



Abstract

Screening recommendations for anemia during pregnancy, etiologies of inherited and noninherited forms of anemia, their impact on maternal–fetal outcomes, and the clinical management of pregnant patients presenting with these conditions are reviewed. Anemia during pregnancy can cause adverse perinatal outcomes including preterm labor, premature rupture of membranes, and increased maternal and fetal mortality. Physiologic (dilutional) anemia and iron deficiency anemia are the two most common noninherited forms of anemia, and some cases may be the result of an underlying comorbidity such as diabetes or lupus. Aplastic anemia and autoimmune hemolytic anemia are uncommon forms of noninherited anemias that also merit discussion. Inherited forms of anemia include sickle cell disease, alpha-thalassemia, and beta-thalassemia. Timely diagnosis and treatment of anemia during pregnancy, whether inherited or noninherited, is imperative to protect mother and baby from potential adverse outcomes associated with these conditions.

Key words: Anemia; Iron deficiency; Pregnancy; Sickle cell anemia; Thalassemia.

ANEMIA IN PREGNANCY: SCREENING AND CLINICAL MANAGEMENT STRATEGIES

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According to the World Health Organization (WHO), approximately 40% of pregnancies worldwide are complicated by anemia (WHO, 2021). Data on anemia for pregnant women in the United States are limited. Adebisi and Strayhorn (2005) estimated a prevalence of 21.55 per 1,000 women when using a classification of hemoglobin concentration less than 10 grams per deciliter. Prevalence of anemia among pregnant women has steadily increased from 9.1% (2004) to 11.5% (2019; World Bank Group, 2021).

The oxygen carrying protein hemoglobin (Hgb) is vital to the sustenance of life and is a necessity for the pregnant patient. To manufacture the vital hemoglobin protein, the body must pull iron molecules from stores in the body. Maternal and fetal outcomes vary according to the mother's hemoglobin and trimester in which anemia is identified. Inherited anemias such as sickle cell disease and thalassemia inhibit normal production of the hemoglobin protein and may require complex clinical management. Noninherited anemias in pregnancy are most commonly classified as physiologic (dilutional) or iron deficiency anemia (IDA) but also include aplastic anemia and autoimmune hemolytic anemia. The purpose of this article is to provide a review of screening recommendations, causes of anemia, and clinical management of these conditions.

Screening Recommendations

The American College of Obstetricians and Gynecologists (ACOG, 2021a) recommends that all pregnant women be screened for anemia in their first trimester using a complete blood cell count (CBC). Based on result of initial screening, further testing may be needed to provide appropriate clinical management of subsequent conditions. A second screening should be conducted between 24 and 28 weeks of pregnancy (ACOG). The primary screening tests consist of serum hemoglobin concentration or hematocrit (ACOG). If IDA is ruled out, the clinician should explore other etiologies (ACOG). Table 1 reflects the diagnostic values of laboratory tests by trimester for anemia (ACOG).

A maternal hemoglobin level indicative of anemia requires additional testing for likely etiologies. Evaluation should include a clinical history as well as laboratory assessment of a CBC and red blood

cell (RBC) indices. An RBC and morphology can aid in categorization of anemia. Mean corpuscular volume (MCV) is the average volume measurement of erythrocytes. The MCV is often decreased in microcytic anemias such as iron deficiency or thalassemias and increased in macrocytic anemias caused by folate and vitamin B12 deficiency. Mean corpuscular hemoglobin is the hemoglobin concentration per RBC count, whereas the mean corpuscular hemoglobin concentration (MCHC) is the hematocrit divided by hemoglobin. These values will typically be decreased in microcytic anemias and increased in macrocytic anemia (Williamson et al., 2011). Ferritin is a protein that stores and releases iron, therefore, serum ferritin levels reflect amount of iron stored in the body for use in the production of hemoglobin. Serum ferritin is the recommended laboratory test to confirm iron deficiency in pregnancy due to the high sensitivity and high specificity of the test (Achebe & Gafer-Gvili, 2017). WHO (2011) recommends monitoring of ferritin concentration as a way of monitoring the impact of interventions on iron status. Iron deficiency is the only known etiology of low ferritin levels, thus highlighting the utility of this test (Auerbach & Landy, 2021). Typically, ferritin levels between 30 and 40 ng/mL are associated with chronic disease processes such as diabetes mellitus and systemic lupus erythematosus. If ferritin levels are borderline, iron studies including serum iron, total iron binding capacity, and transferrin saturation should be evaluated (Auerbach & Landy).

Noninherited Anemias

Physiologic Anemia

The most common form of anemia in pregnancy is physiologic (dilutional) anemia. Normal physiology of pregnancy creates a dilutional anemia secondary to the increased blood volume and increased RBC mass (Blackburn, 2021). Although RBC production increases during pregnancy, there is a decrease in both hemoglobin and hematocrit values during pregnancy because plasma volume increases faster and more than RBC mass (ACOG, 2021a; Blackburn, 2021; Horowitz et al., 2013). As an expected physiologic adaptation, during singleton pregnancy, maternal blood volume increases approximately 40% to 50%, whereas total RBC mass increases approximately 15% to 20% (ACOG). This blood volume expansion supports normal fetal growth and development and anticipated blood loss at birth (ACOG; Vricella, 2017). Despite being a part of normal pregnancy physiology, it's important to distinguish between physiologic anemia and other causes.

The two most common causes of anemia in pregnancy are iron deficiency and acute blood loss.



Iron Deficiency Anemia

In the United States, overall iron deficiency prevalence in pregnancy is near 18%, with anemia affecting 5% of pregnant women (Cantor et al., 2015). Iron deficiency during pregnancy is associated with low birthweight, preterm birth, perinatal mortality, and postpartum depressions (ACOG, 2021a). Hemoglobin levels less than six grams per deciliter (g/dL) have been associated with poor fetal outcomes, including death (ACOG).

Iron is a component of hemoglobin in RBCs and is necessary for the functioning of cellular mechanisms including DNA synthesis. On average, 20 to 25 mg of iron is needed daily for these processes (Lopez et al., 2016). There are two forms of dietary iron. Heme iron is found in animal foods such as meat, poultry, and seafood. Non-heme iron is found in plant and dairy foods and makes up the bulk of consumed iron. However, nonheme iron is not as readily absorbed as heme iron and requires acid digestion for bioavailability (Killip et al., 2007). Dietary intake averages 1 to 2 mg per day. As daily loss (via perspiration, urinary excretion, and other processes) equals the average daily dietary intake, the body relies upon iron stores and its iron-recycling mechanisms for homeostasis. Most of the iron needed for new hemoglobin synthesis comes from recycling of heme from the breakdown of old RBCs. This process is usually efficient, with only small losses, which are replenished by dietary intake. A peptide hormone, hepcidin, regulates iron homeostasis by binding with the iron-exporting protein, FPN1 (Lopez et al.). High expression of hepcidin causes increased binding of this protein and an inability to export iron from cells, low expression decreases this protein binding and increases plasma iron concentration (Lopez et al.). Hepcidin's expression is affected by tissue levels of iron (Lopez et al.).

Iron deficiency results when the body's demands for iron aren't met by dietary absorption. Camaschella (2015) defines IDA as "depressed levels of total body iron in the presence of anemia" (p. 1833). It is a hypochromic, microcytic anemia characterized by low hemoglobin and low MCV, low ferritin, low serum iron, and raised total iron-binding capacity. There are many risk factors that can lead to IDA. Physiologic, pathologic, chronic disease, environmental, genetic, and drug-related factors can all influence risk. Physiologic risk factors include conditions that consume iron stores or require an increased demand such as rapid growth in infancy or adolescence, pregnancy, heavy menstrual blood loss, elite athletes, or in persons who regularly donate blood (Camaschella). Pathologic causes include disorders, which lead to decreased absorption or chronic blood loss. Common

causes of iron malabsorption include the following conditions—celiac disease, gastrectomy, gastric bypass surgery, and *Helicobacter pylori* (Lopez et al., 2016). Other malabsorptive causes include inflammatory bowel diseases such as ulcerative colitis or Crohn's disease or pica syndrome (Camaschella). Nurses should be aware of chronic blood loss disorders that could also lead to IDA. Digestive tract disorders such as esophagitis, gastritis, peptic ulcers, diverticulitis, tumors, hemorrhoids, or parasitic infestation (especially in children) can all cause chronic blood loss. Other causes of chronic blood loss include heavy menses, hematuria, hemodialysis, or causes of intravascular hemolysis, that is, damaged heart valves, malaria. Chronic diseases such as chronic heart failure, cancer, kidney disease, obesity, and rheumatoid arthritis can also be risks for IDA. Environmental causes include poverty, malnutrition, or insufficient dietary intake of iron. Phylates found in cereals can inhibit iron absorption; however, ascorbic acid (Vitamin C) and muscle tissue improve absorption of iron (Lopez et al.). Many drugs can be factorial in IDA including nonsteroidal anti-inflammatory drugs, glucocorticoids and salicylates (increase blood loss risks), and proton-pump inhibitors (decrease iron absorption).

Iron deficiency anemia is never a final diagnosis; identifying and treating the cause is paramount to preventing further iron loss and worsening anemia. Awareness of risk factors and a thorough health history can help screen at-risk patients. WHO (2017) recommendations for the treatment of IDA include increasing iron intake by dietary food fortification and iron supplementation, controlling immunization and infection control for malaria and parasites (primarily hookworm), and improving nutritional B12, folate, and vitamin A deficiencies.

For the treatment of pregnant women with anemia, the United States Preventive Services Task Force (2015) reported that supplementation may improve maternal hematologic indices; however, evidence for routine screening and iron supplementation in prenatal care improving maternal or infant health outcomes is unclear (Cantor et al., 2015). ACOG (2021a) recommends screening all pregnant women for anemia and that all women diagnosed with IDA to be treated with supplemental iron. Daily iron supplementation is positively correlated with decreased risk of anemia at term gestation (Lopez et al., 2016). As a result, mothers who breastfeed are at decreased risk of iron deficiency compared with pregnant women due to iron concentration in breast milk (Lopez et al.). The iron concentration in mature breast milk is 0.20 to 0.80 mg/L, and most mothers who breastfeed are amenorrhoeic (Lopez et al.).

Given the worldwide prevalence, nurses will encounter this disorder in clinical practice. Nurses should be aware that IDA disproportionately affects those of low socioeconomic status and is associated with worse clinical outcomes and diminished quality of life. Burden of this disorder is difficult to discern because its ill effects on a body can be hidden under the surface of other morbidities and measurable statistics. A general understanding of the risk

TABLE 1. CLASSIFICATION OF ANEMIA

Trimester	Hgb	Hct
First	<11 g/dL	<33%
Second	<10.5 g/dL	<32%
Third	<11 g/dL	<33%

Note. Summary of content from ACOG (2021a).

TABLE 2. DAILY VITAMIN RECOMMENDATIONS DURING PREGNANCY

Vitamin/Mineral	Daily Recommendation	Best Sources
Calcium	Age 14–18: 1,300 mg Age 19–50: 1,000 mg	Milk, cheese, yogurt, sardines, dark green leafy vegetables
Iron	27 mg	Lean red meat, poultry, fish, dried beans and peas, iron-fortified cereals, prune juice
Iodine	220 mcg	Iodized table salt, dairy products, seafood, meat, some breads, eggs
Choline	450 mg	Milk, beef liver, eggs, peanuts, soy products
Vitamin A	Age 14–18: 750 mcg Age 19–50: 770 mcg	Carrots, green leafy vegetables, sweet potatoes
Vitamin C	Age 14–18: 80 mg Age 19–50: 85 mg	Citrus fruit, broccoli, tomatoes, strawberries
Vitamin D	600 international units	Sunlight, fortified milk, fatty fish such as salmon and sardines
Vitamin B6	1.9 mg	Beef, liver, pork, ham, whole-grain cereals, bananas
Vitamin B12	2.6 mcg	Meat, fish, poultry, milk (vegetarians should take a supplement)
Folic acid	600 mcg	Fortified cereal, enriched bread and pasta, peanuts, dark green leafy vegetables, orange juice, beans. Also, take a daily prenatal vitamin with 400 mcg of folic acid.

Note. Summary of content from ACOG (2021b).

factors and an awareness of clinical presentation, as well as screening and treatment recommendations for this modifiable disorder will help improve its recognition and result in better health outcomes. Expectant mothers who are at risk for IDA may be encouraged by their providers to increase the amount of iron in their daily diet. Table 2 reflects the recommended daily vitamin and mineral requirements during pregnancy. Incorporating both heme (meat products) and nonheme (fortified cereals and beans) forms of dietary iron may help restore iron levels. A typical diet includes 15 mg of elemental iron per day (ACOG, 2021a). The recommended dietary allowance of ferrous iron for a pregnant woman is 27 mg per day, and 9 mg per day for breastfeeding mothers (ACOG). Thereby, highlighting the importance of iron supplementation during pregnancy. There is inconsistency regarding recommendations for iron supplementation during pregnancy. Auerbach and Landy (2021) recommend an increase of 15 to 30 mg/day, the Centers for Disease Control and Prevention (2020a) recommend universal supplementation of 30 mg/day to meet pregnancy requirements, except in cases of certain genetic disorders; and ACOG (2021a) recommends low-dose supplementation starting in the first trimester for all pregnant women and iron supplementation in addition to prenatal vitamins for those with identified IDA. Iron supplements range from 34 to 106 mg of elemental iron per tablet (ACOG). A 325 mg tablet contains 65 to 106 mg of elemental iron (ACOG). Patients may be advised to take their iron supplementation with vitamin C to increase iron absorption, to avoid combining calcium supplements with iron supplements, and to add a stool softener to their daily regimen because iron supplements may be constipating, especially in pregnancy. Alternate day dosing can be considered for those patients who expe-

rience gastrointestinal adverse effects. Some evidence suggests this regimen improves absorption and tolerability. Supplemental iron should increase hemoglobin levels in approximately 2 weeks. As such, approximately 2 to 3 weeks after initiation of treatment, there should be an increase in hemoglobin of at least 1g/dL, an increase in reticulocytosis and an increase in ferritin into a normal range (Darwish et al., 2019). If lab values remain low, consider potential causes such as intolerance, reduced absorption, or nonadherence. Intravenous (IV) formulations are recommended for patients with severe anemias, malabsorption disease processes, that is, gluten sensitivity, inflammatory bowel disease, gastric bypass surgery, hyperemesis gravidarum, for those patients who are intolerant of oral supplementation, or there is insufficient time to replace iron orally (such as late third trimester) or those whose hemoglobin and/or ferritin levels do not increase with oral iron preparations (Achebe & Gafter-Gvili, 2017). Choice of IV therapy formulation is based on cost, convenience, and provider comfort levels. The three most common IV iron products are ferric gluconate, iron dextran, and iron sucrose. Intravenous iron should be administered in a monitored setting. Intravenous iron products are equally safe and efficient (Auerbach & Landy, 2021).

Aplastic Anemia and Autoimmune Hemolytic Anemia

Aplastic anemia (AA) and autoimmune hemolytic anemia (AIHA) are two uncommon causes of acquired anemia in pregnancy but present unique challenges in clinical management that warrant a brief discussion. The pathophysiology of AA in pregnancy is generally unknown, although there is speculation the disease process is triggered by hormonal changes in pregnancy creating an imbalance between erythropoietin and placental lactogen. Aplastic ane-

mia is diagnosed in pregnancy when testing indicates that pancytopenia is present in combination with hypocellular bone marrow (Townsend, 2013). Aplastic anemia has a very low incidence, averaging just 2 to 14 cases per million per year, mainly occurring most frequently in Asian populations compared with European ones (Schoettler & Nathan, 2018). In the pregnant patient, termination of the pregnancy is often recommended. In approximately one third of cases, aplasia resolves after termination or birth, but relapse may occur in subsequent pregnancies. Clinical management of AA in the pregnant patient includes Human Leukocyte Antigens (HLA)-matched platelet transfusions. After birth, a bone marrow transplant may be indicated if resolution of aplasia does not occur. However, bone marrow transplants are contraindicated during pregnancy due to adverse effects on the fetus (Aitchison et al., 1989).

Autoimmune hemolytic anemia occurs when the immune system targets and destroys its host's red cell antigens. Diagnostically, this presents first as anemia caused by hemolysis; normo- or macrocytic anemia with increased reticulocytes and increased bilirubin among other laboratory markers. Once hemolysis is confirmed, a direct antiglobulin test is performed to determine an autoimmune etiology (Allard & Hill, 2016). As autoimmune diseases are often exacerbated by stress or illness, it is thought that the presentation of AIHA during pregnancy may be due to the stress of gestation on the mother. Another possible cause is an incompatibility between circulating fetal erythrocytes and maternal erythrocytes, similar to the role Rh factor plays in maternal–fetal incompatibility and disease exacerbation. Treatment depends on the subtype of AIHA, but most standards of care begin with steroids as the first course of therapy. It is important to remember that during pregnancy, immunosuppressants may be contraindicated. Removal of the spleen is another therapeutic option, although generally this is not performed during pregnancy. In most cases, a resolution of the hemolytic anemia occurs after birth (Chaplin et al., 1973).

TABLE 3. ADVERSE MATERNAL AND FETAL OUTCOMES OF ANEMIA IN PREGNANCY

Maternal Outcomes	Fetal Outcomes
Abortion	Prematurity
Stillbirth	Low birthweight
Maternal death	Intrauterine growth restriction
Painful crisis	Stillbirth
Acute chest syndrome	Neonatal death
Severe anemia	5 Minute APGAR < 7
Jaundice	
Infections	
Preeclampsia	
Low transverse cesarean birth	

Note. Summary of content from Jain et al. (2019).

Inherited Anemias

Sickle Cell Disease

There are several inherited causes of anemia. “Sickle cell disease (SCD) is the most common inherited hemoglobinopathy with approximately 300,000 neonates born globally every year” (Jain et al., 2019, p. 1). Sickle cell disease is prevalent among those of African descent, Spanish-speaking regions in Central and South America, Saudi Arabia, India, and Mediterranean countries (American Society of Hematology, 2021; Centers for Disease Control and Prevention, 2020b).

Women with SCD experience significant challenges related to fertility, pregnancy, and perinatal outcomes. Nutritional status and sequelae play a significant role in physical and sexual development of patients with SCD (Jain et al., 2019). The onset of menarche is delayed in women with SCD and is strongly associated with the HbSS phenotype compared with the HbSC phenotype. Women with SCD have unique factors that may affect their ability to conceive, including chronic inflammation, oxidative stress, transfusion-related hemochromatosis, and ovarian sickling, causing ischemia and reperfusion injury to the ovaries (Jain et al.). Pregnancy complicated by SCD is associated with increased risk for adverse perinatal outcomes, such as abortion, stillbirth, preeclampsia, sepsis, and prematurity (Table 3; Jain et al.).

Early identification and intervention are important. The prenatal diagnosis may be confirmed by chorionic villus sampling at 10 to 12 weeks gestational age, amniocentesis at 14 to 15 weeks gestational age, or fetal blood sampling (via cordocentesis) at 18 to 19 weeks gestational age (Jain et al., 2019). Confirmation of SCD in pregnancy prompts a comprehensive history and physical exam to develop an individualized and effective plan of care. Pregnant women with SCD should be advised “to avoid precipitating factors of sickle cell crises such as exposure to extreme temperatures, dehydration, and overexertion” (Jain et al.). Management plans should be developed with consideration of six adverse events in pregnancy with SCD—painful crises, acute chest syndrome, pulmonary embolism, strokes, hematological complication, and infections (Jain et al.).

Thalassemias

Thalassemia is an inherited disorder of the blood that inhibits the normal production of hemoglobin. There are two primary types—alpha thalassemia and beta thalassemia. Over 9 million carriers of thalassemia, worldwide, become pregnant annually (Cao & Kan, 2013). In some parts of the world, there is a 40% chance their partners are carriers as well; thereby, increasing the probability of a more severe type of thalassemia to be present in infants (Galanello & Origa, 2010). Although rare, prevalence of thalassemia in the United States has increased by 7.5% over the past 50 years (Sayani & Kwiatkowski, 2015). Depending on severity of the anemia caused by the disease, treatment varies. According to Modell and Darlison (2008), there are approximately 56,000 cases of major thalassemia and 30,000 of those cases require routine blood transfusions.

Alpha Thalassemia

Alpha (α) thalassemia stems from the alpha chains located on chromosome 16. Normally, there are two alpha units per gene, yielding 4 alpha chains. Through gene mutation, they can be expressed as four types of α -thalassemias. The first type of thalassemia is known as the silent carrier, which has 3 functioning genes. Approximately 20% of the world population are carriers of α -thalassemia (Modell & Darlison, 2008). It is prevalent in Southeast Asia, Indonesia, the South Pacific Islands, the Middle East, and the Mediterranean (Chestnut et al., 2014). Women with this type of thalassemia are generally not affected clinically and this condition does not require any intervention during pregnancy. The second type is α -thalassemia trait, which has two functioning alpha subunits. These patients usually present with microcytic anemia and are diagnosed when the use of iron therapy is not effective. The health care provider should perform an alpha gene analysis to confirm presence of the α -thalassemia trait. No other intervention is required during pregnancy and should not affect these patients in the long term.

The third type is known as Hemoglobin H Disease (HbH), or α -thalassemia Intermedia, and has one functioning alpha subunit. This is the most severe, nonfatal form of α -thalassemia. These patients present with severe anemia, general discomfort, fatigue, and splenomegaly (Chestnut et al., 2014). Treatment regimens vary with this population based on their symptoms and whether they have a deletional or nondeletional form of HbH. HbH Constant Spring (HCS) is the most common form of nondeletional HbH in the United States and should be monitored closely. Patients with HCS should be treated aggressively when they present with high fevers as it can lead to severe hemolytic crisis. Complete blood cell counts should be drawn routinely to ensure that the hemoglobin remains within normal limits. If not, it may necessitate blood transfusions when hemoglobin values fall below 6 g/dL (Chonat & Quinn, 2017). Patients may require a splenectomy and monitoring for iron overload may be warranted for patients with HCS. Patients with deletional forms of HbH require more supportive care but may require folic acid therapy (Chui et al., 2003).

The fourth type of α -thalassemia is Hemoglobin Bart's Hydrop Fetalis Syndrome and is characterized by not having any functioning alpha subunits on chromosome 16. Patients with this type of thalassemia present with severe anemia, hepatosplenomegaly, and cardiovascular problems (Chestnut et al., 2014; Chui et al., 2003). This presentation very often results in newborn death immediately following birth (Chestnut et al.; Chui et al.). Significant counseling and education should be made available to the parents and family of infants diagnosed with Hemoglobin Bart's Syndrome.

Beta Thalassemia

In Beta (β) Thalassemia, the production of beta chains is diminished and there is only one beta chain on each gene on chromosome 11. This mutation yields three types of β -thalassemia. The first type, β -thalassemia Major or Cooley's Anemia, occurs when no beta chains are formed. The second type, β -thalassemia Minor, occurs when some production of beta chains exist. The third type, β Thalassemia Intermedia, occurs when beta chains may or may



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The American College of Obstetrics and Gynecology recommends screening all pregnant women for iron deficiency anemia at their first prenatal encounter.

not have been formed (Chestnut et al., 2014). β -thalassemia affects 1 in 100,000 people worldwide and 1 in 10,000 in European regions (Galanello & Origa, 2010). β -thalassemia is prevalent in India, Southeast Asia, the Mediterranean Basin, and the Middle East (De Dreuzy et al., 2016; Modell & Darlison, 2008). Modell and Darlison estimated 350 U.S. births per year compared with 41,000 worldwide of individuals who have β -thalassemia. Prevalence of thalassemia is unknown; however, it is thought to be on the rise with the increased number of people immigrating from affected regions across the world (Sayani & Kwiatkowski, 2015).

Patients with β -thalassemia Major generally present within the first few months of life with severe anemia, tissue hypoxia, skeletal abnormalities, increased iron absorption, jaundice, pallor, and hepatosplenomegaly (Galanello & Origa, 2010). They require iron chelation, surgery to remove the spleen, and frequent blood transfusions for sustainment of life (Chestnut et al., 2014; Galanello & Origa). It is difficult for women with β -thalassemia Major to carry a pregnancy to full term. However, if able, requirements for blood transfusion increase significantly. The goal is to maintain a hemoglobin level greater than 10 g/dL until birth (Chestnut et al.).

In contrast, β -thalassemia Minor requires little-to-no intervention and presents with mild anemia. Pregnancy may be affected by moderate anemia, but overall β -thalassemia Minor has little impact. β -thalassemia Intermedia is not as definitive as the major or minor forms of thalassemia (De Dreuzy et al., 2016). Diagnosis for this type of β -thalassemia is based on the clinical presentation

and the level of intervention required to sustain a normal quality of life. Periodic blood work to ascertain hemoglobin levels may be required to ensure these individuals are not progressing to the more severe β -thalassemia Major.

Thalassemia is a disorder that can be overlooked or misdiagnosed especially in the pregnancy due to the commonality of anemia in this population. In patients with intermedia or minor thalassemias, the health care provider should be hypervigilant in monitoring for subtle signs of cardiac/liver/endocrine dysfunction, as the signs for major thalassemias are more distinct and the aggressive therapy of blood transfusions are commonplace. According to Modell and Darlison (2008), there are approximately 56,000 cases of major thalassemia, and 30,000 of those cases require routine blood transfusions. At a minimum, it would be prudent to monitor for clinical symptoms of thalassemias, order CBCs routinely, and consider iron and folic acid therapy for minor and intermedia thalassemias. For the major thalassemias, chelation therapy and routine blood transfusions may be the norm for this population to sustain the life and the health of the fetus.

Patients with thalassemia should ideally be on a consistent folic acid and vitamin D regimen for at least 3 months prior to becoming pregnant and should speak with their doctor regarding the requirement of additional vaccinations, especially if asplenic. Patients should also be educated regarding changes to their current maintenance therapy. If the patient is receiving blood transfusions with iron chelation therapy, chelation therapy may be halted for the first 20 weeks of pregnancy, as the drugs used are not safe for the developing fetus. Thalassemia increases risk of gestational diabetes and intrauterine growth restriction. Mothers have an increased risk of postpartum deep vein thrombi and may be on anticoagulant therapy for the first 6 weeks postpartum. Education of the pregnant woman with thalassemia should include all of these points, as well as genetic counseling.

Clinical Implications

Much of the literature focuses heavily upon the most common causes of anemia in pregnancy, iron deficiency and physiologic. The United States is a cultural melting pot; thereby, reinforcing importance of nurses to understand other causes of anemias (inherited and acquired). Anemia during pregnancy has been associated with increased risks for adverse maternal–fetal outcomes include low birthweight and preterm birth. However, low socioeconomic factors may be confounding factors in these links. The goal of prenatal care is “to prevent poor perinatal outcomes and provide education to women throughout pregnancy, childbirth, and the postpartum period through a series of one-on-one encounters” between a woman and her obstetrical provider (ACOG, p. e104, 2018). As maternal–child nurses, it is our role and responsibility to empower and support one another in the delivery of care to women, newborns, and families through research, education, and advocacy (Association of Women’s Health, Obstetric, and Neonatal Nurses, 2020). Several inherited and noninherited forms of anemia in pregnancy, including information on current screening recommendations, etiolo-

gies, presentation, and treatment have been presented. Nurses’ knowledge of various anemias during pregnancy is essential to support optimal outcomes.

ACOG (2021a) and other organizations provide excellent preliminary information to help guide clinical practice; however, evidence-based education and clinician knowledge are first steps in management of anemia during pregnancy. To provide patient-centered care and prevent adverse outcomes, establishment of a nurse–patient relationship based on trust and mutual respect is essential. Listening to women, understanding their concerns, and respectful communication in literacy appropriate language is required for nurses to advocate for their patients and tailor therapeutic considerations on a patient-specific level. ❖

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References

- Adebisi, O. Y., & Strayhorn, G. (2005). Anemia in pregnancy and race in the United States: blacks at risk. *Family Medicine*, 37(9), 655–662.
- Achebe, M. M., & Gafter-Gvili, A. (2017). How I treat anemia in pregnancy: Iron, cobalamin, and folate. *Blood*, 129(8), 940–949. <https://doi.org/10.1182/blood-2016-08-672246>
- Aitchison, R. G., Marsh, J. C., Hows, J. M., Russell, N. H., & Gordon-Smith, E. C. (1989). Pregnancy associated aplastic anaemia: A report of five cases and review of current management. *British Journal of Haematology*, 73(4), 541–545. <https://doi.org/10.1111/j.1365-2141.1989.tb00294.x>
- Allard, S., & Hill, Q. A. (2016). Autoimmune haemolytic anaemia. *ISBT Science Series*, 11(S1), 85–92. <https://doi.org/10.1111/vox.12210>
- American College of Obstetricians and Gynecologists. (2018). Group prenatal care (Committee Opinion No. 731). *Obstetrics and Gynecology*, 131(3), e104–e108. <https://doi.org/10.1097/AOG.0000000000002529>
- American College of Obstetricians and Gynecologists. (2007; reaffirmed 2018). Hemoglobinopathies in pregnancy (Practice Bulletin No. 78). *Obstetrics and Gynecology*, 109(1), 229–238. <https://doi.org/10.1097/00006250-200701000-00055>
- American College of Obstetricians and Gynecologists. (2021a). Anemia in pregnancy (Practice Bulletin No. 233). *Obstetrics and Gynecology*, 138(2), e55–e64. <https://doi.org/10.1097/AOG.0000000000004477>
- American College of Obstetricians and Gynecologists. (2021b, March). *Nutrition during pregnancy*. <https://www.acog.org/womens-health/faqs/nutrition-during-pregnancy>
- American Society of Hematology. (2021). *Sickle cell disease*. <https://www.hematology.org/Patients/Anemia/Sickle-Cell.aspx>
- Association of Women’s Health, Obstetric, and Neonatal Nurses. (2020). *About AWHONN*. <https://www.awhonn.org/about-us/>
- Auerbach, M., & Landy, H. (2021). Anemia in pregnancy. In J. Tirnauer & V. Barss (Eds.), *Uptodate*. <https://www.uptodate.com/contents/anemia-in-pregnancy>
- Blackburn, S. T. (2021). Physiologic changes of pregnancy. In K. R. Simpson, P. A. Creehan, N. O’Brien-Abel, C. Roth, & A. Rohan (Eds.). *AWHONN’s Perinatal nursing* (5th ed., pp. 48–65). Wolters Kluwer.
- Camaschella, C. (2015). Iron-deficiency anemia. *The New England Journal of Medicine*, 372(19), 1832–1843. <https://doi.org/10.1056/NEJMra1401038>

- Cantor, A. G., Bougatsos, C., Dana, T., Blazina, I., & McDonagh, M. (2015). Routine iron supplementation and screening for iron deficiency anemia in pregnancy: A systematic review for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*, 162(8), 566–576. <https://doi.org/10.7326/M14-2932>
- Cao, A., & Kan, Y. W. (2013). The prevention of thalassemia. *Cold Spring Harbor Perspectives in Medicine*, 3(2), a011775. <https://doi.org/10.1101/cshperspect.a011775>
- Centers for Disease Control and Prevention. (2020a, June 22). *Micronutrient malnutrition*. <https://www.cdc.gov/nutrition/micronutrient-malnutrition/index.html>
- Centers for Disease Control and Prevention. (2020b, December 16). *Data & statistics on sickle cell disease*. <https://www.cdc.gov/ncbddd/sicklecell/data.html>
- Chaplin, H., Cohen, R., Bloomberg, G., Kaplan, H. J., Moore, J. A., & Dorner, I. (1973). Pregnancy and idiopathic autoimmune haemolytic anaemia: A prospective study during 6 months gestation and 3 months postpartum. *British Journal of Haematology*, 24(2), 219–229. <https://doi.org/10.1111/j.1365-2141.1973.tb05742.x>
- Chestnut, D. H., Polley, L. S., Tsen, L. C., & Wong, C. A. (2014). *Obstetric anesthesia: Principles and practice* (5th ed.). Elsevier.
- Chonlat, S., & Quinn, C. T. (2017). Current standards of care and long term outcomes for thalassemia and sickle cell disease. *Advances in Experimental Medicine and Biology*, 1013, 59–87. https://doi.org/10.1007/978-1-4939-7299-9_3
- Chui, D. H. K., Fucharoen, S., & Chan, V. (2003). Hemoglobin H disease: Not necessarily a benign disorder. *Blood*, 101(3), 791–800. <https://doi.org/10.1182/blood-2002-07-1975>
- Darwish, A. M., Khalifa, E. E., Rashad, E., & Farghally, E. (2019). Total dose iron dextran infusion versus oral iron for treating iron deficiency anemia in pregnant women: A randomized controlled trial. *The Journal of Maternal-Fetal & Neonatal Medicine*, 32(3), 398–403. <https://doi.org/10.1080/14767058.2017.1379988>
- de Dreuzy, E., Bhukhai, K., Leboulch, P., & Payen, E. (2016). Current and future alternative therapies for beta-thalassemia major. *Biomedical Journal*, 39(1), 24–38. <https://doi.org/10.1016/j.bj.2015.10.001>
- Galanello, R., & Origa, R. (2010). Beta-thalassemia. *Orphanet Journal of Rare Diseases*, 5, 11. <https://doi.org/10.1186/1750-1172-5-11>
- Haas, S. de, Ghossein-Doha, C., Kuijk, S. M. van, Drongelen, J. van, & Spaanderman, M. E. A. (2017). Physiological adaptation of maternal plasma volume during pregnancy: A systematic review and meta-analysis. *Ultrasound in Obstetrics & Gynecology*, 49(2), 177–187. <https://doi.org/10.1002/uog.17360>
- Horowitz, K. M., Ingardia, C. J., & Borgida, A. F. (2013). Anemia in pregnancy. *Clinics in Laboratory Medicine*, 33(2), 281–291. <https://doi.org/10.1016/j.cl.2013.03.016>
- Jain, D., Atmapoojya, P., Colah, R., & Lodha, P. (2019). Sickle cell disease and pregnancy. *Mediterranean Journal of Hematology and Infectious Diseases*, 11(1), e2019040–e2019040. <https://doi.org/10.4084/mjhid.2019.040>
- Killip, S., Bennett, J. M., & Chambers, M. D. (2007). Iron deficiency anemia. *American Family Physician*, 75(5), 671–678.
- Lafamme, E. M. (2010). Maternal hemoglobin concentration and pregnancy outcome: A study of the effects of elevation in El Alto, Bolivia. *McGill Journal of Medicine*, 13(1), 47.
- Lopez, A., Cacoub, P., Macdougall, I. C., & Peyrin-Biroulet, L. (2016). Iron deficiency anaemia. *Lancet*, 387(10021), 907–916. [https://doi.org/10.1016/S0140-6736\(15\)60865-0](https://doi.org/10.1016/S0140-6736(15)60865-0)
- Modell, B., & Darlison, M. (2008). Global epidemiology of haemoglobin disorders and derived service indicators. *Bulletin of the World Health Organization*, 86(6), 480–487. <https://doi.org/10.2471/BLT.06.036673>
- Sayani, F. A., & Kwiatkowski, J. L. (2015). Increasing prevalence of thalassemia in America: Implications for primary care. *Annals of Medicine*, 47(7), 592–604. <https://doi.org/10.3109/07853890.2015.1091942>
- Schoettler, M. L., & Nathan, D. G. (2018). The pathophysiology of acquired aplastic anemia: Current concepts revisited. *Hematology/Oncology Clinics of North America*, 32(4), 581–594. <https://doi.org/10.1016/j.hoc.2018.03.001>
- Townsend, D. M. (2013). Hematologic complications of pregnancy. *Seminars in Hematology*, 50(3), 222–231. <https://doi.org/10.1053/j.seminhematol.2013.06.004>
- U.S. Preventive Services Task Force. (2015, September 7). *Iron deficiency anemia in pregnant women: Screening and supplementation*. <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/iron-deficiency-anemia-in-pregnant-women-screening-and-supplementation>
- Vricella, L. K. (2017). Emerging understanding and measurement of plasma volume expansion in pregnancy. *The American Journal of Clinical Nutrition*, 106(Suppl. 6), 1620S–1625S. <https://doi.org/10.3945/ajcn.117.155903>
- Williamson, M., Snyder, L., & Wallach, J. (2011). *Wallach's interpretation of diagnostic tests* (9th ed.). Wolters Kluwer, Lippincott Williams & Wilkins.
- World Bank Group. (2021). *Prevalence of anemia among pregnant women (%) – United States*. <https://data.worldbank.org/indicator/SH.PR.G.ANEM?locations=US>
- World Health Organization. (2008). *Global anaemia prevalence and number of individuals affected*. https://www.who.int/vmnis/anaemia/prevalence/summary/anaemia_data_status_t2/en/
- World Health Organization. (2011). *Serum ferritin concentrations for the assessment of iron status and iron deficiency in populations*. Vitamin and Mineral Nutrition Information System. www.who.int/vmnis/indicators/serum_ferritin.pdf
- World Health Organization. (2017, May 3). *WHO recommendations on antenatal care for a positive pregnancy experience*. <https://www.who.int/publications/i/item/9789241549912>
- World Health Organization. (2021). *Anaemia*. https://www.who.int/health-topics/anaemia#tab=tab_1

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