferrin saturation, and total iron-binding capacity (TIBC), may be performed to rule out iron deficiency anemia (IDA), which can sometimes overlap with NID-A. However, a normal or high ferritin level—often elevated in chronic disease or inflammation—may indicate anemia due to chronic disease rather than iron deficiency. In the case of anemia of chronic disease, a ferritin level greater than 100 ng/mL and a low transferrin saturation are commonly seen.

4. Hemoglobin Electrophoresis and Genetic Testing

In cases where a hemoglobinopathy like sickle cell disease or thalassemia is suspected, hemoglobin electrophoresis is the gold standard for diagnosis. This test separates the various types of hemoglobin in the blood, identifying abnormal forms such as hemoglobin S (in sickle cell disease) or hemoglobin A2 (in thalassemia). Genetic testing may be used to confirm the presence of specific mutations in the hemoglobin genes and to assess whether a woman is a carrier of a genetic disorder, particularly in regions where hemoglobinopathies are prevalent.³³ For thalassemia, additional genetic screening may be required to determine the specific type (alpha or beta thalassemia) and whether the woman is a carrier (thalassemia minor) or affected by the disease (thalassemia major). Similarly, in cases of sickle cell disease, genetic testing can identify whether the woman has sickle cell trait

(heterozygous) or sickle cell disease (homozygous). The identification of these hemoglobinopathies is crucial as it affects the management of pregnancy, including the prevention of complications like vaso-occlusive crises, preterm birth, and fetal growth restriction.

5. Bone Marrow Examination

In rare cases where a bone marrow disorder, such as aplastic anemia or myelodysplastic syndrome, is suspected, bone marrow examination may be necessary. This invasive test involves aspirating a sample from the bone marrow to assess the production of blood cells. Aplastic anemia results from a failure of the bone marrow to produce adequate blood cells, while myelodysplastic syndrome can show abnormal maturation of blood cells. This diagnostic tool is usually reserved for cases with unexplained severe anemia or when other causes of anemia have been excluded. Bone marrow examination can help determine if the anemia is due to marrow failure, hemolysis, or ineffective erythropoiesis.³⁴

6. Infectious Disease Screening

For pregnant women in areas where certain infections are prevalent, screening for malaria, HIV, and other parasitic infections may be crucial. For example, malaria rapid diagnostic tests or blood smears are used to detect *Plasmodium* species, the parasite responsible for malaria. Similarly, HIV testing should be performed to assess whether HIV-related anemia is contributing to the pregnancy complications. These tests are particularly important in endemic regions or in individuals who are at higher risk of these infections. Detection and treatment of underlying infections can significantly reduce the impact of NID-A on both maternal and fetal health.³⁵

Management Strategies

Effective management of non-iron deficiency anemia (NID-A) in pregnancy requires a tailored approach based on the underlying cause of the anemia. While iron supplementation is the cornerstone of treatment for iron deficiency anemia, NID-A demands more specific therapies that target the root cause of the condition, such as vitamin or mineral supplementation, disease-modifying treatments, or addressing any underlying infections or chronic illnesses. The goal of management is to restore normal hemoglobin levels, alleviate symptoms, prevent maternal and fetal complications, and improve overall pregnancy outcomes.³⁶

1. Vitamin and Mineral Supplementation

For pregnant women diagnosed with vitamin B12 or folate deficiency, the primary treatment approach involves supplementation with the deficient vitamin. Folate deficiency can be corrected with oral folic acid supplements, typically at a dose of 400-800 mcg per day, depending on the severity of the deficiency. In severe cases or when there is evidence of megaloblastic anemia, higher doses of folic acid may be needed. Folate supplementation not only helps improve maternal hematologic status but also plays a key role in preventing neural tube defects in the developing fetus.³¹

Vitamin B12 deficiency is commonly treated with parenteral (intramuscular) vitamin B12 injections, especially if the deficiency is severe or if absorption issues are suspected. Oral vitamin B12 supplementation may be considered for less severe cases or as maintenance after initial parenteral therapy. The standard dose of B12 therapy ranges from 1,000 mcg to 2,000 mcg daily, depending on the severity of deficiency. It's crucial to monitor serum levels of both vitamins throughout pregnancy to ensure that the supplementation is effective in restoring normal levels and preventing recurrence.

2. Management of Hemoglobinopathies

Pregnant women with hemoglobinopathies, such as sickle cell disease (SCD) or thalassemia, require specialized care to manage their anemia and prevent complications. For individuals with sickle cell disease, the treatment strategy focuses on pain management, preventing vaso-occlusive crises, and ensuring adequate hydration. Hydroxyurea, an FDA-approved drug for SCD, is generally avoided in pregnancy due to potential teratogenic effects, but it may be considered in extreme cases where the benefit outweighs the risk. Regular blood transfusions are sometimes used to manage severe anemia or to prevent crises, particularly in women with SCD who are at increased risk for complications during pregnancy.³² In thalassemia, management revolves around preventing iron overload, which can occur as a result of blood transfusions or increased iron absorption due to ineffective erythropoiesis. Chelation therapy may be necessary to remove excess iron from the body. Pregnancy management also involves regular monitoring of hemoglobin levels, assessing fetal growth, and counseling on the risks of complications such as intrauterine growth restriction (IUGR) or preterm birth. For both conditions, close multidisciplinary collaboration with hematologists and obstetricians is essential to manage anemia and reduce the risks of maternal and fetal morbidity.

3. Management of Chronic Diseases

Anemia of chronic disease (ACD), often associated with conditions such as chronic kidney disease, rheumatoid arthritis, or autoimmune disorders, requires addressing the underlying inflammatory or infectious process. In cases where chronic kidney disease is contributing to anemia, erythropoiesis-stimulating agents (ESAs) like erythropoietin may be used to stimulate red blood cell production. However, ESAs should be used cautiously in pregnancy and only when the benefit to the mother outweighs the potential risks to the fetus.³³ For women with autoimmune disorders or inflammatory conditions, the treatment of the underlying disease is critical. This may involve the use of immunosuppressive therapy or disease-modifying drugs, which should be carefully chosen to minimize risks during pregnancy. Corticosteroids are commonly used to control inflammation, but their use should be limited and closely monitored due to potential side effects such as hyperglycemia and fetal growth restriction. In some cases, biologic therapies may be used, depending on the

specific disease and its severity. Monitoring of inflammatory markers, such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), can provide insights into disease activity and help guide treatment decisions.

4. Infection Management

Infection-induced anemia, such as malaria or HIV-related anemia, requires prompt treatment with appropriate antimicrobial agents. Malaria is a major cause of anemia in pregnancy in many regions, particularly in sub-Saharan Africa. Pregnant women diagnosed with malaria should be treated with safe, pregnancy-approved antimalarial drugs, such as artemisinin-based combination therapies (ACTs), while ensuring that the treatment regimen does not harm the developing fetus. In some cases, blood transfusion may be necessary to manage severe anemia caused by malaria, especially when associated with acute illness.³⁴ For HIV-positive pregnant women with anemia, antiretroviral therapy (ART) plays a crucial role in managing both the underlying HIV infection and associated anemia. The use of ART can prevent HIV progression, reduce opportunistic infections, and improve overall maternal health. In cases of HIV-related anemia, managing the HIV infection can alleviate the anemia by improving bone marrow function. Blood transfusions may be needed if anemia becomes severe or symptomatic. Additionally, monitoring CD4 counts and viral loads throughout pregnancy ensures optimal management of both anemia and the HIV infection.

5. Blood Transfusions and Other Supportive Care

In cases of severe anemia where other management strategies are insufficient, blood transfusions may be necessary to improve oxygen delivery to the tissues and prevent maternal or fetal complications. Blood transfusions are typically reserved for women with significant anemia (hemoglobin levels below 7-8 g/dL) who are symptomatic or at risk of hemodynamic instability. The decision to transfuse should consider both maternal and fetal well-being, and transfusions should be matched for blood type to reduce the risk of transfusion reactions.³⁵ Supportive care may also involve maintaining proper hydration, optimizing nutrition, and monitoring fetal growth. In cases of severe anemia, close fetal monitoring is crucial to assess for signs of intrauterine growth restriction (IUGR), preterm labor, or fetal distress. Regular ultrasounds and non-stress tests can help track fetal well-being and guide management decisions.

6. Prevention and Education

Preventing non-iron deficiency anemia in pregnancy is key to improving maternal and fetal health outcomes. This involves early screening during prenatal care visits to identify at-risk women and initiate early interventions. Women who are at risk for vitamin B12, folate, or hemoglobinopathies should receive appropriate supplementation and counseling. Those with chronic conditions should be managed to reduce the risk of anemia exacerbation during pregnancy. Health education on proper nutrition, including the

consumption of folate-rich foods, vitamin B12, and adequate protein intake, can play a role in reducing the incidence of deficiencies.³⁶ Genetic counseling is also an essential component of care for women with a family history of hemoglobinopathies, helping them understand the risks of passing these conditions to their offspring. Additionally, screening for infections, such as malaria and HIV, in areas where these conditions are endemic can help identify at-risk individuals and prevent anemia-related complications. Regular monitoring of hematologic parameters throughout pregnancy is vital to detect any changes early and adjust treatment plans accordingly.

Conclusion

Non-iron deficiency anemia in pregnancy is a multifaceted condition with various underlying causes, including vitamin deficiencies, hemoglobinopathies, chronic diseases, and infections. Effective management of this condition is essential to prevent adverse maternal and fetal outcomes, such as preterm birth, intrauterine growth restriction, and maternal morbidity. A personalized approach to treatment is critical, involving the identification of the specific cause and the use of targeted therapies, such as vitamin supplementation, disease-modifying drugs, infection management, and, in some cases, blood transfusions. Timely and accurate diagnosis is crucial for effective intervention. Diagnostic strategies should be comprehensive, including detailed maternal history, laboratory tests, and possibly genetic screening for inherited hemoglobinopathies. Once the underlying cause is identified, management can be tailored to the individual's needs, ensuring optimal health for both mother and fetus.

Conflict of Interest: Author declares no potential conflict of interest with respect to the contents, authorship, and/or publication of this article.

Source of Support: Nil

Funding: The authors declared that this study has received no financial support.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data supporting in this paper are available in the cited references.

Ethics approval: Not applicable.

References

1. Owais A, Merritt C, Lee C, Bhutta ZA. Anemia among women of reproductive age: an overview of global burden, trends, determinants, and drivers of progress in low-and middle-income countries. *Nutrients*. 2021; 13(8):2745. <https://doi.org/10.3390/nu13082745> PMID:34444903 PMCID:PMC8401240
2. World Health Organization. Worldwide prevalence of anaemia 1993-2005: WHO global database on anaemia. 2008.
3. Agreen FC, Obeagu EI. Anaemia among pregnant women: A review of African pregnant teenagers. *Journal of Public Health and Nutrition*. 2023;6(1):138.

4. Obeagu EI, Obeagu GU, Chukwueze CM, Ikpenwa JN, Ramos GF. Evaluation of protein C, protein S and fibrinogen of pregnant women with malaria in Owerri metropolis. Madonna University journal of Medicine and Health Sciences. 2022; 2(2):1-9.
5. Means RT. Iron deficiency and iron deficiency anemia: implications and impact in pregnancy, fetal development, and early childhood parameters. *Nutrients*. 2020; 12(2):447. <https://doi.org/10.3390/nu12020447> PMID:32053933 PMCID:PMC7071168
6. Obeagu EI, Adepoju OJ, Okafor CJ, Obeagu GU, Ibekwe AM, Okpala PU, Agu CC. Assessment of Haematological Changes in Pregnant Women of Ido, Ondo State, Nigeria. *J Res Med Dent Sci*. 2021 Apr;9(4):145-8.
7. Obeagu EI, Obeagu GU. Neonatal Outcomes in Children Born to Mothers with Severe Malaria, HIV, and Transfusion History: A Review. *Elite Journal of Nursing and Health Science*. 2024; 2(3): 38-58
8. Sapehia D, Mahajan A, Srinivasan R, Kaur J. Pre-natal dietary imbalance of folic acid and vitamin B12 deficiency adversely impacts placental development and fetal growth. *Placenta*. 2023; 132:44-54. <https://doi.org/10.1016/j.placenta.2023.01.003> PMID:36657272
9. Obeagu EI, Obeagu GU. Sickle cell anaemia in pregnancy: a review. *International Research in Medical and Health Sciences*. 2023 Jun 10;6(2):10-3. <https://doi.org/10.22270/ijmspr.v10i2.103>
10. Obeagu EI, Obeagu GU. Hemolysis Challenges for Pregnant Women with Sickle Cell Anemia: A Review. *Elite Journal of Haematology*. 2024;2(3):67-80.
11. Obeagu EI, Ezimah AC, Obeagu GU. Erythropoietin in the anaemias of pregnancy: a review. *Int J Curr Res Chem Pharm Sci*. 2016;3(3):10-8. <https://doi.org/10.22270/ijmspr.v10i2.95>
12. Muñoz M, Peña-Rosas JP, Robinson S, Milman N, Holzgreve W, Breyman C, Goffinet F, Nizard J, Christory F, Samama CM, Hardy JF. Patient blood management in obstetrics: management of anaemia and haematonic deficiencies in pregnancy and in the post-partum period: NATA consensus statement. *Transfusion medicine*. 2018; 28(1):22-39. <https://doi.org/10.1111/tme.12443> PMID:28722245
13. Breyman C. Iron deficiency anemia in pregnancy. In *Seminars in hematology* 2015; 52(4):339-347. WB Saunders. <https://doi.org/10.1053/j.seminhematol.2015.07.003> PMID:26404445
14. Obeagu EI, Influence of Hemoglobin Variants on Vaso-Occlusive Phenomena in Sickle Cell Anemia: A Review, *International Journal of Medical Sciences and Pharma Research*. 2024;10(2):54-59 <https://doi.org/10.22270/ijmspr.v10i2.104>
15. Rashid S, Meier V, Patrick H. Review of Vitamin B12 deficiency in pregnancy: a diagnosis not to miss as veganism and vegetarianism become more prevalent. *European journal of haematology*. 2021; 106(4):450-455. <https://doi.org/10.1111/ejh.13571> PMID:33341967
16. Jagnade RS, Bharat R, Singh P. Association Between Systemically Healthy Chronic Periodontitis Pregnant Female Subjects and Anemia of Chronic Diseases: A Clinical Study. *Journal of Advanced Medical and Dental Sciences Research*. 2018;6(9):88-95.
17. Barrera-Reyes PK, Tejero ME. Genetic variation influencing hemoglobin levels and risk for anemia across populations. *Annals of the New York Academy of Sciences*. 2019; 1450(1):32-46. <https://doi.org/10.1111/nyas.14200> PMID:31385320
18. Guyatt GH, Oxman AD, Ali M, Willan A, McIlroy W, Patterson C. Laboratory diagnosis of iron-deficiency anemia: an overview. *Journal of general internal medicine*. 1992; 7:145-53. <https://doi.org/10.1007/BF02598003> PMID:1487761
19. Eweis M, Farid EZ, El-Malky N, Abdel-Rasheed M, Salem S, Shawky S. Prevalence and determinants of anemia during the third trimester of pregnancy. *Clinical Nutrition ESPEN*. 2021;44:194-199. <https://doi.org/10.1016/j.clnesp.2021.06.023> PMID:34330465
20. Babker AM, Di Elnaïm EO, Hematological changes during all trimesters in normal pregnancy, *Journal of Drug Delivery and Therapeutics*. 2020;10(2):1-4 <https://doi.org/10.22270/jddt.v10i2.3958>
21. Siteti MC, Namasaka SD, Ariya OP, Injete SD, Wanyonyi WA. Anaemia in pregnancy: Prevalence and possible risk factors in Kakamega County, Kenya. *Science journal of public health*. 2014;2(3):216-222. <https://doi.org/10.11648/j.sjph.20140203.23>
22. Kumar SB, Arnipalli SR, Mehta P, Carrau S, Ziouzenkova O. Iron deficiency anemia: efficacy and limitations of nutritional and comprehensive mitigation strategies. *Nutrients*. 2022; 14(14):2976. <https://doi.org/10.3390/nu14142976> PMID:35889932 PMCID:PMC9315959
23. Pai RD, Chong YS, Clemente-Chua LR, Irwinda R, Huynh TN, Wibowo N, Gamilla MC, Mahdy ZA. Prevention and management of iron deficiency/iron-deficiency anemia in women: an Asian expert consensus. *Nutrients*. 2023; 15(14):3125. <https://doi.org/10.3390/nu15143125> PMID:37513543 PMCID:PMC10383547
24. Muñoz M, Peña-Rosas JP, Robinson S, Milman N, Holzgreve W, Breyman C, Goffinet F, Nizard J, Christory F, Samama CM, Hardy JF. Patient blood management in obstetrics: management of anaemia and haematonic deficiencies in pregnancy and in the post-partum period: NATA consensus statement. *Transfusion medicine*. 2018;28(1):22-39. <https://doi.org/10.1111/tme.12443> PMID:28722245
25. Shi H, Chen L, Wang Y, Sun M, Guo Y, Ma S, Wang X, Jiang H, Wang X, Lu J, Ge L. Severity of anemia during pregnancy and adverse maternal and fetal outcomes. *JAMA network open*. 2022;5(2):e2147046-. <https://doi.org/10.1001/jamanetworkopen.2021.47046> PMID:35113162 PMCID:PMC8814908
26. World Health Organization. Guideline: daily iron and folic acid supplementation in pregnant women. World Health Organization; 2012.
27. Obeagu EI, Obeagu GU. Sickle cell anaemia in pregnancy: a review. *International Research in Medical and Health Sciences*. 2023 Jun 10;6(2):10-3. <https://doi.org/10.22270/ijmspr.v10i2.103>
28. Obeagu EI, Ubosi NI, Uzoma G. Antioxidant Supplementation in Pregnancy: Effects on Maternal and Infant Health. *Int. J. Adv. Multidiscip. Res*. 2023;10(11):60-70.
29. Obeagu EI, Ubosi NI, Uzoma G. Antioxidant Supplementation in Pregnancy: Effects on Maternal and Infant Health. *Int. J. Adv. Multidiscip. Res*. 2023;10(11):60-70.
30. Obeagu EI, Obeagu GU. Enhancing Maternal and Fetal Well-being: The Role of Antioxidants in Pregnancy. *Elite Journal of Medical Sciences*. 2024;2(4):76-87.
31. Obeagu EI, Obeagu GU. Antioxidant Supplementation and Prevention of Early Pregnancy Loss: A Narrative Review. *Int. J. Curr. Res. Chem. Pharm. Sci*. 2024;11(9):28-37. <https://doi.org/10.22270/ijmspr.v10i4.120>
32. Obeagu EI, Obeagu GU. Molar Pregnancy: Update of prevalence and risk factors. *Int. J. Curr. Res. Med. Sci*. 2023;9(7):25-8. <https://doi.org/10.19080/JGWH.2023.25.556169>
33. Obeagu EI, Obeagu GU. Hypoxia-induced Metabolic Changes in Pregnancy: Clinical Perspectives. *Elite Journal of Medicine*. 2024;2(8):50-9.
34. Obeagu EI, Obeagu GU. Hemolysis Challenges for Pregnant Women with Sickle Cell Anemia: A Review. *Elite Journal of Haematology*. 2024;2(3):67-80.
35. Obeagu EI, Obeagu GU, Ezeonwumelu JO. Safety and Efficacy of Blood Transfusions in Pregnant Women. *Elite Journal of Haematology*, 2024; 2 (3):.96-106.
36. Obeagu EI, Obeagu GU. Hypoxia in Pregnancy: Implications for Fetal Development. *Int. J. Curr. Res. Chem. Pharm. Sci*. 2024;11(7):39-50. <https://doi.org/10.22270/ijmspr.v10i4.123>