

Microcytic Anemia in Pregnancy: Causes and Clinical Management

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Abstract

Microcytic anemia is a common hematologic complication in pregnancy, primarily caused by iron deficiency due to increased maternal iron demands and, less frequently, by genetic hemoglobinopathies such as thalassemia. Characterized by a reduced mean corpuscular volume (MCV), microcytic anemia often manifests with symptoms like fatigue, pallor, and shortness of breath, which may be mistaken for typical pregnancy discomforts, leading to delayed diagnosis. Early identification and appropriate management of microcytic anemia are essential, as the condition is associated with adverse maternal and fetal outcomes, including preterm birth, low birth weight, and increased maternal morbidity. This review examines the etiological factors contributing to microcytic anemia in pregnancy, highlighting iron deficiency anemia (IDA) as the predominant cause. Other contributing factors, including anemia of chronic disease and, in rare cases, deficiencies in vitamin B6, are also discussed. Effective diagnosis relies on a combination of laboratory tests, including complete blood count (CBC), iron studies, and, in select cases, hemoglobin electrophoresis. These tests help distinguish between iron deficiency and other causes of microcytic anemia, allowing for precise and personalized treatment approaches.

Keywords: *Microcytic anemia, pregnancy, iron deficiency anemia, thalassemia, hypochromic anemia, maternal health, fetal outcomes, clinical management.*

Introduction

Microcytic anemia is a common and significant hematologic concern in pregnancy, often affecting maternal health and fetal outcomes. Characterized by a decreased mean corpuscular volume (MCV) below 80 fL, microcytic anemia frequently presents with hypochromia, indicating that red blood cells are both smaller than average and contain less hemoglobin. This condition can have a range of causes, from nutritional deficiencies to genetic hemoglobinopathies, and it often leads to symptoms such as fatigue, pallor, and shortness of breath. These symptoms can be challenging to distinguish from general pregnancy-related fatigue and discomfort, leading to the possibility

of undiagnosed or delayed treatment. Given the risks associated with untreated microcytic anemia, particularly in pregnant women, understanding its causes, consequences, and effective treatment strategies is crucial for optimal maternal and fetal health.¹ The primary cause of microcytic anemia in pregnant women is iron deficiency anemia (IDA), which arises from increased iron requirements during pregnancy to support fetal development, placental growth, and expanded maternal blood volume. Iron deficiency affects approximately 20–40% of pregnant women globally, making IDA a leading concern for maternal health in both developing and developed nations. Despite the increased access to prenatal care and iron supplementation guidelines in many

countries, a significant proportion of pregnant women continue to experience iron deficiency due to dietary limitations, gastrointestinal issues affecting iron absorption, or a history of chronic blood loss. Iron deficiency not only impacts the mother's health but also poses risks to the fetus, including increased likelihood of preterm birth, low birth weight, and cognitive or developmental delays in infancy.²

In addition to iron deficiency, other less common causes of microcytic anemia include hemoglobinopathies such as α -thalassemia and β -thalassemia. These inherited conditions, prevalent in certain regions including Southeast Asia, the Middle East, and parts of Africa, lead to abnormal hemoglobin production and typically require specific diagnostic and management approaches. Screening for thalassemia is especially important in areas with high prevalence, as carriers are often asymptomatic but can still pass the trait to their offspring. When undiagnosed or poorly managed, thalassemia during pregnancy can lead to severe maternal anemia and a higher risk of adverse outcomes, necessitating specialized care and genetic counseling.³ Anemia of chronic disease (ACD) is another potential contributor to microcytic anemia, though it is less commonly seen in pregnant women compared to iron deficiency or thalassemia. ACD is usually linked to chronic inflammatory conditions, which alter iron metabolism and result in sequestration of iron in macrophages, making it less available for erythropoiesis despite normal or elevated iron stores. While not as frequent in pregnancy, ACD may complicate the clinical picture when present, requiring healthcare providers to distinguish it from other forms of microcytic anemia to avoid unnecessary iron supplementation and target treatment toward the underlying inflammatory condition.⁴ The clinical implications of microcytic anemia in pregnancy are profound, affecting both the mother and fetus. Untreated or poorly managed microcytic anemia is associated with several adverse maternal outcomes, such as increased risk of preeclampsia, postpartum hemorrhage, and infection. Additionally, pregnant women with anemia are more likely to experience fatigue, decreased immune function, and poorer

overall health, potentially impacting their ability to carry out daily activities and care for their newborns. Fetal and neonatal risks include increased rates of preterm birth, low birth weight, and perinatal mortality, highlighting the importance of early detection and effective management of this condition.⁵

Causes of Microcytic Anemia in Pregnancy

The causes of microcytic anemia in pregnancy are diverse and can often be multifactorial, involving both nutritional deficiencies and genetic factors.

1. Iron Deficiency Anemia (IDA)

Iron deficiency anemia is the most prevalent cause of microcytic anemia in pregnancy, resulting from inadequate iron intake, increased physiological demands, or impaired iron absorption. During pregnancy, the body's iron requirements increase substantially to support fetal growth, increased maternal blood volume, and placental development. If dietary intake and iron stores cannot meet this increased demand, iron deficiency develops, leading to microcytic and hypochromic red blood cells. Risk factors include a diet low in iron-rich foods, frequent pregnancies with short intervals, gastrointestinal issues affecting iron absorption, and chronic blood loss (e.g., from gastrointestinal sources or heavy menstrual periods before pregnancy).⁶⁻⁷

2. Thalassemia

Thalassemia is a genetic disorder that affects hemoglobin synthesis, commonly causing microcytic anemia. Two main forms, α -thalassemia and β -thalassemia, are prevalent in certain regions, including the Mediterranean, Southeast Asia, the Middle East, and parts of Africa. In pregnancy, thalassemia can lead to severe anemia if both parents carry the trait and pass it to the fetus. Pregnant women with thalassemia trait may also experience microcytic anemia and may require specialized management to distinguish it from IDA, as traditional iron supplementation could be counterproductive or

unnecessary. Prenatal screening and genetic counseling are essential in areas with high prevalence to guide management for both the mother and potential offspring.⁸

3. Anemia of Chronic Disease (ACD)

Anemia of chronic disease is a type of anemia seen in individuals with long-standing inflammatory or chronic conditions, such as autoimmune disorders, chronic infections, or certain cancers. Though less common in pregnancy, ACD can contribute to microcytic anemia in pregnant women with underlying chronic conditions. ACD is characterized by the body's altered iron metabolism in response to inflammation, which leads to iron sequestration in macrophages and a decrease in serum iron availability for red blood cell production. Unlike IDA, ACD does not respond to iron supplementation and requires targeted treatment to manage the underlying chronic disease.⁹

4. Vitamin B6 Deficiency

While rare, vitamin B6 (pyridoxine) deficiency is another cause of microcytic anemia. Vitamin B6 is essential for hemoglobin synthesis, and a deficiency impairs the production of heme, a component of hemoglobin, leading to the formation of small, hypochromic red blood cells. Pregnant women with poor dietary intake or specific metabolic disorders may develop vitamin B6 deficiency. While uncommon, this cause of microcytic anemia should be considered in cases unresponsive to iron therapy, and supplementation with vitamin B6 may be required.¹⁰

5. Lead Poisoning

Lead poisoning, although rare in most populations, can also lead to microcytic anemia. Lead interferes with heme synthesis, resulting in anemia characterized by small, hypochromic red blood cells. Pregnant women with significant environmental exposure to lead through contaminated water, paint, or soil may be at risk. Lead poisoning should be considered as a

differential diagnosis in cases of microcytic anemia unresponsive to conventional therapies, especially in areas where lead exposure is a known issue.¹¹

6. Sideroblastic Anemia

Sideroblastic anemia, though uncommon, is a condition where the bone marrow produces ringed sideroblasts rather than healthy red blood cells due to a defect in mitochondrial iron processing. This can be congenital or acquired, though in pregnancy it is rare. In cases where sideroblastic anemia is suspected, specific testing and genetic counseling may be necessary to manage the condition and prevent complications.¹²

Clinical Presentation

The clinical presentation of microcytic anemia in pregnancy can vary in severity, often depending on the underlying cause, the degree of anemia, and individual patient factors. Symptoms may develop gradually, and since pregnancy itself can cause some fatigue and other similar symptoms, microcytic anemia is sometimes underdiagnosed until it becomes more severe.¹³

1. General Symptoms of Anemia

- **Fatigue and Weakness:** One of the most prominent symptoms, fatigue occurs due to decreased oxygen transport to tissues, leading to reduced energy levels.
- **Pallor:** Pale skin, especially noticeable in the face, palms, and conjunctiva of the eyes, is a common sign due to reduced hemoglobin levels.
- **Shortness of Breath:** Reduced oxygen-carrying capacity can lead to dyspnea, particularly during physical activity, as the body struggles to meet its oxygen demands.
- **Dizziness and Lightheadedness:** These symptoms may be due to insufficient oxygen supply to the brain, resulting in frequent feelings of dizziness or, in severe cases, fainting.¹⁴

2. Cardiovascular Symptoms

- **Palpitations:** The heart may beat faster to compensate for low oxygen levels, causing palpitations or a noticeable “pounding” heartbeat.
- **Exertional Chest Pain:** In more severe cases, the heart may be overburdened, leading to chest discomfort or pain with physical exertion.

3. Neurological Symptoms

- **Headaches:** Oxygen deficiency can lead to persistent or recurring headaches.
- **Difficulty Concentrating:** Cognitive function may be impacted, resulting in difficulty focusing or impaired memory, often compounded by pregnancy-related hormonal changes.

4. Specific Symptoms Related to Iron Deficiency Anemia

- **Pica:** A unique symptom of iron deficiency anemia, pica is the craving for non-nutritive substances such as ice, clay, or dirt, which can exacerbate iron deficiency if left unaddressed.
- **Restless Leg Syndrome:** Iron deficiency in pregnancy is also associated with restless leg syndrome, causing an uncomfortable urge to move the legs, particularly at night, which can affect sleep quality.

5. Signs Related to Thalassemia

- **Jaundice:** In some cases of thalassemia, hemolysis (the destruction of red blood cells) occurs, leading to mild jaundice. This may manifest as a yellowing of the skin and eyes.
- **Splenomegaly:** Enlargement of the spleen is sometimes seen in severe cases, as the spleen works harder to filter abnormal red blood cells, though this is less common in pregnancy.

6. Physical Examination Findings

- **Delayed Capillary Refill Time:** A slower capillary refill time in the nail beds may be observed as a sign of anemia.
- **Heart Murmur:** In severe anemia, a functional systolic murmur can sometimes be detected due to increased blood flow across the heart valves as a compensatory mechanism.
- **Angular Cheilitis and Glossitis:** Cracks at the corners of the mouth (angular cheilitis) and inflammation of the tongue (glossitis) are often seen in severe iron deficiency anemia cases.¹⁵

Diagnostic Approach

Diagnosis of microcytic anemia in pregnancy requires a comprehensive approach to differentiate between iron deficiency and other etiologies.

1. **Complete Blood Count (CBC) and Peripheral Blood Smear**
 - a. A CBC can identify low hemoglobin, hematocrit, and MCV levels. A peripheral blood smear may reveal hypochromic, microcytic red cells, especially in iron deficiency anemia.
2. **Iron Studies**
 - a. **Serum Ferritin:** A low ferritin level suggests depleted iron stores and is diagnostic for IDA.
 - b. **Serum Iron and Total Iron-Binding Capacity (TIBC):** Low serum iron with high TIBC is indicative of iron deficiency.
3. **Hemoglobin Electrophoresis**
 - a. Hemoglobin electrophoresis is essential for diagnosing thalassemia and other hemoglobinopathies, especially in high-prevalence populations.

4. Serum Inflammatory Markers

- a. Tests such as C-reactive protein (CRP) can be used to evaluate underlying chronic disease if anemia of chronic disease is suspected.¹⁶

Clinical Management

The clinical management of microcytic anemia in pregnancy is determined by the underlying cause of the anemia. Effective treatment requires an accurate diagnosis to address specific etiologies, optimize maternal and fetal health outcomes, and prevent complications. Here is an outline of clinical management strategies for the most common causes of microcytic anemia in pregnancy:

1. Iron Deficiency Anemia (IDA)

Iron Supplementation:

- **Oral Iron:** Oral iron supplementation is the first-line treatment for iron deficiency anemia in pregnancy, with ferrous sulfate being the most commonly prescribed form. The typical dosage is 60-120 mg of elemental iron daily. To improve absorption, iron should be taken on an empty stomach, with vitamin C-rich foods or supplements, and separately from calcium-containing foods or supplements.¹⁷
- **Intravenous Iron:** For women who cannot tolerate oral iron due to gastrointestinal side effects (e.g., nausea, constipation) or who fail to respond adequately, intravenous (IV) iron is recommended. IV iron is also indicated for women with severe anemia later in pregnancy when rapid correction is needed to prevent adverse outcomes.¹⁸

Dietary Modification:

- Emphasis on iron-rich foods, such as lean meats, fish, eggs, legumes, and leafy

greens, can support iron stores during pregnancy. Vitamin C-rich foods (e.g., citrus fruits, bell peppers) help enhance iron absorption.¹⁹

Monitoring:

- Follow-up hemoglobin and ferritin levels are important to assess treatment effectiveness and guide ongoing supplementation. Typically, hemoglobin levels should rise by at least 1-2 g/dL within four weeks of therapy initiation if treatment is effective.

2. Thalassemia

Genetic Counseling and Prenatal Screening:

- In areas with high prevalence, prenatal screening for thalassemia is recommended to assess the risk of transmission to the fetus. Genetic counseling is crucial for parents who are both carriers, as they have a risk of having a child with severe thalassemia major.

Avoidance of Unnecessary Iron Supplementation:

- Unlike iron deficiency anemia, thalassemia does not benefit from iron supplementation unless there is a confirmed concurrent iron deficiency. Regular iron studies can help determine if supplementation is needed, as excessive iron intake can be harmful in thalassemia patients, potentially causing iron overload.²⁰

Folate Supplementation:

- Women with thalassemia often benefit from folate supplementation, as folate is essential for red blood cell production. Folate requirements increase in pregnancy, and supplementation may support red blood cell health in women with thalassemia.

Transfusion and Monitoring in Severe Cases:

- In severe cases, such as thalassemia intermedia or major, blood transfusions may be required to maintain adequate hemoglobin levels. Women with severe thalassemia may require specialized monitoring by a hematologist and obstetrician experienced in managing high-risk pregnancies.

3. Anemia of Chronic Disease (ACD)**Management of Underlying Condition:**

The primary approach for anemia of chronic disease is treating the underlying inflammatory or chronic condition (e.g., autoimmune disorder, chronic infection). Successfully managing the underlying disease often improves anemia without the need for direct anemia-specific treatment.

Erythropoiesis-Stimulating Agents (ESAs):

In some cases, particularly where hemoglobin levels are significantly low and the underlying condition cannot be controlled, erythropoiesis-stimulating agents may be used. However, these are generally used cautiously in pregnancy and only when potential benefits outweigh risks.²¹

Avoidance of Iron Supplementation:

Iron supplementation is typically not effective in ACD, as the condition is driven by altered iron metabolism and iron sequestration rather than a true deficiency. Excess iron can exacerbate inflammation and should be avoided unless concurrent iron deficiency is confirmed.

4. Vitamin B6 Deficiency**Vitamin B6 Supplementation:**

If vitamin B6 deficiency is confirmed as the cause of microcytic anemia, pyridoxine supplements are administered. Typical doses range from 25-50 mg daily, which should help resolve symptoms and

improve red blood cell production in cases of pyridoxine-responsive anemia.

Dietary Sources:

Pregnant women should be encouraged to consume vitamin B6-rich foods such as poultry, fish, potatoes, bananas, and fortified cereals to support their nutritional needs.

5. Lead Poisoning**Removal from Exposure Source:**

If lead poisoning is identified as the cause of microcytic anemia, it is essential to remove the pregnant woman from the source of lead exposure. Sources could include contaminated water, soil, or workplace hazards. Public health agencies may need to be involved to ensure safe living conditions.

Chelation Therapy (If Severe):

In cases of significant lead poisoning with high blood lead levels, chelation therapy may be necessary. Chelation therapy during pregnancy, however, is approached cautiously and typically reserved for cases with severe toxicity.

6. Sideroblastic Anemia**Treatment of Underlying Causes:**

If sideroblastic anemia is due to a reversible cause, such as vitamin B6 deficiency, treating the deficiency can improve anemia. Other acquired forms may require more specialized hematological intervention.²²

Hematology Referral and Supportive Care:

Women with sideroblastic anemia may benefit from referral to a hematologist for specialized management. Blood transfusions may be needed in severe cases, especially if other treatments are ineffective.

Monitoring and Follow-up

All pregnant women with microcytic anemia require close follow-up, including regular CBCs and iron studies, to monitor treatment effectiveness and anemia progression. Optimal management also includes addressing nutritional needs, patient education on anemia prevention, and regular consultation with a multidisciplinary team when necessary, including obstetricians, hematologists, and nutritionists.²³

Risks and Complications

Microcytic anemia in pregnancy carries several risks and potential complications for both the mother and the fetus, emphasizing the need for timely diagnosis and management.

1. Maternal Risks

1.1 Increased Risk of Preterm Labor and Delivery:

Microcytic anemia, particularly when due to iron deficiency, has been linked to an elevated risk of preterm labor and premature delivery. Low hemoglobin levels reduce oxygen supply to the uterus, which can induce labor prematurely and result in infants born before 37 weeks of gestation.²⁴

1.2 Postpartum Hemorrhage:

Pregnant women with microcytic anemia have an increased risk of postpartum hemorrhage (PPH) due to the reduced ability of anemic blood to clot effectively. Severe anemia reduces platelet count and function, impairing coagulation and increasing the likelihood of heavy bleeding during and after delivery, which can be life-threatening if not managed promptly.

1.3 Fatigue and Decreased Physical Resilience:

Anemia can exacerbate pregnancy-induced fatigue, leading to diminished physical stamina, increased stress, and reduced quality of life. Fatigue can also interfere with a mother's ability

to care for her newborn postpartum, potentially impacting breastfeeding and bonding experiences.

1.4 Cardiac Stress and Complications:

Chronic anemia places additional strain on the heart as it works harder to deliver oxygen to tissues. Pregnant women with severe anemia may develop tachycardia (elevated heart rate), palpitations, and in extreme cases, heart failure, especially if they have pre-existing cardiovascular conditions.

2. Fetal Risks

2.1 Intrauterine Growth Restriction (IUGR):

Microcytic anemia impairs oxygen delivery to the fetus, which is essential for proper growth and development. Low maternal hemoglobin can lead to IUGR, where the fetus does not reach optimal size for gestational age, resulting in a low birth weight baby. IUGR is associated with long-term health risks, including developmental delays and chronic illnesses.²⁵

2.2 Low Birth Weight and Small for Gestational Age (SGA):

Fetuses born to mothers with microcytic anemia are more likely to have a low birth weight (<2500 grams) or be small for gestational age, both of which increase neonatal morbidity and mortality risks. Low birth weight infants often require special medical care, including time in a neonatal intensive care unit (NICU), and face greater risks of infections and respiratory issues.

2.3 Preterm Birth:

Anemia-related hypoxia can trigger the release of stress hormones that may stimulate labor, increasing the risk of preterm birth. Preterm infants are more vulnerable to various health challenges, including respiratory distress syndrome, sepsis, and feeding difficulties.

2.4 Neurodevelopmental Issues:

Iron plays a crucial role in fetal brain development. Maternal iron deficiency and subsequent fetal iron deficiency can disrupt neurodevelopment, increasing the risk of cognitive and motor impairments. These developmental delays may impact learning abilities, behavior, and overall quality of life.

3. Complications Related to Specific Causes of Microcytic Anemia

3.1 Iron Deficiency Anemia Complications:

Beyond the general complications of anemia, iron deficiency specifically increases risks of infection due to compromised immune function. Pregnant women with untreated iron deficiency anemia may have an elevated risk of postpartum depression and impaired physical recovery.

3.2 Thalassemia-Related Complications:

For women with thalassemia, pregnancy poses additional risks, especially in severe forms like thalassemia major. These patients may face transfusion-related complications, such as iron overload, which can lead to organ damage if not managed carefully. Thalassemia carriers also face a risk of passing the condition to their child, necessitating genetic counseling.

3.3 Lead Poisoning Complications:

If microcytic anemia results from lead exposure, there are unique complications to consider, as lead toxicity can harm both mother and fetus. Lead exposure has been linked to increased rates of miscarriage, stillbirth, and congenital anomalies, as well as developmental and behavioral issues in the child.

4. Impact on Postpartum Health and Future Pregnancies

4.1 Postpartum Anemia:

Women with untreated or inadequately treated microcytic anemia may experience persistent anemia postpartum, leading to prolonged recovery, increased fatigue, and challenges with infant care. This is particularly concerning for women who may wish to have subsequent pregnancies, as starting a new pregnancy with pre-existing anemia can compound health risks.

4.2 Risk of Complications in Future Pregnancies:

Microcytic anemia can recur in future pregnancies, especially if it stems from chronic causes such as thalassemia or recurrent iron deficiency. Women with a history of anemia in pregnancy are at a higher risk of experiencing the same condition in subsequent pregnancies, which may lead to cumulative maternal and fetal risks if not addressed early.

4.3 Maternal Mental Health and Well-Being:

The physical strain and complications associated with untreated microcytic anemia can also impact maternal mental health. Increased physical fatigue and stress, coupled with the demands of caring for a newborn, may lead to higher rates of postpartum depression and anxiety, which can affect overall family dynamics and mother-infant bonding.²⁶

Conclusion

Microcytic anemia in pregnancy is a multifactorial condition with significant implications for maternal and fetal health. Its most common causes—iron deficiency, thalassemia, anemia of chronic disease, vitamin B6 deficiency, and, rarely, lead poisoning—necessitate a nuanced diagnostic approach to ensure accurate identification and appropriate treatment. Untreated microcytic anemia poses substantial risks, including preterm birth, low birth weight, intrauterine growth restriction, and postpartum hemorrhage, all of which increase morbidity and potential mortality for both mother and child. Clinical management tailored to the underlying cause of microcytic anemia is essential for effective treatment. Iron deficiency is

generally managed with oral or intravenous iron supplementation, dietary counseling, and regular follow-up to monitor treatment response. For genetic conditions like thalassemia, genetic counseling and a multidisciplinary approach are crucial, particularly in severe cases. Addressing these causes early in pregnancy can mitigate risks, promote normal fetal development, and support maternal well-being.

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