The American Journal of Clinical Nutrition 117 (2023) 1059–1060

American Society for Nutrition
Excellence in Nutrition Research and Practice

The American Journal of CLINICAL NUTRITION

journal homepage: https://ajcn.nutrition.org/

Editorial

Iron Deficiency in Pregnancy: A Health Inequity

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In 2022, the WHO estimated that anemia affects >40% of pregnant women worldwide [1], making it an important priority for women's health globally. However, as has been noted previously [2], the choice of hemoglobin threshold values is of course of utmost importance when one defines anemia. There are variable reference ranges by sex, race, and gestational status that have physiologic bases that accurately reflect health, but what could be the rationale for cutoffs based on a social construct, such as race?

In this issue of *the American Journal of Clinical Nutrition*, Kang et al. [3] analyzed a 10-y retrospective study of pregnant women at a single urban academic medical center to describe hemoglobin concentrations across gestation and reported race and ethnicity. Anemia was defined as hemoglobin concentration of <11.0 g/dL in trimesters 1 and 3 and <10.5 g/dL during the second trimester. As suggested by the United States CDC, race-adjusted cutoffs for anemia in pregnant Black women were used; these are 0.8 g/dL lower than that for pregnant White women [4]. Iron deficiency (ID) was defined as SF concentration of <15 ng/mL for all groups. Twenty percentage of the population self-identified as Black. More than one quarter of the study population was anemic at any stage of gestation, and the prevalence of anemia increased throughout gestation. Black women showed a significantly lower mean hemoglobin concentration than White women by a mean of 0.8 g/dL. The authors found a 5-fold increase in anemia as pregnancy progressed. Black women also demonstrated lower increase in hemoglobin from the nadir to term than other groups. The RRs of anemia among Black compared with White women were 3.23 in the first trimester, 6.18 in the second trimester, and 2.59 in the third trimester, without applying CDC race-adjusted anemia cutoffs. The effect of ID in this cohort was also assessed. Iron supplements were prescribed to 11% of the population. Of the 41,226 pregnancies, only 2.3% (n = 965) had ferritin data recorded. This is an atrociously low number of women screened given the prevalence and severity of ID during pregnancy. Of patients with anemia and ferritin values, 52.9% (288/544) had ferritin concentration of <15 ug/ml. Importantly, many hematologists believe that ferritin concentration of >50 ng/mL is an optimal marker for iron repletion, 30–50 ng/mL is consistent with iron insufficiency, and <30 ng/mL is consistent with ID [5]. However, many studies—including this one by Kang et al. [3]—use much lower ferritin thresholds to identify ID. Thus, more than half of the screened patients in this study showed severe ID, and the number of patients with any ID (ferritin concentration <50 ng/mL) was likely significantly higher. Notably, hemoglobin concentrations after 30 wks of gestation were significantly higher among women with any supplemental iron dose than in those not taking supplemental iron. This study adds to the large body of literature that observes high rates of anemia and ID among pregnant women with low rates of assessing and properly addressing ID [6]. The rates of anemia were substantial, were higher among Black women than those among White women, and increased throughout pregnancy.

How are we to understand the higher rates of anemia in Black women? There is a clear physiologic justification for different hemoglobin ranges for men and women attributed to sex hormones and for differences in gestational trimesters owing to differential increases in erythrocytes and blood volume [7]. In addition, the CDC and various other bodies have also suggested different hemoglobin ranges by race; NHANES recommends hemoglobin lower limit of 11.3 g/dL for Black women compared with 12.2 g/dL for White women [8], and the American College of Obstetrics and Gynecology recommends an anemia threshold of <11 g/dL for non-Black women and <10.2 g/dL for Black women [9]. The physiologic basis of these thresholds is unclear. Race, unlike biological sex, chronological age, or gestational age, is a social construct with no biologic or scientific underpinnings [10]. In fact, there is often more genetic variation within races than between races [11]. There is now increasing recognition of the dangers of race-based medicine owing to unacceptable excess harm toward

DOI of original article: https://doi.org/10.1016/j.ajcnut.2023.01.022.

Abbreviations: ID, Iron deficiency.

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https://doi.org/10.1016/j.ajcnut.2023.04.024
Received 24 March 2023; Received in revised form 18 April 2023; Accepted 19 April 2023
Available online 21 April 2023

non-White populations when race-based algorithms are used [12]. When one applies differential cutoffs to signify diseases that are without a physiologic basis, one is essentially defining a group to a lower standard, normalizing pathology, and excluding a group from appropriate treatment.

Race is likely an indirect proxy for the true causes of higher rates of anemia in Black women at a population level, such as baseline ID because of lack of access to iron-rich foods, higher rates of inaccessibility to the health care system, lower rates of screening for ID, and pervasive normalization of lower hemoglobin concentrations. If despite the adjusted hemoglobin, lower limits in Black women rates of anemia are as high as noted in the study by Kang et al., [3] the true prevalence in Black women is certainly even higher. Reference intervals are the foundation of how we view normal and abnormal values. If the reference ranges do not accurately reflect states of health for all people, we inappropriately normalize the states of disease.

Despite the well-known high prevalence of ID in pregnancy, at best, only 40% of pregnant women are screened, and women of lower socioeconomic status are less likely to be screened [13]. Both anemia as a late complication of ID and ID alone contribute to poor maternal and fetal outcomes, including postpartum hemorrhage and adverse neurodevelopmental outcomes [14]. In its most recent statement on the matter, the United States Preventative Services Task Force stated that "current evidence is insufficient to assess the balance of benefits and harms of screening for iron deficiency anemia in pregnant women to prevent adverse maternal health and birth outcomes" [15]. Indeed, although there is a plethora of evidence showing iron supplementation in pregnancy improves hemoglobin [14], data on patient-centered maternal and infant outcomes are lacking. The United States Preventative Services Task Force is currently updating guidance on ID anemia in pregnant women; we await their recommendations with cautious optimism.

Our obligation in medicine is to investigate and identify why there are differences in anemia rates by the social construct of race, rather than merely adjust reference ranges to normalize lower hemoglobin concentrations. Anemia in pregnancy remains a significant health burden affecting women. We need consensus on the definition of ID and anemia. Ultimately, we need pragmatic clinical trials powered to elucidate superior strategies to identify and manage ID and anemia during pregnancy, which will result in improved maternal, fetal, and infant outcomes, and implementation plans of action to ensure uptake by the medical community. The problem of ID and anemia during pregnancy is an example of the intersection of systemic medical sexism and racism. Multiple, sustained, systematic interventions will be required to address this inequity. Creating a healthier world is dependent on improvements in the health of all women.

Funding

The authors reported no funding received for this study.

Acknowledgments

The authors responsibilities were as follows – LEM: wrote the first draft of the manuscript; MOA: edited the manuscript; and both authors: read and approved the final manuscript.

MOA is a member of the Scientific Advisory Board of Pharmacosmos, the manufacturer of Monofer and reports a relationship with Pogust Goodhead US that included paid expert testimony. LEM reports no conflicts of interest.

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Update

The American Journal of Clinical Nutrition
Volume 118, Issue 5, November 2023, Page 1069

DOI: https://doi.org/10.1016/j.ajcnut.2023.09.024

The American Journal of Clinical Nutrition 118 (2023) 1069

The American Journal of CLINICAL NUTRITION

journal homepage: https://ajcn.nutrition.org/

Corrigendum to 'Iron Deficiency in Pregnancy: A Health Inequity' Am J Clin Nutr. 2023 Jun;117(6):1059-1060

The authors regret the following errors:

1) In the sentence "As suggested by the United States CDC, race-adjusted cutoffs for anemia in pregnant Black women were used; these are 0.8 g/dL lower than that for pregnant White women.", the editorial references #4 which is M. M. Achebe et al and not reference #2 Earl and Woteki for the IOM report, which is the actual source for the statements, not CDC.

Response:

This statement is corrected to "As suggested by an Institute of Medicine (now National Academy of Medicine) report, race-adjusted cutoffs for anemia in pregnant Black women were utilized; these are 0.8 g/dL lower than that for pregnant White women".

A reference that was present in earlier versions of the editorial manuscript, Sachdev H.S et al. Lancet Glob Health. 2021 Jun;9(6):e822-e831, got deleted inadvertently and subsequent references, such as Earl and Woteki, became misaligned.

2) Additional comments attributed specifically to CDC cite reference #8 ACOG clinical guidance instead of reference #7 Vital Health Statistics by CDC authors.

These references were also misaligned by the same error.

3) The 2007 retired ACOG clinical guidance is cited instead of the 2021 ACOG current guidance, which explicitly reverses prior 2007 guidance and states on page e58 "There are disparities in the distribution of hematocrit and hemoglobin by race. The National Academy of Medicine (formerly known as the Institute of Medicine) historically recommended a change in the threshold for diagnosis of anemia based on race for this reason (18). However, since the etiology of these disparities is unknown and using a different standard may result in a failure to identify and treat people at risk for adverse pregnancy outcomes related to anemia, the same criteria should be used for all populations."

This statement is corrected to reflect the updated guidance in 2021. The correction is as follows:

Remarkably, in contradistinction to American College of Obstetrics and Gynecology (ACOG) 2007 recommendation of an anemia threshold of <11 g/dL for non-Black women and <10.2 g/dL for Black women, ACOG 2021 current guidance notes that disparities of unknown cause attributed to race may result in a failure to identify and treat people at risk for adverse pregnancy outcomes related to anemia, therefore the same criteria should be used for all populations [1]. The authors agree with this update.

The authors would like to apologize for any inconvenience caused.

Reference

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DOI of original article: https://doi.org/10.1016/j.ajcnut.2023.04.024.

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https://doi.org/10.1016/j.ajcnut.2023.09.024

Available online 6 October 2023