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■ **Clinical Practice Guideline**

Management and the Prevention of Anaemia in Pregnancy: SOGON Clinical Practice Guidelines

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ABSTRACT

Anaemia during pregnancy is a significant public health concern in this country. With 40% of the population living in poverty and 63% facing multidimensional poverty as reported by the National MPI 2022, it is not surprising that women often have poor diets, making them more prone to iron and folate deficiency anaemia, which are the leading causes of anaemia during pregnancy. Other factors contributing to anaemia during pregnancy include having multiple pregnancies in quick succession, giving birth to multiple babies, pre-pregnancy menorrhagia, worm infestation, severe and prolonged hyperemesis gravidarum, among others. Anaemia during pregnancy can cause serious complications for the fetus, such as preterm birth and low birth weight. It can also affect the mother's well-being, with severe anaemia increasing the risk of death or near misses. Recent evidence also suggests that anaemia during pregnancy significantly increases the risk of postpartum haemorrhage caused by uterine atony. It's crucial for healthcare providers to be aware of the issues associated with anaemia during pregnancy and the measures for preventing and detecting high-risk pregnancies early. Healthcare providers must understand the different types of anaemia, common symptoms, and treatment options to recognize the warning signs of anaemia and avoid complications. This clinical guideline is designed for obstetricians and midwives to help manage pregnant women with anaemia appropriately. The document's layout and practical step-by-step approach to managing anaemia during pregnancy are commendable, and the team of experts who produced this high-quality document under the chairmanship of Prof Abiodun Aboyeji deserves appreciation. All members of the committee deserve commendation for a job well done. Healthcare practitioners should use this guideline to manage anaemia during pregnancy effectively, reducing complications for both mother and foetus, and ultimately reducing the burden of high maternal and perinatal mortality and morbidity related to anaemia. This is one of four clinical guidelines to be produced by the SOGON Executive under my leadership. The other three will be rolled out shortly.

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INTRODUCTION

Anaemia is a global public health challenge and is among the commonest medical disorders of pregnancy. It is a significant contributor to maternal and perinatal morbidity and mortality, particularly in low resource countries. The global prevalence of anaemia in pregnancy is 36.5%[1], but in Nigeria, the prevalence of anaemia in pregnancy ranges between 37.6% and 76.5%. Studies from northern and southern Nigeria have reported prevalence rates of Iron deficiency Anaemia (IDA) in pregnancy of 12.3 - 65.1%[2–6]

Definition

The World Health Organization (WHO) defines anaemia in pregnancy as a haemoglobin (Hb) concentration of less than 11g/dl and postpartum less than 10g/dl.[1] However in obstetrics in the tropics, the cut off for anaemia in pregnancy is generally accepted as Hb concentration less than 10g/dl or a Packed Cell volume of 30%. This is because of mean Hb values among the populace and the fact that side effects associated with anaemia are not commonly found at Hb values above 10g/dl.

Consequences of Anaemia in Pregnancy

Anaemia in pregnancy can lead to maternal and foetal complications including preterm deliveries, postpartum haemorrhage, infections and depression.[6,7] Anaemia has socioeconomic implications and also contributes to suboptimal work performance, reduced mental function, and productivity, hence reduced earning capacity.[8] The foetus may suffer from foetal growth restriction and stillbirth, while the infant of an affected mother may develop neurodevelopmental impairment and diseases in adult life.[6,7]

AETIOLOGY

In Nigeria, the common causes of anaemia in pregnancy include nutritional deficiencies (iron, folate and vitamin B12), haemoglobinopathies (sickle cell disorder), blood loss (antepartum and postpartum haemorrhage), infections and infestations (malaria, urinary tract infection, HIV and hookworm).[4,9] Other less common causes include drugs, Glucose-6-Phosphatase dehydrogenase (G6PD) deficiency and autoimmune disorders.[4,9]

Classification

Anaemia in pregnancy can be classified based on severity into mild (Hb = 10.0 – 10.9 g/dl), moderate (Hb = 7.0 – 9.9g/dl) and severe (Hb = < 7.0 g/dl).[10] The incidence of associated complications will rise with progression from mild to severe forms.

Anaemia can also be classified morphologically into various types, where the morphology of the RBCs can indicate the cause of the anaemia. The first is normocytic normochromic anaemia, which can be due to physiologic haemodilution of pregnancy. Secondly, it can be Microcytic hypochromic anaemia which is typical of Iron deficiency. Thirdly it can be Macrocytic (megaloblastic) anaemia which occurs in Vitamin B12 and Folic acid deficiency. There may be mixed picture when the cause of the anaemia is multifactorial.

Anaemia can also be classified based on kinesis into those from excessive destruction of RBCs which can occur in haemolysis like Haemoglobinopathies, autoimmune disorders, infestations (like malaria), severe infections, uraemia and others. Second, it can occur from excessive blood loss that can occur in acute or chronic bleeding. Thirdly, anaemia can occur from inadequate production of RBs like in Iron, folate and Vitamin B12 deficiency, severe malnutrition, bone marrow atrophy like in aplastic anaemia or bone marrow infiltration by malignant cells.

Anaemia can also result from other severe medical conditions like severe endocrine, liver and kidney diseases among others. Knowing the cause of anaemia in pregnancy is critical to manage it correctly and successfully, in order to prevent maternal and perinatal morbidity and mortality.

DIAGNOSIS

Considering the various causes of anaemia, the knowledge of the aetiology is important to ensure correct management of the condition. This entails taking a thorough history including symptoms, pre-existing disease conditions, dietary history, family and social history, obstetrics, gynaecologic and drug history. The symptoms and duration of the condition should also be looked for. This should be followed by comprehensive examination and relevant investigations.

Clinical Features

In most cases women with anaemia in pregnancy are asymptomatic. The asymptomatic anaemias are majorly chronic, while the acute anaemia, usually from acute blood loss or sequestration tend to be more symptomatic. As severity of anaemia increases, they may present with symptoms such as weakness, tiredness, lassitude, easy fatiguability, dizziness, fainting attacks, headaches, breathlessness on exertion, palpitation, and swollen legs, while anaemia from acute blood loss can lead to hypovolaemia and haemorrhagic shock.

History of prescription and recreational drug use should be sought, presence of passage of frequent

stool, cough, weight loss, fever, urinary symptoms, parity and occupational history will be relevant. There may also be associated foetal complications including abortion, foetal distress or demise, preterm delivery and growth restriction in chronic anaemia.

Physical Examination

The commonest sign of anaemia is pallor, which may present in varying degrees. The pallor can be elicited from the conjunctiva, buccal mucosa and palmar surface, but this can be affected by other factors like crying, exposure to smoke (conjunctiva), conditions like liver diseases (palms) and diet (buccal mucosa). Other signs of moderate to severe anaemia include generalized oedema, jaundice, fever, petechial haemorrhages and hepatosplenomegaly. Dyspnoea, heart failure, glossitis, stomatitis, pharyngeal webs and koilonychia may also develop.

Patients should be examined for lymphadenopathy, hepatomegaly and splenomegaly. The size and regularity of the uterus and the presence of abdominopelvic masses should be looked for. Pelvic examination and digital rectal exam should also be performed as indicated.

With increasing severity, anaemia can progress through three clinical phases. It can begin with compensation with episodes of dyspnea with activity, then progress to the phase of decompensation with dyspnea at rest, and if uncorrected can lead to cardiac failure.

The clinical findings will determine the appropriate Investigations that should be requested in managing the patient.

Investigations

General

1. Full blood count (FBC). This is the most important test in the evaluation of anaemia and it includes the Hb concentration, packed cell volume (PCV), red blood cell count (RBC), white blood cell count (WBC), platelet count and reticulocyte count, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC).
   - ⇒ Normal reticulocyte is 1-2.5% and it may be increased (haemolytic anaemia or acute blood loss) or decreased (iron, B12, or folic deficiency and anaemia of chronic disorders.
   - ⇒ Mean Corpuscular Volume (MCV) may be < 80fL(microcytic), 80-100fL (normocytic) or >100 fL(macrocytic).
   - ⇒ Mean Corpuscular haemoglobin (MCH). It is the average amount of hemoglobin in a person's red blood cells and normal value is 34pg/dl.
   - ⇒ Mean Corpuscular Haemoglobin Concentration (MCHC) may be high (> 34pg/dl) in macrocytic anaemia), normal (17–34pg/dl) or low (<17pg/dl) in microcytic anaemia.
2. Peripheral blood films: It is useful in showing characteristic abnormalities of red blood cell shape, size and appearance, also the presence of precursor RBCs and platelet count.
   - ⇒ It may be microcytic (iron deficiency, thalassemia, chronic disease), macrocytic (folate deficiency, vitamin B12 deficiency, drug induced haemolytic anaemia, liver disease), normocytic (haemorrhagic anaemia, early iron deficiency anaemia, chronic disease, autoimmune haemolytic anaemia) or dimorphic (iron deficiency and folate deficiency).[11,12]
   - ⇒ Others may show hypochromic (Iron deficiency), spherocytes (immune hemolysis, microangiopathic haemolysis), sickle cells (sickle cell anaemia) or target cells (thalassemias).[12]
3. Haemoglobin Genotype: To diagnose haemoglobinopathies.
4. Malaria test: Blood film for identification of malaria parasites, or malaria rapid diagnostic tests
5. HIV test: Rapid test according to Nigerian national HIV testing guidelines
6. Stool microscopy: To check for the presence of ova of hookworm and the count.
7. Urinalysis and microscopy, culture and sensitivity: To diagnose urinary tract infection.

Specialized tests (These tests should only be done when indicated)

8. Iron studies: Serum ferritin has the highest sensitivity and specificity in pregnancy and is recommended when it is necessary to determine the cause of anaemia.[13] As Serum ferritin is sometimes elevated in the presence of inflammation, C-Reactive Protein may also be necessary.[14] The serum ferritin threshold for the diagnosis of IDA is < 30µg/L.[13,15]
9. Biochemical parameters: These include liver function tests (increased LDH, increased Indirect bilirubin), renal function tests, thyroid function tests, serum haptoglobin and haemoglobinuria. These are indicated when clinical features of the specific disease conditions are elicited.
10. Direct Antiglobulin test (DAT): To distinguish immune causes (DAT-positive) from non-immune causes (DAT-negative).
11. Vitamins and Micronutrients: Serum vitamin B12 level, folate levels, copper and zinc.
12. Bone marrow studies: Should only be done in collaboration with haematologist.

TREATMENT

The treatment of anaemia in pregnancy varies depending on the cause, severity, the symptoms and gestational age.

A. Iron Deficiency Anaemia

Maternal iron deficiency anaemia impairs neurodevelopmental function and learning in children.[16–18] It is therefore important to treat pregnant women promptly even when presenting with mild asymptomatic IDA. IDA is treated with oral and parenteral iron, and blood transfusion. Hb concentration rise of > 1g/dl in two weeks after treatment with oral iron is seen as evidence of iron deficiency anaemia if properly taken. To enhance absorption, pregnant women should be advised to take oral iron one to two hours after meals preferably with 100mg of vitamin C. Oral iron should also not be taken with antacids or with caffeine containing beverages including tea and coffee.[19] Parenteral iron preparations are also available and can be used if indicated. Older dextran-based preparations have been associated with hypersensitivity reactions, but newer preparations are largely known to be safe.

In most cases packed red blood cell (pRBC) is preferable for blood transfusion except in acute blood loss, severe anaemia close to term and when the patient is clinically unstable. The benefits of blood transfusion must be assessed to outweigh the associated risks (infections, transfusion reactions, sensitization in rhesus negative, volume overload and others).

In the management of IDA folic acid 5mg daily should also be administered. Adjuvant recombinant human erythropoietin (rHuEPO) 4000 units subcutaneously, three times a week should be used in patients who refuse blood transfusions. Table 1 below shows the treatment of IDA based on gestational age and severity.

Table 1: Treatment of IDA Based on Gestational Age and Severity of Anaemia in Pregnancy.

	Trimesters of pregnancy		
Severity of anaemia	**First**	**Second**	**Third**
Mild (Hb = 10 – 10.9g/dl)	Oral elemental iron 60mg bd. If no rise of 1g/dl in 4 weeks, administer parenteral iron in second trimester	Oral elemental iron 60mg bd. If no rise of 1g/dl in 4 weeks, administer parenteral iron	Oral elemental iron 60mg bd. If no rise in 4 weeks, administer parenteral iron
Moderate (Hb = 7 - 9.9g/dl)	If asymptomatic, administer oral elemental iron 60mg bd. If no rise in Hb of up to 1g/dl in 2 weeks, administer parenteral iron in second trimester. If symptomatic administer pRBC,	If asymptomatic, administer oral elemental iron 60mg bd. If no rise in Hb of 1g/dl in 2 weeks, administer parenteral iron. If symptomatic administer pRBC,	If asymptomatic, administer oral elemental iron 60mg bd. If no rise in Hb of 1g/dl in 2 weeks, administer parenteral iron If symptomatic or close to delivery transfuse pRBC
Severe (Hb < 7g/dl)	Transfuse pRBC,	Transfuse pRBC,	Transfuse pRBC,

NB: Dose of iron stated in the table above refers to elemental iron.

Blood transfusion should be considered in acute blood loss where patient is decompensated, when the foetus is affected, when the Hb is very low, and when delivery is close. The benefits should outweigh the risks.

The following doses of oral iron commonly used, correspond to 60mg elemental iron - ferrous sulphate 200mg, ferrous gluconate 500mg, ferrous fumarate 180mg.

The recommended intravenous iron preparation is intravenous sucrose because of its relative safety and availability. The formula for calculating the dose of intravenous iron: Weight (Kg) X (110g/L – initial Hb) X 0.24 + 500mg (replacement of iron stores).[20]

Other Causes of Anaemia

Table 2 below refers to the treatment of other common causes anaemia in pregnancy.

Table 2: Treatment of Other Causes of Anaemia in Pregnancy

Causes	**First**	**Second**	**Third**
Malaria	Quinine or Artemether Lumefantrine	Artemether Lumefantrine (AL)	Artemether Lumefantrine (AL)
Infections	Appropriate antimicrobial for pregnancy	Appropriate antimicrobial for pregnancy	Appropriate antimicrobial for pregnancy
Sickle cell disease	Transfuse packed AA RBCs, if consistently less than steady state, or less than 6g/dl	Transfuse packed AA RBCs, if consistently less than steady state, or less than 6g/dl	Transfuse packed AA RBCs, if consistently less than steady state, or less than 6g/dl
Folate deficiency	Folic acid 5mg daily	Folic acid 5mg daily	Folic acid 5mg daily
Haemorrhage	Transfusion of whole blood if symptomatic or Hb < 9g/dl Administer oral iron if stable and Hb ≥ 9g/dl	Transfusion of whole blood if symptomatic or Hb < 9g/dl Administer oral or parenteral iron if stable or Hb≥9g/dl	Transfusion of whole blood if symptomatic or Hb < 9g/dl Administer oral or parenteral iron if stable or Hb≥9g/dl
Hookworm or other Helminths	Defer treatment till second trimester	Albendazole 400mg single dose or Mebendazole 500mg single dose	Albendazole 400mg single dose or Mebendazole 500mg single dose

PREVENTION OF ANAEMIA IN PREGNANCY

Anaemia is an indicator of both poor nutrition and poor health.[21] Maternal undernutrition is highly prevalent in Nigeria and is recognized as a key determinant of poor perinatal outcomes.[21] Measures to improve maternal malnutrition are good preventive strategies to prevent anaemia in pregnancy. Prevention of other common causes of maternal anaemia should occur as early as possible during or before pregnancy.
The preventive measures include:

1. Preconception care for women of reproductive age with emphasis on good nutrition, genotype awareness, and appropriate care for heavy and/or prolonged menstrual bleeding.[21,22]
2. Pregnant women should be encouraged to register for antenatal care in the first trimester.[21]
3. Specific health education on optimal nutrition during pregnancy.[21,22]

4. Screen all pregnant women for anaemia using haemoglobin concentration or PCV at booking.[21]
5. Commence prophylactic iron supplementation (60mg of elemental iron daily) for all pregnant women from booking till six weeks post-partum (except those with sickle cell disorder) - (WHO Recommendations on ANC). Although oral iron supplementation was found to increase malaria and other infection rates in children in some malaria endemic settings, a review of the literature did not find any epidemiological evidence that daily maternal supplementation with 60mg elemental iron, leads to increased maternal P. falciparum infection.[16]
6. Commence prophylactic folic acid 5mg daily (ideally from 12 weeks before conception) throughout pregnancy.[21]
7. Commence malarial chemoprophylaxis with monthly Sulphadoxine-Pyrimethamine regime starting from the second trimester till delivery.[21]

Summary of Recommendations

1. The World Health Organization (WHO) defines anaemia in pregnancy as a haemoglobin concentration of less than 110g/l (11g/dl) and postpartum less than 100g/l (10g/dl).[10]
2. Anaemia in pregnancy is classified based on severity into mild (Hb = 10.0 – 10.9 g/dl), moderate (Hb = 7.0 – 9.9g/dl) and severe (Hb = < 7.0 g/dl).[10]
3. Full blood count (FBC) is the most important test in the evaluation of anaemia, and it includes the Hb concentration, packed cell volume (PCV), red blood cell count (RBC), white blood cell count (WBC), platelet count and reticulocyte count, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC).
4. Serum ferritin has the highest sensitivity and specificity in pregnancy and is recommended when it is necessary to determine the cause of anaemia. The serum ferritin threshold for the diagnosis of IDA is < 30µg/L.[13,15]
5. IDA should be treated with oral and parenteral iron, and blood transfusion. Packed red blood cell (pRBC) is preferable for blood transfusion except in acute blood loss, severe anaemia close term and when the patient is clinically unstable.
6. In the management of IDA folic acid 5mg daily should also be administered.
7. Adjuvant recombinant human erythropoietin (rHuEPO) 4000 units subcutaneously, three times a week should be used in patients who refuse blood transfusions.
8. Hb concentration rise of > 1g/dl in two weeks after treatment with oral iron is seen as evidence of iron deficiency anaemia.[23,24]
9. The doses of elemental oral iron for prophylaxis and treatment of IDA in pregnancy should be 60mg daily and 60mg twice daily, respectively.
10. Preventive strategies during and before pregnancy, including IPTp should be emphasised in women of reproductive ages and their partners.

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