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Original Research Article

Hemoglobin distributions and prevalence of anemia in a multiethnic United States pregnant population

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A B S T R A C T

Background: Few normative longitudinal hemoglobin data are available to estimate the prevalence and risk factors for anemia among a multiethnic United States pregnant population.

Objectives: The aim of this study was to characterize hemoglobin distributions and prevalence of anemia in a pregnant population receiving care at a large urban medical center.

Methods: A retrospective medical chart review was undertaken in 41,226 uncomplicated pregnancies of 30,603 pregnant individuals who received prenatal care between 2011 and 2020. Mean hemoglobin concentrations and anemia prevalence in each trimester and incidence of anemia during pregnancy in a subset of 4821 women with data in each trimester were evaluated in relation to self-reported race and ethnicity and other possible risk factors. Risk ratios (RRs) of anemia were determined using generalized linear mixed-effects models. Smoothed curves describing changes in hemoglobin across pregnancy were created using generalized additive models.

Results: The overall prevalence of anemia was 26.7%. The observed fifth percentiles of the hemoglobin distributions were significantly lower than the United States CDC anemia cutoffs in the second and third trimesters (T3). The RR (95% CI) of anemia were 3.23 (3.03, 3.45), 6.18 (5.09, 7.52), and 2.59 (2.48, 2.70) times higher in Black women than that in White women in each trimester, respectively. Asian women recorded the lowest risk of anemia compared with other racial groups in T3 (compared with White womenRR: 0.84; 95% CI: 0.74, 0.96). Hispanic women presented a higher risk of anemia in T3 than non-Hispanic women (RR: 1.36; 95% CI: 1.28, 1.45). In addition, adolescents, individuals with higher parity, and those carrying multiple fetuses experienced a higher risk of developing anemia in late gestation.

Conclusions: Anemia was evident in more than one-quarter of a multiethnic United States pregnant population despite current universal prenatal iron supplementation recommendations. Prevalence of anemia was higher among Black women and lowest among Asian and White women.

Keywords: hemoglobin, anemia, pregnancy, multiethnicity, race and ethnicity, electronic health records, longitudinal data

Introduction

Gestational anemia has been associated with adverse maternal and neonatal birth outcomes including preeclampsia, maternal mortality, low birth weight, small-for-gestational age, preterm birth, stillbirth, and perinatal and neonatal mortality [1–3]. Universal prenatal iron supplementation is recommended in the United States to combat anemia, but in 2015, the United States Preventive Services Task Force concluded that although routine iron supplementation during pregnancy improved maternal hematologic indexes, existing evidence was insufficient to recommend routine iron supplementation during pregnancy to prevent adverse maternal health and birth outcomes, and more data on risks and benefits of routine iron supplementation were needed [4]. The NIH Office of Dietary Supplements followed up on this report with a workshop highlighting the limited amount of national cross-sectional data and total absence of any national longitudinal data on the prevalence of iron deficiency (ID) and IDA among United States pregnant individuals [4]. Data indicated that ID screening among

Abbreviations: EHR, electronic health records; GWG, gestational weight gain; Hb, hemoglobin; HEIRS, Hemochromatosis and Iron Overload Screening; ID, iron deficiency; RR, risk ratio; SMH, Strong Memorial Hospital; T1, first trimester; T2, second trimester; T3, third trimester.

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pregnant individuals is not common [5,6], and ferritin stores are often not evaluated in those with anemia to determine whether anemia is due to ID [7]. These knowledge gaps have been highlighted by the most recent American College of Obstetricians and Gynecologists Practice Bulletin [8].

Accurate definitions of anemia are needed to effectively identify those who will benefit from iron supplementation. The current gestational anemia cutoffs were first proposed in 1968 [9], based on data from European women [10–14]. Technical meetings held by both WHO and American Society of Hematology in 2017 concluded that these cutoffs merited reevaluation [15]. The existing United States CDC cutoffs for gestational anemia were derived from the European studies undertaken >4 decades ago ($n = 394$), in a population where 83% of the pregnant individuals studied received a high-dose oral iron supplementation [16–19]. Characteristics of current United States pregnant individuals are dramatically different from the CDC reference populations in race and ethnic composition, prepregnancy BMI, and supplemental prenatal iron intake [20].

To address existing gaps in the literature, we undertook a 10-y retrospective medical chart review of all pregnant individuals receiving prenatal care at an urban academic medical center to characterize hemoglobin (Hb) distributions across gestation as a function of self-reported race and ethnicity. Hb distributions were compared with the current CDC anemia cutoffs, and risk factors associated with anemia were characterized.

Methods

Study design

A retrospective medical chart review was undertaken in pregnant individuals who received prenatal care between 2011 and 2020 at Strong Memorial Hospital (SMH) and Highland Hospital in Rochester, NY. Deidentified data on maternal demographic, anthropometric, and health-related characteristics were obtained from electronic health records (EHR) by an honest broker. This study was approved by the Institutional Review Boards of the University of Rochester and Cornell University.

Demographic and biometric measurements and definitions

Demographic information included maternal age at delivery and self-reported race and ethnicity following NIH race/ethnicity reporting criteria. Race was grouped into one of four categories for analysis purposes: Asian, Black, White, or other, as detailed in Supplemental Table 1. Ethnicity was grouped into one of three categories: Hispanic, Non-Hispanic, or unknown, as detailed in Supplemental Table 1. Anthropometric data included maternal height measured during the first trimester (T1), self-reported prepregnancy body weight, and measured maternal weight across gestation. Prepregnancy BMI (in kg/m^2) was classified as underweight (<18.5); healthy weight (18.5 to <25.0); overweight (25.0 to <30.0); obesity (30.0 to <40) or severely obesity (≥40.0) [21]. Gestational weight gain (GWG) was calculated based on the third trimester (T3) weight minus the prepregnancy weight and categorized as less than, equal to, or greater than recommended based on the Institute of Medicine guidelines [22]. Self-reported smoking status was reported as "never smoked," "passive smoking," "quit smoking," or "currently smoking." Adequacy of prenatal care was determined using Kotelchuck method [23]. Over this period of time, prenatal iron-containing supplements were universally recommended for all pregnant individuals. If the medical chart indicated that the individual had been prescribed iron supplements (in addition to their prenatal supplementation), this information was abstracted and documented.

Biochemical analyses and definitions

The primary outcome in this study was the Hb concentration during pregnancy. Hb and SF analyses were undertaken at SMH in a CLIA-certified laboratory. For individuals who had multiple Hb measurements within the same trimester of pregnancy, the mean concentration was used for analysis purposes. For those who had two Hb measurements ($n = 154$) on the delivery date, the higher Hb value was used. Anemia was defined using CDC criteria as Hb < 11.0 g/dL in T1/T3, or <10.5 g/dL during the second trimester (T2) [24]. Anemia was also evaluated using race-adjusted cutoffs in Black individuals (lowered by 0.8 g/dL) as indicated by CDC [20]. In people diagnosed with anemia, IDA was defined if SF data were available, and any values obtained were <15 μg/L [25].

Statistical analyses

Descriptive statistics were calculated as the mean ± SD or median (IQR) for continuous variables or counts and percentages for categorical variables. The weeks of gestation at which the nadir or peak Hb concentrations occurred was estimated based on bootstrapping resamples ($n = 10,000$) of the population. Smoothed curves describing changes in Hb values across pregnancy were created using generalized additive models. Slopes of the change in Hb values across gestation were constructed using linear models setting race or anemia status as interaction terms in each descending and ascending gestational windows. Mixed-effects multivariable Poisson regression models (with a log-link) were used to identify risk factors associated with prevalence of anemia in each trimester and incidence of anemia during pregnancy. Potential factors for gestational anemia such as maternal age, race, ethnicity, prepregnancy BMI, GWG, parity, multiple gestation pregnancy, smoking status, and prenatal care index were included in the model as independent variables, and mother was set as the random effect to consider individuals who recorded more than one pregnancy in a given trimester. Risk of anemia was evaluated using risk ratios (RRs) with a 95% CI. The statistical testing was 2-sided, and P values of <0.05 were considered statistically significant. All statistical analyses were conducted using R 4.0.3 (R Foundation for Statistical Computing).

Results

Characteristics of the study population

Between 2011 and 2020, 54,453 pregnancies occurred. Those with complicated pregnancies were excluded, resulting in a database that included 42,117 pregnancies (Figure 1). The data set was further cleaned to eliminate data points that were deemed to be biologically implausible: Hb > 20.0 g/dL ($n = 5$) or <5.0 g/dL ($n = 7$), body weight < 35.0 kg ($n = 16$) or >300.0 kg ($n = 6$), or height >2.0 m ($n = 8$) or <1.2 m ($n = 16$). Among the 42,117 uncomplicated pregnancies, 2% ($n = 891$) had no Hb data and, thus, were excluded. The final sample included 41,226 births to 30,603 individuals (Figure 1). Characteristics

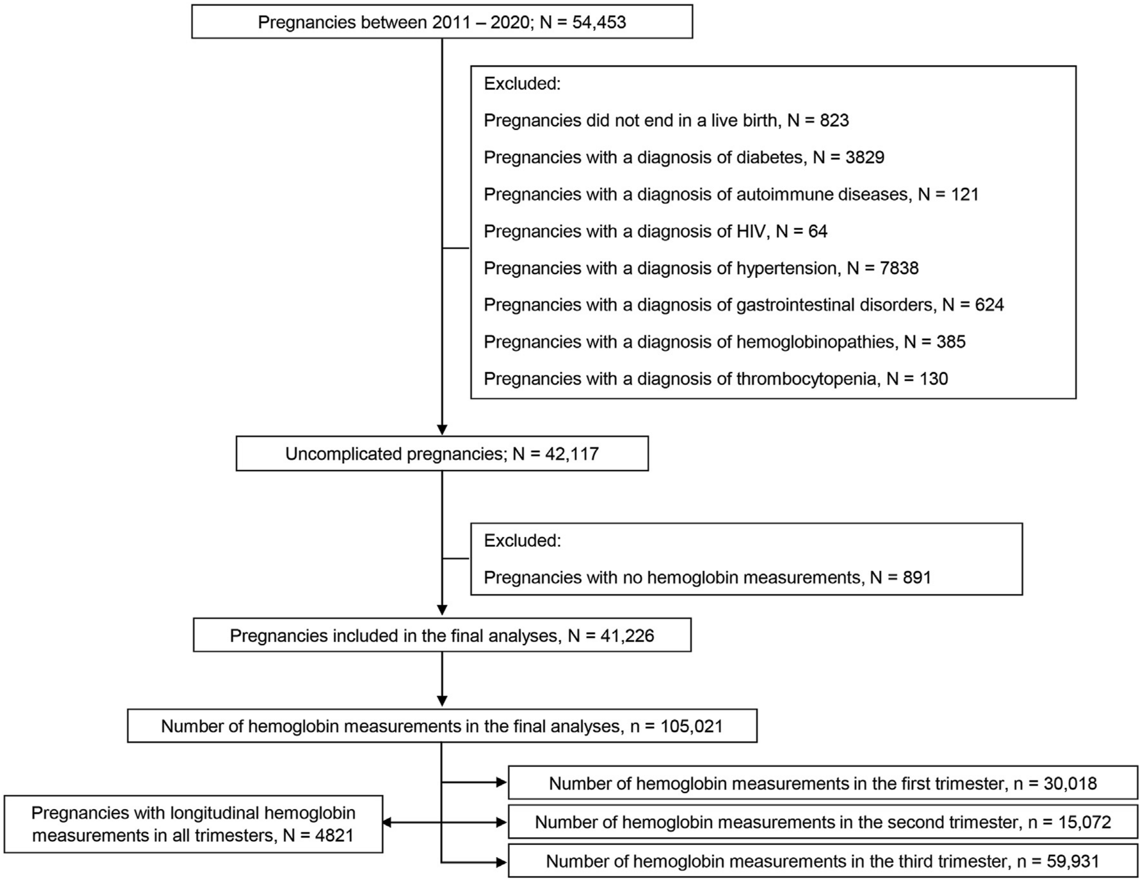

Figure 1. Flow chart of the study population identified from the retrospective medical chart review.

of the final population are presented in Table 1. Among all eligible pregnant individuals included in this study, race was self-identified as Asian (3.9%), Black (20.2%), White (66.5%), or other (9.4%). Most of this population (87.5%) self-identified their ethnicity as non-Hispanic. Among those who received a transfusion during pregnancy (1.4%, n = 588), 4.4% self-identified as Asian, 25.3% as Black, 60.2% as White, and the remaining 10.0% as other.

An average of 2.5 Hb measures were obtained per woman across gestation. Of all Hb measures, 28.6% were obtained in T1, 14.4% in T2, and 57.0% in T3, and 78% of pregnancies had longitudinal Hb data (Figure 1). Among pregnancies with longitudinal Hb data, 0.5% (n = 168) had Hb values measured in T1 and T2, 21.2% (n = 6801) in T2 and T3, 63.3% (n = 20,331) in T1 and T3, and 15.0% (n = 4821) in each trimester of pregnancy (Figure 1). Only 2.3% (n = 965) of the final pregnancy sample had SF data in their EHR. Most of the SF analyses (41.2%) were obtained during T3, followed by T1 (30.2%) and T2 (28.5%). Among pregnancies with available SF data, 20% (n = 192) had more than one SF measure across pregnancy. A total of 150 individuals had SF data available in more than one trimester, of these 24.7% (n = 37) had SF measured in T1 and T2, 34.0% (n = 51) in T2 and T3, 22.7% (n = 34) in T1 and T3, and 18.6% (n = 28) during each trimester. In those with available SF data, self-reported race and ethnicity was 3.9% (Asian), 31.1% (Black), and 56.2% (White). Race distributions among those with SF data differed from the larger population studied, with a greater representation from those who self-reported race as Black (31.1% compared with 20.2%) and a lower representation of data from those who self-identified their race as White (20.2% compared with 66.5%).

Hb distributions and prevalence of anemia among study population

More than one-quarter of the study population (26.7%) was diagnosed with anemia at any stage of gestation, and prevalence of anemia significantly and progressively increased from T1 to T3 (Table 2). Iron supplements were prescribed to 11% of the population (Table 1), and 64.6% of those who were prescribed iron supplements had anemia documented in their medical record in at least one trimester of pregnancy. Those who were prescribed an iron supplement tended to have significantly lower Hb concentrations ($P < 0.001$) and a significantly higher prevalence of anemia ($P < 0.001$). In addition, pregnant adolescents, Black or Hispanic individuals, and those who were underweight were significantly more likely to have documentation of prescribed iron supplementation in their medical records ($P < 0.05$). In the subgroup of individuals with SF data, 52.9% (288/544) of the anemia identified could be attributed to IDA (anemia and SF <15 μg/L). In the population as a whole, the highest mean Hb concentration (13.1 g/dL; 95% CI: 12.9, 13.2 g/dL) was found at 4 weeks of gestation (95% CI: 4, 6 wk), and the nadir of the Hb distribution (11.0 g/dL; 95% CI: 10.9, 11.0 g/dL) occurred at 30 weeks of gestation (95% CI: 27, 31 wk). Marked differences in observed changes in Hb over gestation were evident when stratifying the population by anemia status (Figure 2A). Pregnant individuals with anemia had a more pronounced

Table 1
Characteristics of a multiethnic pregnant population receiving prenatal care in Rochester, NY from 2011 to 2020

Variable	Groups	Mean (SD) or median (IQR)	Total $N = 41,226$, % (n)
Maternal age (y)		29.8 (5.5)[1]	
	<20	18 (2)	3.4 (1405)
	20–35	28.4 (3.9)[1]	76.7 (31,608)
	≥35	37 (4)	19.9 (8213)
Race			
	Asian		3.9 (1594)
	Black		20.2 (8325)
	White		66.5 (27,417)
	Other		9.4 (3890)
Ethnicity			
	Hispanic		8.6 (3556)
	Non-Hispanic		87.5 (36,061)
	Unknown		3.9 (1609)
Prepregnancy BMI (kg/m^2)[2]		25.4 (8.7)	
	Underweight (<18.5)	17.8 (1.0)	3.3 (350)
	Healthy weight (18.5 to <25)	22.0 (1.7)[1]	44.4 (4665)
	Overweight (25.0 to <30)	27.3 (1.4)[1]	25.2 (2643)
	Obesity (30.0 to <40)	34.1 (2.8)[1]	21.2 (2233)
	Severe obesity (≥40.0)	43.8 (5.4)	5.9 (616)
Gestational weight gain (kg)[3]		8.7 (5.7)[1]	
	Underweight (<18.5)	10.0 (5.3)	
	Healthy weight (18.5 to <25)	9.8 (5.4)	
	Overweight (25.0 to <30)	8.9 (5.3)[1]	
	Obesity (30.0 to <40)	6.3 (6.2)[1]	
	Severe obesity (≥40.0)	3.6 (8.2)	
	Less than recommended		53.9 (5614)
	Recommended		27.2 (2838)
	More than recommended		18.9 (1967)
Parity		1 (2)	
	Nulliparous (parity = 0)	0 (0)	39.6 (16,330)
	Primiparous (parity = 1)	1 (0)	34.1 (14,056)
	Multiparous (parity > 1)	2 (1)	26.2 (10,788)
	Unknown		0.1 (52)
Use of assisted reproduction technology			
	Yes		0.7 (271)
	No		99.3 (40,955)
Blood transfusion during pregnancy			
	Yes		1.4 (588)
	No		98.6 (40,638)
Weeks of Gestation		39 (2)	
	Preterm (< 37 wk)	34 (4)	8.6 (3533)
	Not preterm (≥ 37 wk)	39 (1)	91.4 (37,693)
Multiple pregnancy			
	No		97.7 (40,278)
	Yes		2.2 (920)
	Unknown		0.1 (28)
Delivery type			
	Vaginal		71.8 (29,600)
	C-section		26.2 (10,802)
	VBAC		1.1 (445)
	Unknown		0.9 (379)
Adequacy of prenatal care utilization index			
	Inadequate		16.1 (6640)
	Intermediate		2.4 (1000)
	Adequate		8.2 (3365)
	Adequate plus		7.8 (3202)
	Unknown		65.5 (27,019)
Prenatal vitamins prescribed during pregnancy			
	Yes		34.8 (14,346)
	No		65.2 (26,880)
Iron supplementation prescribed during pregnancy			
	Yes		11.1 (4560)
	No or unknown		88.9 (36,666)
Smoking status			
	Never		66.6 (27,464)
	Passive or yes		8.0 (3277)

(*continued on next page*)

Table 1 (*continued*)

Variable	Groups	Mean (SD) or median (IQR)	Total $N = 41{,}226$, % (n)
	Quit		19.5 (8033)
	Not asked or unknown		5.9 (2452)

VBAC, vaginal birth after a cesarean section.

1 Data are presented as median (IQR).

2 The total number of pregnancies with available prepregnancy BMI data was 10,507.

3 The total number of pregnancies with available gestational weight gain data was 10,419.

decline (slope:−0.067; 95% CI:−0.069, −0.067) in Hb values from entry into prenatal care compared with the observed nadir observed among nonanemic individuals (slope:−0.100; 95% CI:−0.102, −0.098; $P < 0.001$), whereas, in late gestation, nonanemic individuals had a greater increase in Hb compared with those who were anemic (slope: 0.080; 95% CI: 0.077, 0.084 compared with 0.038; 95% CI: 0.033, 0.043; $P < 0.001$). After the observed changes in Hb values over gestation were stratified by self-reported race (Figure 2B), Asian women recorded a significantly smaller decrease in Hb values from entry to the nadir (slope: −0.071; 95% CI: −0.077, −0.064) compared with other racial groups (slopes in Black women: −0.080; 95% CI: −0.082, −0.078; other: −0.085; 95% CI: −0.089, −0.082; White women: −0.083; 95% CI: −0.085, −0.082; $P < 0.001$). Black women recorded a significantly lower increase in Hb values from the nadir to term (slope: 0.075; 95% CI: 0.068, 0.082) compared with other groups (slope among Asian women: 0.110; 95% CI: 0.088, 0.133; slope among women classified as other: 0.102; 95% CI: 0.091, 0.114; and slope among women self-identifying as White: 0.099; 95% CI: 0.094, 0.104; $P < 0.001$) (Figure 2C). Of note, the nadir of the Hb distribution occurred significantly later in individuals with anemia (33 wk; 95% CI: 31, 34 wk) compared with nonanemic individuals (26 wk; 95% CI: 20, 25 wk). After excluding individuals with anemia, the descending slopes of Hb concentrations were not significantly different by race, but Asian women had a more pronounced increase in Hb values from week 26 until term (slopes: 0.094; 95% CI: 0.085, 0.103) compared with other racial groups (slopes in Black women: 0.060; 95% CI: 0.055, 0.064; slope among women classified as other: 0.065; 95% CI: 0.059, 0.071; slope among women classified as White: 0.099; 95% CI: 0.063, 0.068; $P < 0.001$) (Figure 2D).

The CDC fifth percentile values in T1, T2, and T3 corresponded to the fifth percentile of our population in T1 but represented the 16th and 27th percentile of the observed Hb distribution in our population at T2 and T3, respectively (Figure 3A). The reported CDC 95th percentile of Hb concentration (15.0 g/dL) was above the 99th percentile in our population, and only 0.55% ($n = 226$) of those studied exceeded this cutoff (Table 2). The data used to develop the CDC criteria were obtained in individuals ingesting ≤200 mg supplemental iron per day. When the original reference data used to generate CDC anemia cutoffs were plotted according to the amount of supplemental iron intake ingested for each of the reference groups (65, 100, or 200 mg/d), the significant effect of the supplemental iron intake on Hb concentrations across gestation was evident (Figure 3B).

Hb distributions and prevalence of anemia by race and ethnicity

The mean Hb concentration was significantly lower among individuals who self-identified as Black than that of those who self-identified as White by an average of −0.8 (T1), −0.7 (T2), and −1.0 g/dL (T3) ($P < 0.001$). Hispanic women recorded significantly lower Hb (mean ± SD: 12.5 ± 1.0 g/dL and 11. 5 ± 1.3 g/dL) than non-Hispanic women (mean ± SD: 12.6 ± 1.0 g/dL and 11.8 ± 1.3 g/dL; $P < 0.001$) in T1 and T3, respectively.

The prevalence of anemia in each trimester as a function of self-reported race/ethnicity and in relation to other characteristics is summarized in Table 3 and Supplemental Table 2, respectively. The prevalence of anemia was highest among Black women in each trimester, whereas White women recorded the lowest prevalence of anemia in T1 and T2 and Asian women the lowest prevalence of

Table 2

Hemoglobin and anemia prevalence across gestation in a multiethnic pregnant population receiving prenatal care in Rochester, NY, from 2011 to 2020

		T1 ($n = 25{,}622$)	T2 ($n = 12{,}101$)	T3 ($n = 40{,}445$)
Hemoglobin (g/dL)[1]	Mean ± SD	12.6 ± 1.0	11.6 ± 1.1	11.8 ± 1.3
Anemia prevalence[2]	% (95% CI)	4.5 (4.3, 4.8)	14.1 (13.4, 14.7)	25.1 (24.7, 25.6)
Anemia prevalence (race-adjusted)[3]	% (95% CI)	2.9 (2.7, 3.1)	8.6 (8.1, 9.1)	20.3 (19.9, 20.7)
Hemoglobin >15 g/dL[4]	% (95% CI)	0.4 (0.3, 0.5)	0.08 (0.04, 0.02)	0.3 (0.2, 0.3)
Observed hemoglobin distribution (g/dL)	5th Percentile	11.0 (10.9, 11.0)	9.8 (9.8, 9.9)	9.6 (9.6, 9.7)
	Median	12.7 (12.7, 12.8)	11.6 (11.5, 11.6)	11.8 (11.8, 11.9)
	95th Percentile	14.1 (14.1, 14.1)	13.3 (13.2, 13.3)	13.8 (13.8, 13.9)
CDC anemia cutoffs[5]		11.0	10.5	11.0

T1, first trimester; T2, second trimester; T3, third trimester.

1 Mean hemoglobin concentrations reflect from the mean hemoglobin concentration observed in each trimester. Differences in mean hemoglobin concentrations between trimesters were significant ($P < 0.001$) as evaluated by linear mixed-effects models.

2 Anemia was defined as hemoglobin <11.0 g/dL in T1/T3 or <10.5 g/dL in T2. Differences between trimesters were significant ($P < 0.001$) as evaluated by mixed-effects multivariable Poisson regression models.

3 Anemia was defined as hemoglobin <10.2 g/dL in T1/T3 or <9.7 g/dL in T2 in Black pregnant individuals and as hemoglobin <11.0 g/ in T1/T3 or <10.5 g/dL in T2 in all other groups. Differences between trimesters were significant ($P < 0.001$) as evaluated by mixed-effects multivariable Poisson regression models.

4 15 g/dL was the 95th percentile of the CDC reference data. Differences between trimesters cannot be evaluated because of the small sample size of pregnant individuals with hemoglobin >15 g/dL.

5 The fifth percentiles of the hemoglobin distribution as reported from the CDC reference data in each respective trimester.

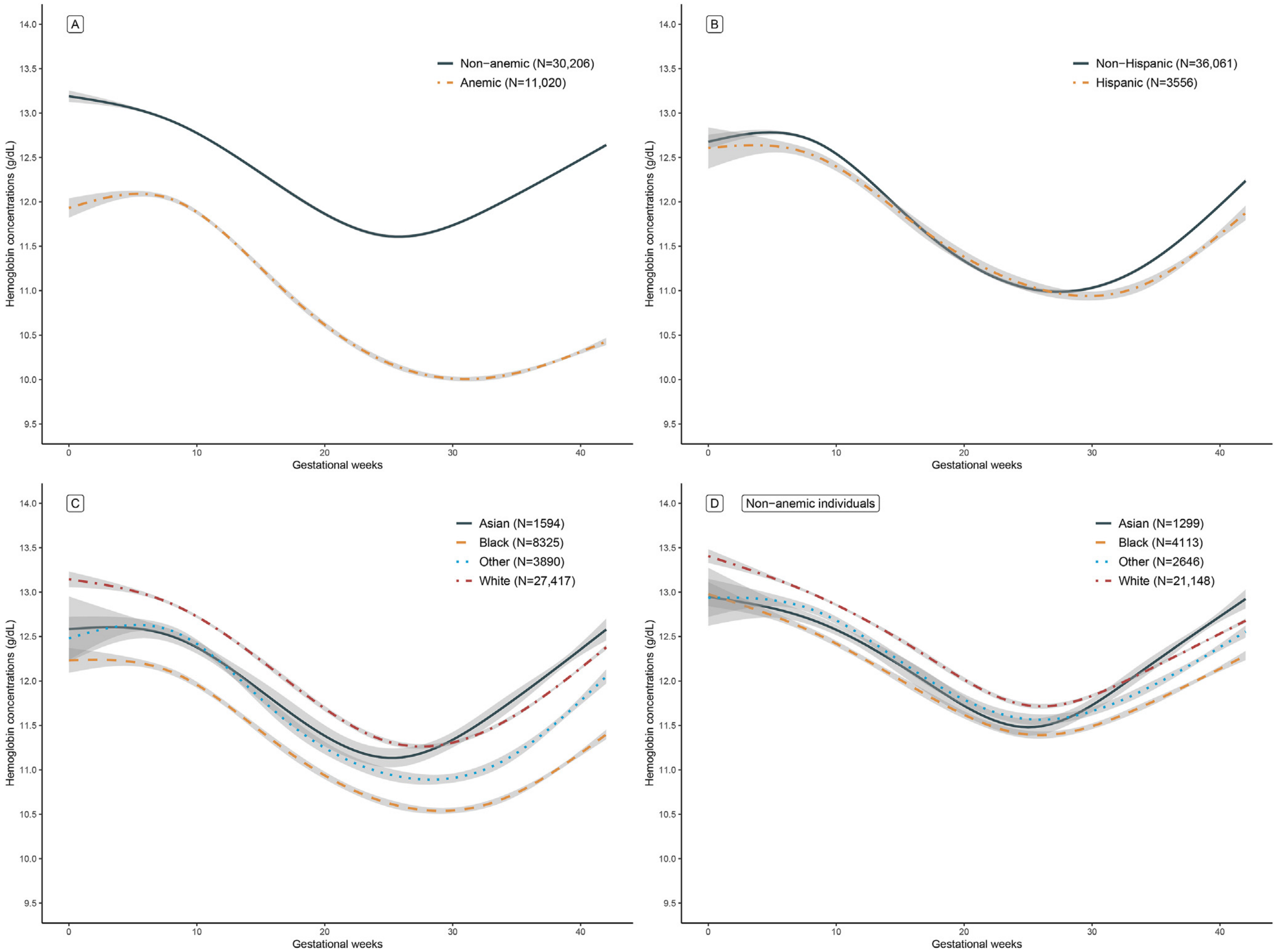

Figure 2. Hemoglobin concentrations across gestation in a multiethnic pregnant population receiving prenatal care in Rochester, NY, from 2011 to 2020. Smoothed curves were created using generalized additive models. Gray areas indicate the CI. Change in hemoglobin across gestation by anemia status (A). Change in hemoglobin concentrations across gestation by ethnic group (B). Mean hemoglobin concentrations across gestation by racial group (C). Mean hemoglobin concentrations across gestation by racial group in nonanemic pregnant individuals (D).

anemia in T3. The RR (95% CI) of anemia among Black women was 3.23 (3.03, 3.45), 6.18 (5.09, 7.52), and 2.59 (2.48, 2.70) times relative to White women in each respective trimester. The RR of anemia did not significantly differ between Asian women and White women in T1 or T2 but in T3: Asian women showed a significantly lower risk of anemia than White women (RR: 0.84; 95% CI: 0.74, 0.96). If applying CDC race-adjusted anemia cutoffs for Black women, the prevalence of anemia remained significantly higher among Black women (24.7%) than that of Asian women (18.5%) or White women (19.2%; $P < 0.001$). The RR of anemia did not significantly differ between Hispanic and non-Hispanic women in T1 or T2, but Hispanic women recorded a significantly higher risk of anemia in T3 than non-Hispanic women (RR: 1.36; 95% CI: 1.28, 1.45).

Risk factors associated with anemia prevalence during pregnancy

We further assessed maternal risk factors associated with the prevalence of anemia in each trimester (Table 4). Self-reported race as Black or other, higher parity, and carrying multiple fetuses were associated with a higher risk of anemia in each trimester. Although some studies have noted an increased risk of anemia among pregnant individuals with obesity [26], no significant association between overweight or obesity and anemia was evident in our study population.

Risk factors associated with the incidence of anemia during pregnancy

We further calculated the incidence of anemia during pregnancy in the subgroup of the population ($n = 4821$) that had longitudinal Hb measures in each trimester of pregnancy. Individuals in this subgroup showed significantly lower mean Hb concentrations (mean ± SD: 11.7 ± 1.0 g/dL and 12.0 ± 1.1 g/dL; $P < 0.001$) and a significantly higher prevalence of anemia across pregnancy (42.0% compared with 24.7%; $P < 0.001$) than the overall cohort. In addition, individuals with younger age, those who self-identified as Black or Hispanic, those who were obese, those with higher parity, and those carrying multiple fetuses were significantly more likely to have Hb measurements documented in their medical records in all trimesters of pregnancy ($P < 0.05$).

The incidence of anemia was 13.1% (586/4475) from T1 to T2, 33.1% (1483/4475) from T1 to T3, and 29.0% (1162/4007) from T2 to T3. Maternal risk factors associated with the incidence of anemia are presented in Table 5. Self-reported Black or other race and individuals

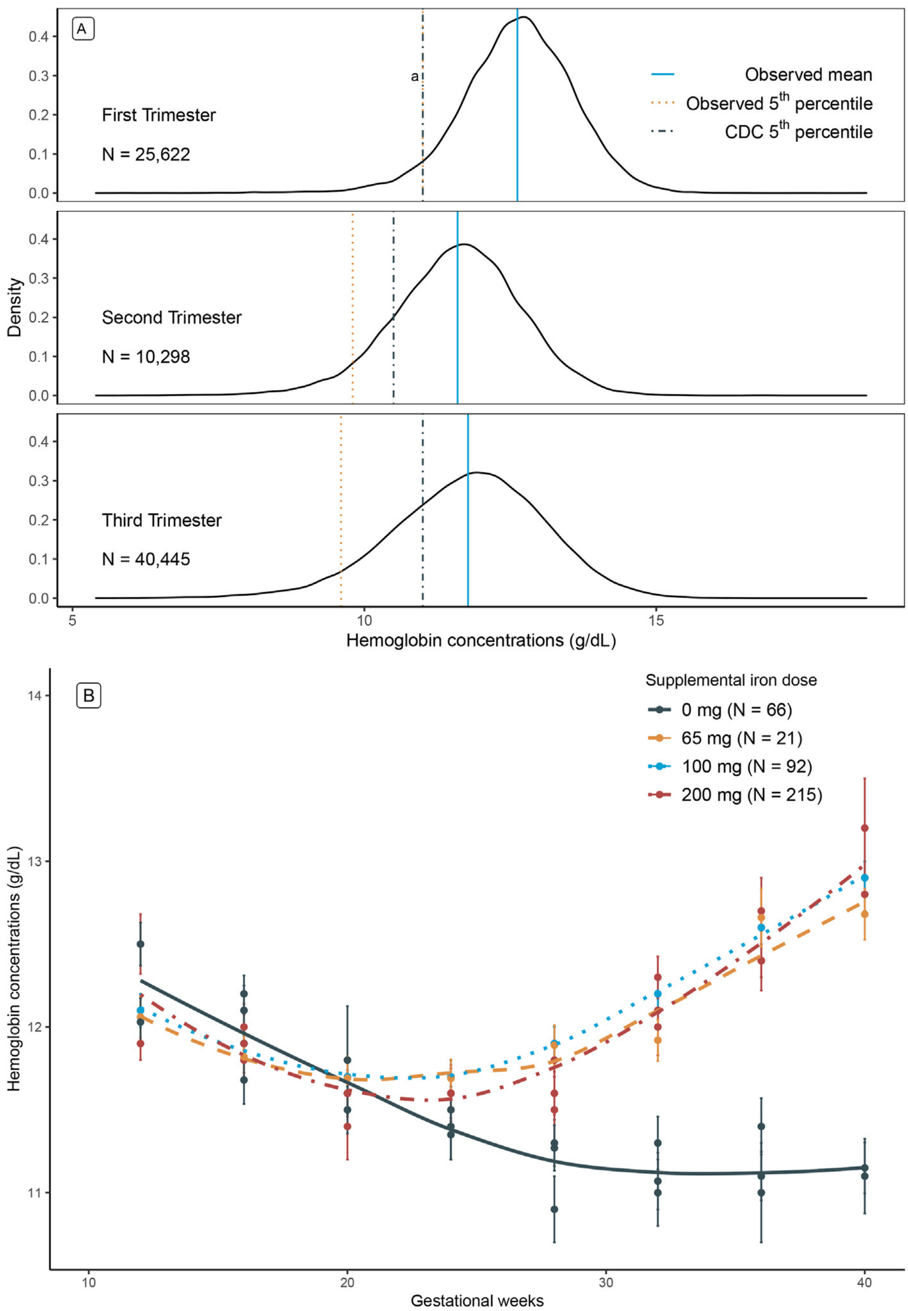

Figure 3. Hemoglobin distributions across gestation in a multiethnic pregnant population receiving prenatal care in Rochester, NY from 2011 to 2020 and in CDC reference population. Hemoglobin distributions in each trimester in a multiethnic pregnant population receiving prenatal care between 2011 and 2020 at Strong Memorial Hospital and Highland Hospital in Rochester, NY (A). Average hemoglobin concentrations (means and SEs) across gestation in the CDC reference population by the supplemental iron dose. Iron supplementation started at 12 or 16 weeks of gestation (B). [a]The observed fifth percentile of the hemoglobin concentration in our population overlapped with the CDC anemia cutoff (11.0 g/dL) in the first trimester but significantly shifted to the left during the second and third trimesters of pregnancy.

carrying multiple fetuses exhibited a higher risk of developing anemia from T1 to T2. Although adolescents, Black individuals, Hispanic women, and those with higher parity recorded a significantly higher risk of developing anemia from early or mid-gestation to late gestation. Pregnant women aged 35 y or older experienced a lower risk of developing anemia in late gestation.

Discussion

To our knowledge, this study is the largest study to evaluate normative longitudinal and cross-sectional data on Hb concentrations and to present the incidence of anemia across gestation in a multiethnic United States pregnant population. Anemia was evident in more than a quarter of these otherwise healthy pregnant individuals using the current CDC anemia cutoffs, and prevalence of anemia increased 5-fold as pregnancy progressed. Black women showed the highest risk of gestational anemia and highest incidence of anemia during gestation, whereas the prevalence of anemia was lowest among White women and Asian women. Non-Hispanic women recorded significantly a higher average Hb and lower risk of developing anemia in late gestation than Hispanic women. Notably, the current CDC anemia cutoffs represented the 5th, 16th, and 27th percentiles of our population in T1, T2, and T3, respectively, and the observed fifth percentiles in our population in T2 and T3 were significantly lower than the fifth percentile values of the reference population used to define the CDC anemia cutoffs.

The prevalence of anemia in this large population was 2–6.5 times higher than that previously reported using data from NHANES, which had a much smaller sample size of 1283 and only included singleton pregnancies [27–29]. Moreover, the NHANES had a lower percentage

Table 3
Anemia prevalence across gestation as a function of self-reported race/ethnicity in a multiethnic pregnant population receiving prenatal care in Rochester, NY from 2011 to 2020[1]

Self-reported race/ethnicity	Prevalence of anemia in pregnancy[2]	Anemia prevalence in T1	Anemia prevalence in T2	Anemia prevalence in T3
Race[3]				
Asian	18.5 (295/1594)[a]	5.7 (57/997)[a]	9.4 (42/449)[ab]	15.3 (241/1572)[a]
Black	50.6 (4212/8352)[c]	13.6 (608/4477)[c]	24.2 (946/3904)[c]	47.6 (3877/8142)[d]
Other	32.0 (1244/3890)[b]	6.1 (132/2175)[b]	15.0 (212/1413)[b]	29.2 (1116/3821)[c]
White	19.2 (5269/27,417)[a]	2.0 (364/17,973)[a]	7.9 (500/6335)[a]	18.3 (4928/26,910)[b]
Ethnicity[4]				
Hispanic	35.1 (1249/3556)[B]	5.1 (139/2748)	13.3 (182/1374)	29.4 (1455/4949)[B]
Non-Hispanic	26.1 (9415/36,061)[A]	4.5 (1019/22,800)	14.1(1462/10,338)	25.5 (8678/35,369)[A]

T1, first trimester; T2, second trimester; T3, third trimester.
[1] Data are presented as % (*n*/total *N*). Differences between racial groups or ethnic groups were evaluated by mixed-effects multivariable Poisson regression models.
[2] The prevalence of women who were classified as anemic at any point over pregnancy (ever-anemic) was calculated based on those who were diagnosed as anemic at any stage of gestation. Anemia was defined as hemoglobin <11.0 g/dL in T1/T3 or <10.5 g/dL in T2.
[3] For different racial groups, values in a column that do not share a lowercase superscript significantly differ from one another ($P < 0.05$).
[4] For ethnic groups, values in a column that do not share a capital letter superscript significantly differ from one another ($P < 0.001$).

of White women (53.5% compared with 66.5%) than our population. In our population, Hb concentrations reached a nadir at 30 weeks of gestation, comparable with what has been reported in the literature [30]. However, the Hb nadir occurred at a significantly later stage of gestation in anemic compared with nonanemic individuals. We speculate that anemic individuals had limited body iron stores, which necessitated a greater use of the maternal Hb pool to meet gestational iron demands.

Notably, the current CDC anemia cutoffs represented the fifth percentile identified in this much larger population in T1, but our Hb

Table 4
Risk factors associated with anemia prevalence in a multiethnic pregnant population receiving prenatal care in Rochester, NY, from 2011 to 2020

Variables	RR (95% CI)		
	T1 (n = 6387)	T2 (n = 4730)	T3 (n = 10,126)
Maternal age (y)			
<20	1.14 (0.66, 1.96)	1.28 (0.97, 1.71)	1.39 (1.20, 1.60)
20–35	Ref	Ref	Ref
≥35	1.09 (0.77, 1.55)	1.03 (0.80, 1.33)	0.77 (0.69, 0.86)
Race			
Asian	2.18 (1.03, 4.62)	1.41 (0.87, 2.28)	0.92 (0.72, 1.18)
Black	6.34 (4.68, 8.59)	3.24 (2.67, 3.93)	2.02 (1.87, 2.19)
Other	2.87 (1.71, 4.83)	2.24 (1.62, 3.08)	1.31(1.14, 1.51)
White	Ref	Ref	Ref
Ethnicity			
Hispanic	1.05 (0.64, 1.07)	0.88 (0.65, 1.19)	1.16 (1.02, 1.31)
Non-Hispanic	Ref	Ref	Ref
Prepregnancy BMI (kg/m^2)			
Underweight (<18.5)	1.09 (0.80, 1.49)	0.90 (0.74, 1.10)	1.07 (0.97, 1.17)
Healthy weight (18.5 to <25)	Ref	Ref	Ref
Overweight (25.0 to <30)	1.09 (0.80, 1.49)	0.90 (0.74, 1.10)	1.07 (0.97, 1.17)
Obesity (30.0 to <40)	0.75 (0.53, 1.04)	0.76 (0.61, 0.94)	0.99 (0.90, 1.08)
Severe obesity (≥40.0)	1.20 (0.77, 1.89)	0.81 (0.59, 1.11)	1.12 (0.97, 1.28)
Gestational weight gain			
Less than recommended	1.03 (0.78, 1.37)	1.07 (0.89, 1.29)	1.13 (1.04, 1.23)
Recommended	Ref	Ref	Ref
More than recommended	0.81 (0.56, 1.18)	0.93 (0.73, 1.19)	0.91 (0.82, 1.02)
Parity			
Nulliparous (parity = 0)	Ref	Ref	Ref
Primiparous (parity = 1	1.08 (0.80, 1.47)	1.25 (1.03, 1.52)	1.38 (1.26, 1.51)
Multiparous (parity > 1)	1.55 (1.14, 2.11)	1.19 (0.96, 1.46)	1.66 (1.52, 1.83)
Multiple pregnancy			
Singleton	Ref	Ref	Ref
Multiples	1.64 (0.81, 3.32)	2.51 (1.82, 3.47)	1.61 (1.31, 1.96)
Smoking status			
Never	Ref	Ref	Ref
Yes or passive	1.02 (0.68, 1.54)	1.04 (0.82, 1.32)	1.09 (0.97, 1.21)

RR, risk ratio; T1, first trimester; T2, second trimester; T3, third trimester. RRs indicate adjusted risk ratios of anemia analyzed using mixed-effect multivariable Poisson regression models.

distribution was significantly shifted to the left for the remainder of pregnancy. A similarly left-shifted Hb distribution was noted in pooled Hb data from 257 population-representative data from 107 countries [31]. An international study of Hb distributions in 3502 healthy pregnant individuals carrying singletons reported similar fifth centile values at T2 and T3 (9.7 and 10.4 g/dL, respectively) [32]. In addition, a recent study of 2000 United States pregnant individuals (self-identified predominantly as White (21.3%) or Hispanic (48.6%) who were prescribed 325 mg ferrous sulfate daily [(65 mg elemental iron) throughout pregnancy] also reported comparable Hb fifth centiles as 11.0 g/dL in T1, 10.3 g/dL in T2, and 10.0 g/dL predelivery [33]. In the CDC reference population of 397 pregnant European individuals, >80% of individuals studied ingested 65–200 mg supplemental iron per day starting at 12 weeks of gestation. This load of supplemental iron is 2–7 times higher than the current United States recommended daily allowance for pregnant population (27 mg/d) [20]. In one of the CDC reference population groups, the authors noted that those receiving therapeutic doses of prenatal iron ($n = 21$) remained normocytic through T3, whereas compromised erythropoiesis was evident in non–iron-supplemented individuals ($n = 24$) [17]. Based on the abovementioned data, we speculate that the markedly lower doses of iron contained in typical prenatal supplements (27 mg) may contribute to the left-shifted Hb distribution in our population because few differences were evident in the first trimester of pregnancy. Another possible concern with the CDC reference data are their exclusion of pregnant individuals with Hb concentrations <12 [19], <10 [18], or <11 g/dL [16], which may have skewed their Hb distribution.

Disparities in Hb concentrations were evident in our population, with a greater risk of anemia among Black women, a finding consistent with many previous epidemiologic studies [27–29,34]. The relative differences in Hb concentrations observed in our population are comparable with the CDC data as mean Hb concentrations were 0.8 g/dL lower in Black women than in White women. Whether this difference in Hb concentrations is due to genetic determinants or other socioeconomic factors is not known, and more information on the factors responsible for these disparities is needed to avoid risk of underdiagnosing anemia or withholding needed blood transfusions.

In this large population of pregnant individuals, Asian women showed a lower prevalence of anemia across gestation and the highest Hb concentrations in late gestation. It is interesting to note that the largest epidemiologic study to date that evaluated iron stores by ethnicity, the Hemochromatosis and Iron Overload Screening (HEIRS) study, also found Asian adults recorded the highest risk of elevated iron status and lower prevalence of ID than Black women or Hispanic women [35,36]. A secondary analysis of the HEIRS data evaluated iron stores in a much smaller cohort that were studied while pregnant or breastfeeding ($n = 1962$), and results also noted that Asian women was associated with a significantly decreased risk of gestational ID compared with White women or Black women [37]. In agreement with these data, direct measures of iron absorption adjusted to a fixed amount of storage iron found a significantly higher iron absorption among nonpregnant Asian women than those of White women [38]. Because excess iron stores cannot be eliminated from the body, using a universal guideline for iron supplementation among nonanemic pregnant individuals may lead to elevated iron stores at maturity and increased risks of diseases associated with iron overload in populations that may have increased iron absorption or greater iron stores [39]. Other studies have found that intermittent iron supplementation regimens may provide fewer side effects than daily supplementation while also optimizing iron absorption [40–42].

This study has some limitations. No data on birth outcomes or neonatal iron status were available to address the effect of gestational anemia on adverse maternal/neonatal birth outcomes or on neonatal iron stores at birth. Data on maternal educational level and socioeconomic status were too scarce to be analyzed and data on C-reactive protein or hepcidin were not available from the EHR because these

Table 5
Risk factors associated with incidence of anemia during pregnancy in a multiethnic pregnant population receiving prenatal care in Rochester, NY, from 2011 to 2020[1]

Variables	T1–T2 ($n = 4609$)	T1–T3 ($n = 4609$)	T2–T3 ($n = 4,609$)
Maternal age (y)			
<20	1.06 (0.70, 1.60)	1.37 (1.07, 1.75)	1.47 (1.11, 1.93)
20–35	Ref	Ref	Ref
≥35	1.02 (0.80, 1.30)	0.76 (0.65, 0.89)	0.71 (0.59, 0.86)
Race			
Asian	1.33 (0.81, 2.18)	0.78 (0.54, 1.13)	0.89 (0.60, 1.31)
Black	2.15 (1.78, 2.60)	1.57 (1.40, 1.76)	1.38 (1.21, 1.57)
Other	1.78 (1.27, 2.49)	0.95 (0.77, 1.18)	0.92 (0.72, 1.16)
White	Ref	Ref	Ref
Ethnicity			
Hispanic	0.91 (0.66, 1.26)	1.39 (1.16, 1.67)	1.39 (1.13, 1.70)
Non-Hispanic	Ref	Ref	Ref
Parity			
Nulliparous (parity = 0)	Ref	Ref	Ref
Primiparous (parity = 1	0.96 (0.78, 1.18)	1.28 (1.12, 1.46)	1.41 (1.21, 1.63)
Multiparous (parity > 1)	0.95 (0.77, 1.17)	1.42 (1.24, 1.63)	1.51 (1.30, 1.77)
Multiple pregnancy			
Singleton	Ref	Ref	Ref
Multiples	2.30 (1.67, 3.15)	1.46 (1.15, 1.86)	1.02 (0.74, 1.41)
Smoking status			
Never	Ref	Ref	Ref
Yes or passive	1.15 (0.89, 1.48)	0.94 (0.79, 1.11)	0.92 (0.76, 1.12)

T1, first trimester; T2, second trimester; T3, third trimester
[1] Data are presented as RR (95% CI). RRs indicate adjusted risk ratios of incidence of anemia analyzed using mixed-effect multivariable Poisson regression models.

biomarkers were not screened. Data on compliance with prescribed prenatal supplementation were not available in the EHR; thus, we were not able to investigate differences as a function of supplementation compliance. The EHR practices evolved across this 10-y period, leading to differences in the medical chart data available across the study interval, and the COVID-19 pandemic occurred during the last year (2020) of this data collection period, which likely affected hospital screening visits.

In conclusion, anemia was evident in more than one-quarter of a multiethnic United States pregnant population who received current universal prenatal iron supplementation recommendations. Prevalence and incidence of anemia was higher among Black women and lowest among Asian women and White women. Our study provides the largest published data to date to describe cross-sectional changes in maternal Hb and longitudinal Hb data to investigate the incidence of anemia during pregnancy in a multiethnic United States pregnant population. Reference data in large obstetric populations that are representative of the current BMI, ethnic diversity, and prenatal supplemental iron intakes are needed to inform guidelines and avoid misclassification of gestational anemia. Future studies are needed to address risks and benefits of universal iron supplementation on maternal health outcomes and neonatal birth outcomes and to investigate the appropriate prenatal iron supplementation dose to optimize maternal and neonatal health outcomes. In addition, data are needed to evaluate maternal iron status in relation to the iron endowment of the newborn when evaluating iron intake recommendations to ensure that the in utero environment supports healthy birth outcomes.

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Author contributions

The authors' responsibilities were as follows—WK, KOO: designed the research, analyzed and interpreted the data, and wrote the manuscript; CI, YW, AC, ZG: assisted with the design of the research, analysis and interpretation of the data, and preparation of the manuscript; KOO: had primary responsibility for final content; and all authors participated in the revision and writing of the manuscript and read and approved the final version of the manuscript.

Conflict of Interest

All authors have no conflicts of interest to declare.

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Data Availability

Data described in the manuscript, code book, and analytic code will be made available on request pending application to the corresponding author and approval.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajcnut.2023.01.022.

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