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Pregnancy-Associated Anemia and Its Relationship with Gestational Age: A Review

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Abstract: Pregnancy-associated anemia is a prevalent and complex condition affecting a significant proportion of pregnant women worldwide, with higher incidence rates in low-resource settings. Defined as low hemoglobin levels that fail to meet the increased physiological demands of pregnancy, this condition poses serious health risks to both mother and child, including complications such as preterm birth, low birth weight, and increased maternal morbidity. The prevalence and severity of anemia are closely related to gestational age, with higher rates observed in the second and third trimesters due to factors like expanded blood volume and rising fetal demands. Gestational age influences the pathophysiology of anemia in pregnancy, with maternal and fetal demands intensifying as pregnancy progresses. During the first trimester, anemia is less common as blood volume expansion and fetal demands are lower; however, in the second trimester, these demands escalate, leading to increased rates of iron deficiency anemia if adequate supplementation is not provided. By the third trimester, maternal iron stores are often strained by rapid fetal growth and placental development, placing mothers with pre-existing nutritional deficiencies or multiple pregnancies at greater risk. This gestational-age-dependent progression underscores the need for trimester-specific screening and interventions to prevent severe anemia and associated complications.

Keywords: Pregnancy-Associated Anemia, Gestational Age, Maternal Health, Fetal Development, Anemia Prevalence.

Review Paper

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INTRODUCTION

Pregnancy-associated anemia is a condition that has profound implications for maternal and neonatal health, representing a significant public health challenge globally, particularly in low- and middle-income countries. Anemia in pregnancy is most commonly caused by iron deficiency, as the body's demand for iron and other essential nutrients increases significantly to support the developing fetus and accommodate maternal physiological changes. Defined by hemoglobin levels falling below 11 g/dL, pregnancy-associated anemia can lead to a cascade of health complications if left untreated, affecting maternal energy levels, immune function, and pregnancy outcomes. Despite advancements in prenatal care, anemia continues to affect nearly 40% of pregnant women worldwide, with severe cases correlating with increased maternal and perinatal morbidity and mortality [1, 2]. The prevalence and severity of pregnancy-associated anemia are influenced by gestational age due to the physiological demands at each pregnancy stage. During the first trimester, the maternal body begins to adjust to the needs of the growing fetus, but the blood volume increase remains relatively modest. As pregnancy progresses into the second trimester, the body undergoes significant blood volume expansion to accommodate fetal growth, increasing the demand for iron and other nutrients. By the third trimester, this demand intensifies as the fetus rapidly grows and the placenta completes its development, causing hemoglobin levels to drop in women who cannot meet these demands. This gestational age-dependent variation in anemia prevalence necessitates trimester-specific monitoring and intervention strategies to prevent the development of severe anemia [3, 4].

Gestational age thus serves as an essential factor in understanding the pathophysiology of anemia in pregnancy. Hemodilution, resulting from increased plasma volume, lowers hemoglobin concentration and can cause physiological anemia even in healthy pregnancies. However, when nutritional deficiencies exist, this hemodilution effect is compounded, increasing the risk of anemia. For many pregnant women, particularly those in resource-limited settings, dietary iron intake and supplementation may not suffice to offset the increased needs, leading to progressively lower hemoglobin levels as pregnancy advances. Analyzing the

relationship between gestational age and anemia development helps clarify when interventions are most needed and how healthcare providers can best support pregnant women to prevent complications [5, 6]. The health implications of pregnancy-associated anemia extend beyond maternal morbidity, affecting fetal growth and development, as well as neonatal health. For mothers, anemia can lead to fatigue, reduced immunity, and an elevated risk of complications such as preterm labor, preeclampsia, and postpartum hemorrhage. For the fetus, chronic anemia in the mother can result in intrauterine growth restriction (IUGR), low birth weight, and even preterm birth, as the placenta cannot adequately transfer oxygen and nutrients. These risks underscore the need for effective anemia management throughout pregnancy, with an emphasis on preventing moderate anemia from escalating into severe anemia during the later stages [7, 8]. Current approaches to managing pregnancy-associated anemia include preventive measures, routine anemia screening, iron and folic acid supplementation, and, in severe cases, intravenous iron or blood transfusions. Prenatal care guidelines commonly recommend iron and folic acid supplementation for all pregnant women as a baseline preventive measure; however, personalized approaches tailored to gestational age are crucial in managing cases where supplementation alone does not suffice. For women who develop moderate to severe anemia during the second or third trimester, timely and intensive interventions, such as higher iron doses or alternative iron administration methods, are necessary to quickly elevate hemoglobin levels and prevent complications around childbirth [9, 10].

Gestational Age and Physiological Changes in Pregnancy-Associated Anemia

Gestational age plays a pivotal role in the development and progression of pregnancy-associated anemia, influencing both maternal physiology and fetal demands. As pregnancy progresses, several physiological changes occur in the maternal body that can impact hemoglobin levels, with these changes varying across each trimester. In particular, blood volume expansion, altered iron metabolism, and increased fetal nutrient demands are key factors in the onset and severity of anemia during pregnancy [11]. In the first trimester, the physiological changes in pregnancy are relatively modest compared to the later stages. Blood volume expansion begins to occur, but it is not as pronounced as in the second and third trimesters. At this stage, maternal blood volume increases by about 10–15%, primarily as a result of plasma expansion, rather than a substantial increase in red blood cell mass. This hemodilution effect can cause a mild decrease in hemoglobin levels, though it is often not severe enough to be classified as anemia. However, for women with pre-existing nutritional deficiencies or other health issues, this natural decrease in hemoglobin can exacerbate any existing anemia. Additionally, iron stores from the first trimester may not be sufficient to meet the increasing demands of later pregnancy, making it important to address nutritional deficiencies early [12,13].

During the second trimester, the body's demands for iron, folate, and other essential nutrients increase significantly as the fetus begins to grow rapidly. By this time, blood volume expansion becomes more pronounced, with plasma volume increasing by about 30%, while red blood cell mass continues to grow at a slower rate. This creates a greater hemodilution effect, further lowering hemoglobin concentrations. As fetal growth accelerates, the placenta begins to develop its vascular network, increasing the need for iron to support the expanding blood volume. The second trimester is a critical period for screening and early intervention, as this is when women are most likely to develop iron deficiency anemia, particularly if they have not been taking appropriate iron supplements or maintaining an iron-rich diet [14, 15]. In the third trimester, the maternal body faces the highest physiological demands. Blood volume expansion continues, with the total blood volume increasing by as much as 50% by the end of the pregnancy. This volume increase continues to be driven by plasma expansion, which again results in hemodilution of red blood cells and further decreases in hemoglobin concentration. In addition, the fetal growth rate reaches its peak, and the growing fetus places additional pressure on maternal iron stores. At this stage, maternal iron reserves can become significantly depleted, particularly if iron supplementation has been inadequate or if there are other contributing factors such as multiple pregnancies, chronic diseases, or malnutrition. Without adequate iron, women in the third trimester are at a high risk for severe anemia, which can lead to complications such as preterm labor, low birth weight, or maternal fatigue and weakness [16, 17]. The relationship between gestational age and pregnancy-associated anemia emphasizes the need for trimester-specific interventions. In the first trimester, early screening for anemia and iron deficiency should be prioritized, especially for women at higher risk. This can be achieved through blood tests that assess hemoglobin and serum ferritin levels. In the second and third trimesters, more intensive supplementation or alternative treatments may be necessary to meet the increasing demands of both the mother and the fetus. Iron supplementation, either oral or intravenous, is typically used to address the escalating anemia risk during these stages, while folic acid and vitamin B12 are also important for supporting overall maternal and fetal health [18].

Impact of Pregnancy-Associated Anemia on Maternal and Fetal Outcomes

Pregnancy-associated anemia, particularly when severe, can have significant negative effects on both maternal and fetal health. The impact of anemia

extends across a range of complications, with the severity of these outcomes often correlating with the degree of anemia and the gestational age at which it occurs. Early detection, adequate management, and timely interventions are crucial in mitigating these adverse outcomes. Both maternal and fetal systems are vulnerable to the reduced oxygen-carrying capacity of the blood, which can impair normal development and lead to long-term health consequences if left untreated [19]. For the mother, the primary risks of pregnancy-associated anemia are related to cardiovascular stress, reduced immune function, and an increased susceptibility to infections. Severe anemia reduces the oxygen supply to vital organs, placing additional strain on the heart as it works harder to compensate for the decreased hemoglobin levels. This can lead to heart failure, particularly in women with pre-existing heart conditions or during the later stages of pregnancy when blood volume is at its highest. Additionally, anemia weakens the immune system, leaving mothers more vulnerable to infections, particularly postpartum. In severe cases, anemia may lead to complications such as preeclampsia, eclampsia, or placental abruption, all of which can result in poor maternal outcomes, including death. Furthermore, women with anemia are at higher risk for postpartum hemorrhage due to reduced clotting ability, which can lead to significant blood loss after delivery [20].

From a fetal perspective, pregnancy-associated anemia is associated with increased risk of intrauterine growth restriction (IUGR), preterm birth, and low birth weight. As maternal hemoglobin levels drop, the oxygen and nutrient supply to the developing fetus diminishes, which can impair normal fetal development. This is particularly critical in the second and third trimesters when the fetus is undergoing rapid growth and the placenta is responsible for transferring nutrients and oxygen. Inadequate oxygenation can lead to a lower birth weight, which is a well-established risk factor for neonatal morbidity and mortality. Newborns with low birth weight are more likely to suffer from respiratory distress syndrome, developmental delays, and other long-term cognitive and motor impairments. Moreover, fetal anemia due to maternal iron deficiency can affect the fetus's ability to produce its own hemoglobin, further complicating neonatal health [21]. The risk of preterm birth is also significantly heightened by severe anemia, particularly in the later stages of pregnancy. When maternal anemia reaches a severe level, the body may initiate preterm labor as a response to the decreased oxygen supply, or complications like preeclampsia may trigger early labor. Preterm birth carries with it numerous risks for the infant, including compromised organ development, particularly of the lungs, leading to higher rates of respiratory distress syndrome and the need for extended neonatal care. The neurological development of the preterm infant may also be affected, with some studies suggesting an increased risk for cognitive delays and behavioral disorders later in life [22]. Additionally, severe anemia during pregnancy can have a profound impact on the placenta, affecting placental perfusion and function. Inadequate placental blood flow due to maternal anemia can result in poor fetal oxygenation and nutrient transfer, increasing the likelihood of complications such as IUGR, preterm delivery, and stillbirth. Placental insufficiency caused by anemia can also contribute to long-term health issues for the child, including an increased risk for chronic diseases such as cardiovascular problems and metabolic disorders in adulthood [23].

Current Interventions for Pregnancy-Associated Anemia by Gestational Age

Pregnancy-associated anemia requires tailored interventions that vary by gestational age to ensure the health and safety of both the mother and the fetus. The progression of pregnancy and the associated physiological changes, such as increased blood volume and heightened nutritional demands, necessitate different strategies at each trimester to manage anemia effectively. Early detection, appropriate supplementation, and timely medical interventions are crucial in preventing the adverse effects of anemia. Below is an overview of the current interventions for pregnancy-associated anemia according to gestational age [24].

First Trimester: Early Detection and Nutritional Support

The first trimester of pregnancy is characterized by the onset of blood volume expansion and the early development of the fetus. However, the demands for iron and folic acid are relatively low compared to later stages. Despite this, nutritional deficiencies, particularly iron deficiency, can begin to develop. Early intervention in this trimester focuses on preventing the onset of anemia, particularly for women at high risk, such as those with a history of anemia, poor dietary intake, or other pre-existing conditions. The primary intervention in the first trimester involves promoting adequate iron intake through dietary modifications, including iron-rich foods such as red meat, leafy greens, and legumes. Supplementation with folic acid, typically prescribed at a dose of 400–800 mcg daily, is essential to prevent folate deficiency and its associated complications, such as neural tube defects [25]. If anemia is detected early in the first trimester, iron supplementation is recommended, with oral ferrous sulfate being the most common treatment. However, for women with severe nausea or gastrointestinal side effects, alternative forms of iron supplements, such as iron bisglycinate or liquid iron preparations, may be considered. Hemoglobin levels should be monitored regularly, and further intervention should be escalated if levels fall below 11 g/dL, indicating the onset of anemia. Additionally, health providers should screen for other potential causes of anemia, such as vitamin B12 deficiency or chronic infections, and address these concurrently.

Second Trimester: Iron Supplementation and Monitoring

The second trimester represents a period of rapid fetal growth and significant blood volume expansion in the mother. The plasma volume increases, leading to hemodilution, which can naturally lower hemoglobin concentrations. Iron demands increase during this period to support the developing fetus and the expanding placenta. For women who are at risk of developing anemia during this stage, iron supplementation is crucial to prevent more severe complications in later trimesters. Routine screening for anemia is typically conducted between 24 and 28 weeks of gestation. Women identified with mild anemia (hemoglobin levels between 10.5 and 11 g/dL) are usually treated with oral iron supplements, commonly in the form of ferrous sulfate, to replenish iron stores. The standard recommended dose is 60–120 mg of elemental iron daily. For women who cannot tolerate oral iron or those who have more severe anemia (hemoglobin below 10.5 g/dL), intravenous iron may be considered, particularly if oral supplementation fails to adequately raise hemoglobin levels or if gastrointestinal side effects are problematic. Intravenous iron preparations, such as iron sucrose or ferric carboxymaltose, are effective alternatives that provide faster correction of iron deficiency and are safe during pregnancy when administered by a trained healthcare provider [26].

Third Trimester: Intensive Management and Special Considerations

The third trimester is the most critical period for managing pregnancy-associated anemia, as the risk of severe anemia and its associated complications increases due to the high demands of fetal growth and the maturation of the placenta. By this stage, blood volume expansion reaches its peak, which can lead to significant hemodilution, further reducing hemoglobin levels. Inadequate iron stores or poor adherence to supplementation can exacerbate anemia and lead to maternal fatigue, preterm labor, or other complications such as preeclampsia or postpartum hemorrhage. Women in the third trimester who have iron deficiency anemia are typically treated with higher doses of oral iron, though intravenous iron may be necessary for women with severe anemia or for those who cannot tolerate oral iron. Blood transfusions may be considered in extreme cases, especially if hemoglobin levels drop significantly below 7–8 g/dL, or if there are concerns about the mother's cardiovascular stability or other complications. In addition to iron supplementation, folic acid (1 mg daily) and vitamin B12 supplementation should be continued throughout the third trimester to support the optimal development of both the mother and the fetus [22]. Monitoring hemoglobin levels closely during the third trimester is essential, especially for women with known risk factors for anemia. Early signs of anemia-related complications, such as dizziness, shortness of breath, or excessive fatigue, should be assessed promptly. Special consideration should also be given to women carrying multiples, as the increased fetal demands for iron and nutrients further elevate the risk of anemia. In cases of severe anemia that is not responsive to oral or intravenous iron supplementation, blood transfusions may be required to prevent serious maternal and fetal outcomes [23].

Postpartum Considerations: Continued Monitoring and Management

Although pregnancy-associated anemia primarily impacts the course of pregnancy, postpartum anemia remains a concern for many women, particularly those who had anemia during pregnancy. In the postpartum period, the body requires time to restore blood volume and iron stores, and women may continue to experience fatigue and weakness as a result of ongoing iron deficiency. Continued iron supplementation is typically recommended for up to 6 weeks postpartum to replenish iron stores, particularly for women who had severe anemia during pregnancy or experienced significant blood loss during delivery [24, 25]. Breastfeeding women, in particular, should be carefully monitored for signs of anemia, as iron deficiency can affect milk production and the health of the infant. For women who experienced substantial blood loss during childbirth or had complicated deliveries, intravenous iron or blood transfusions may still be necessary. Regular follow-up care and postnatal screening for anemia should be an integral part of maternal healthcare to ensure complete recovery and prevent long-term complications [26].

CONCLUSION

Pregnancy-associated anemia is a significant public health concern that poses substantial risks to both maternal and fetal health. Its management requires a comprehensive, stage-specific approach tailored to the unique physiological changes and nutritional demands during each trimester. Early detection, routine screening, and appropriate interventions—primarily through iron supplementation—are essential in preventing and addressing anemia. The first trimester focuses on dietary support and early supplementation to prevent deficiency, while the second and third trimesters require more intensive management to address the increased iron demands of the growing fetus and the expanding maternal blood volume. In severe cases, intravenous iron or blood transfusions may be necessary, particularly when oral supplementation fails or when anemia is diagnosed late in pregnancy. Timely interventions during the third trimester are particularly critical, as untreated anemia can lead to preterm birth, low birth weight, and an increased risk of maternal complications such as cardiovascular strain and postpartum hemorrhage. Additionally, the postpartum period should not be

overlooked, with continued monitoring and supplementation to restore iron levels and prevent persistent anemia.

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