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Brief: Anemia in Pregnancy

Anemia remains a daunting global health challenge. USAID promoted the creation of an Anemia Task Force (ATF) to advise its project USAID Advancing Nutrition. The ATF developed a report characterizing key elements of the biology, assessment, and approaches to interventions to address this challenge. The comprehensive report conceptualized anemia as a multifactorial condition that represents an "ecology" of interacting internal (biology, genetics, health) and external (social, behavioral, demographic and physical) environments.[1] The complexity of this ecology and its implications for diagnosis and treatment is exemplified by the intersection of anemia and pregnancy.

As highlighted in the ATF report, the etiology of anemia can be either nutritional or non-nutritional. The following is a brief review of approaches to addressing this dichotomy focused on pregnancy.

Key Messages

- The net iron requirement in pregnancy is 0.5–1 grams (g).
- World Health Organization (WHO) guidelines recommend daily iron and folic acid supplementation. Thus far, use of multiple micronutrient supplements (MMS), containing iron and folic acid, is recommended only under rigorous research conditions (WHO 2020b).
- Infections during pregnancy pose unique challenges with regards to treatment.
- Anemia during pregnancy can increase the risk of postpartum hemorrhage (PPH), the most common cause for maternal death globally.

Nutritional Causes of Anemia in Pregnancy

Increased Iron Requirements during Pregnancy

Pregnant women are a population sub-group at greatest risk of anemia and its adverse health consequences. A key factor underlying that risk is the biology of iron, which is characterized by the following features:

- Iron requirements are highest in pregnant women, who have a recommended dietary allowance of 27 milligrams (mg)/day in diets with high iron bioavailability; pre-menopausal women's requirements are also high (18 mg/day). (NHMRC 2006; NIH 2021).
- Despite a nine-fold increase in iron absorption during pregnancy to supply a 30 percent expansion of the hemoglobin mass (Bothwell 2000), absolute iron deficiency (i.e., depleted or insufficient iron stores) may account for half of all anemia in pregnancy in low- and middle-income countries (Geller et al. 2006).
- Iron lost during bleeding in childbirth and lactation is incompletely offset by increased absorption and amenorrhea (i.e., the absence of a menstrual period) in the postpartum period.
- Overall, the net pregnancy iron requirement is substantial (500 mg to 1 g) and despite increased iron absorption, the dietary supply may be insufficient to reach the additional iron demand (Bothwell 2000; Georgieff 2020).

[1] Several manuscripts are being prepared based on the content of the ATF report. The plan is to publish them in a peer-reviewed journal.

Providing Iron during Pregnancy[2]

Currently, there is no harmonized guidance on universal screening for anemia during pregnancy (WHO 2016). The American College of Obstetricians and Gynecologists (ACOG), for example, recommends screening all pregnant women for anemia in the first trimester and again at 24 0/7–28 6/7 weeks of gestation. ACOG suggests treating those identified with anemia caused by iron deficiency with supplemental iron, in addition to prenatal vitamins (ACOG 2008). A summary of existing options for meeting iron and anemia-related micronutrient needs for pregnant persons follows.

Iron-Folic Acid Supplementation

WHO guidelines for pregnant women recommend daily oral iron and folic acid supplementation with 30 to 60 mg of elemental iron and 0.4 mg folic acid during pregnancy to prevent maternal anemia and related adverse outcomes (e.g., postpartum hemorrhage, low birthweight, and preterm birth) (WHO 2020a).

Iron-Folate Supplements versus Multiple Micronutrient Supplements (MMS)

In highly vulnerable populations affected by malnutrition, current evidence suggests that giving MMS during pregnancy may reduce the risk of low birth weight and of small size for gestational age, compared with just iron and folic acid supplementation. However, there are important gaps in the evidence, both biologically and programmatically, and the WHO currently only recommends MMS use for pregnant women under rigorous research conditions (WHO 2020b).

Approaches to Non–Nutritional Causes of Anemia in Pregnancy

Management of Parasitic Infections during Pregnancy

Malaria

Malaria during pregnancy poses a unique challenge for anemia prevention and control due to adverse effects on both the mother and the fetus (WHO 2015). In areas where *Plasmodium falciparum* malaria transmission is stable and pregnant women are semi-immune, infections are mostly asymptomatic, making diagnosis difficult and hampering targeted prevention programs through the use of malaria screening.

WHO guidelines recommend a focus on prevention of malaria infection with intermittent preventive treatment using drugs such as sulfadoxine-pyrimethamine (IPTp-SP) (COSMIC Consortium 2019). When implemented effectively, IPTp-SP reduces maternal malaria episodes, maternal and fetal anemia, placental parasitemia, low birth weight, and neonatal mortality (Cutts et al. 2020; WHO 2015; COSMIC Consortium 2019). The WHO guidelines provide a holistic approach to malaria management in pregnant women and those of reproductive age by integrating the use of long-lasting insecticide-treated nets as a prevention tool in the home along with effective and early diagnosis and management (WHO 2015).

In the face of emerging drug resistance and the uncertain safety of repeated doses during pregnancy, an alternate regimen for malaria control in pregnancy is the use of rapid diagnostic screening during the antenatal period, with immediate treatment if the mother tests positive. Available evidence suggests that a newer therapy, such as artemisinin-based combination therapy with dihydroartemisinin-piperaquine, is superior to the current standard of two or three doses of IPTp-SP (Cutts et al. 2020).

Other Parasitic Infections

Other parasitic infections causing anemia during pregnancy include infection with helminths (i.e., a diverse group of intestinal parasites including round-, whip- and hookworms) and schistosomes. The

[2] Intravenous iron therapy is a strategy to improve iron status; however, the application of this therapy in low- and middle-income countries is still a research topic.

parasite species, maternal nutritional status, and presence of comorbidities such as malaria and human immunodeficiency virus (HIV) influence the extent of morbidity (Aderoba et al. 2015; Blackwell 2016).

Population-based deworming programs recommended by WHO consider mass drug administration, targeted chemotherapy, and selective therapy (WHO 2017). However, the available evidence is limited. Cochrane systematic reviews of the interventions informing the guidelines showed very low to moderate strength evidence to support the impact of deworming on anemia reduction (Salam et al. 2015). A review of four trials showed a significant impact of a single anthelmintic dose on third trimester anemia, but the quality of the evidence was considered low (Salam et al. 2015).

Evidence from single studies shows positive effects of deworming. In Calabar, Nigeria, women who received deworming regimens during pregnancy only had half the prevalence of anemia in the peripartum period compared to those not receiving the intervention (Akpan et al. 2018). A four-month program of weekly deworming and folic acid supplementation among women of reproductive age resulted in a lower prevalence of low-birth-weight infants compared to controls (Passerini et al. 2012).

Postpartum Hemorrhage

- Anemia during pregnancy can increase the risk of PPH (≥ 500 milliliters blood loss < 24 hours after delivery).
- PPH occurs in 6 percent of all births globally and is the most common cause of maternal deaths across the world.
- PPH is responsible for more than 25 percent of maternal deaths annually and contributes to postpartum anemia in 31–75 percent of cases.
- Effective tools for prevention and treatment of PPH are available, but most are not feasible or practical for use where many births still occur at home with untrained birth attendants.
- Many uterotonics (i.e., drugs that produce adequate uterine contraction) known to be effective in reducing PPH in tertiary care settings may not be useful in community settings because they require refrigeration and/or skilled administration.

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