Prevalence of Iron Deficiency and Iron-Deficiency Anemia in US Females Aged 12-21 Years, 2003-2020

Iron deficiency and iron-deficiency anemia are common, underappreciated conditions with significant morbidity and mortality despite widespread availability of effective treatment. Historically, the focus of screening has been preschool-aged and pregnant persons. The Centers for Disease Control and Prevention recommends anemia screening for nonpregnant female adolescents and women every 5 to 10 years,[1] whereas the US Preventive Services Task Force does not address screening for these populations.[1]

Supplemental content

Although screening for anemia by measurement of hemoglobin level is recommended, there is benefit in identifying and treating iron deficiency in those without anemia because supplementation improves exercise performance and reduces fatigue, and iron deficiency is associated with increased all-cause mortality.[2,3] We examined iron deficiency prevalence among females aged 12 to 21 years to inform future screening strategies.

Methods | This study used National Health and Nutrition Examination Survey (NHANES) cycles from 2003-2010 and 2015-March 2020 (ferritin level was not measured in 2011-2014). NHANES is a series of nationally representative surveys consisting of interviews and physical examinations. Response rates ranged from 51% to 80%. The study protocol was approved by the ethics review board of the National Center for Health Statistics and participants provided informed consent.

Data were extracted for nonpregnant females aged 12 to 21 years. Individuals were excluded for missing data, inflammation, and kidney or liver dysfunction (additional information appears in the eMethods in Supplement 1). The proportion of the population with iron deficiency (ferritin <25 μg/L)[4] was described; and the ferritin cutoffs of 15 μg/L and 50 μg/L were assessed as sensitivity analyses. The prevalence of iron-deficiency anemia (hemoglobin <12 mg/dL by World Health Organization definition and ferritin <25 μg/L) was examined as well as using the hemoglobin cutoffs of 12.5 mg/dL and 13 mg/dL, given debate around this definition.[5] Quasibinomial models were used to generate independent adjusted odds ratios to assess the associations among race and ethnicity, income, food security, menstruation, and body mass index and having iron deficiency or iron-deficiency anemia. Self-reported race and ethnicity (using categories defined by NHANES) were collected to evaluate for associations between social determinants of health and iron deficiency.

The models restricted to menstruating individuals were generated to evaluate the association with years menstruating. The counts were unweighted and the percentages were weighted to account for nonresponse. A 2-sided $\alpha < .05$ was considered statistically significant. Analyses were conducted using the survey package in R version 4.2.2 (R Foundation for Statistical Computing).

Results | There were 4052 individuals who met inclusion criteria and 3490 who had complete data. Of these 3490 individuals, 188 were premenarchal (5.4% [95% CI, 4.2%-6.6%]) (**Table 1**). The overall prevalence of iron deficiency was 38.6% (95% CI, 35.8%-40.9%); 17% (95% CI, 15.4%-19.2%) using a 15-μg/L ferritin cutoff and 77.5% (95% CI, 75.7%-79.3%) using a 50-μg/L cutoff. Premenarchal individuals had a prevalence of iron deficiency of 27.1% (95% CI, 17.1%-37.0%) using a 25-μg/L ferritin cutoff.

The overall prevalence of iron-deficiency anemia was 6.3% (95% CI, 5.2%-7.4%); 11.0% (95% CI, 9.5%-12.6%) using a 12.5-mg/dL hemoglobin cutoff and 17.2% (95% CI, 15.3%-19.1%) using a 13-mg/dL cutoff. Among individuals with iron deficiency, it was not associated with iron-deficiency anemia for 83.6% (95% CI, 80.8%-86.4%).

Table 1. Sample Description Stratified by Iron Deficiency and Iron-Deficiency Anemia Status

	Total (N = 3490)		Iron deficiency (n = 1413)		Iron deficiency anemia (n = 271)	
Characteristics	No.	% (95% CI)[a]	No.	% (95% CI)[a]	No.	% (95% CI)[a]
Age, median (IQR), y		16 (14-18)		16 (14-18)		17 (15-18)
Race and ethnicity[b]						
Non-Hispanic Black	968	14.1 (11.9-16.3)	399	34.2 (27.1-41.2)	143	34.3 (27.2-41.4)
Hispanic	1224	19.0 (16.0-22.1)	544	21.6 (14.1-29.1)	69	21.7 (14.2-29.3)
Non-Hispanic White	1039	59.4 (55.7-63.1)	364	38.0 (28.9-47.0)	42	37.6 (28.5-46.7)
Other[c]	259	7.4 (6.1-8.8)	106	6.3 (2.9-9.7)	17	6.3 (2.9-9.8)
Income-to-poverty ratio, median (IQR)		2.3 (1.1-4.1)		2.3 (1.0-3.9)		1.8 (1.0-3.4)
Below 130% of federal poverty level	1519	32.0 (28.9-35.0)	655	35.0 (30.7-39.3)	125	37.4 (29.8-45.0)
Food insecurity	1355	29.0 (26.5-31.6)	547	29.5 (25.6-33.3)	128	42.8 (35.8-49.8)
Premenarchal	188	5.4 (4.2-6.6)	41	3.8 (2.1-5.6)	3	0.4 (<0.01-0.9)
Body mass index, median (IQR)[d]		22.3 (19.8-26.2)		22.3 (19.9-25.8)		23.1 (20.6-27.0)

[a] Unless otherwise indicated. The percentages were weighted to account for nonresponse.

[b] Self-reported and defined by the National Health and Nutrition Examination Survey.

[c] American Indian or Alaska Native, Asian, Native Hawaiian or Pacific Islander, non-Hispanic multiracial, or other or not listed.

[d] Calculated as weight in kilograms divided by height in meters squared.

Table 2. Adjusted Associations Between Demographic and Menstruation Characteristics and Odds of Iron Deficiency or Iron-Deficiency Anemia

Characteristics	Iron deficiency Adjusted OR (95% CI)	Iron deficiency P value	Iron deficiency anemia Adjusted OR (95% CI)	Iron deficiency anemia P value
Age	0.99 (0.95-1.02)	.57	1.04 (0.98-1.11)	.20
Race and ethnicity[a]				
Non-Hispanic Black	1.37 (1.06-1.68)	.02	4.05 (2.59-6.33)	<.001
Hispanic	1.34 (1.07-1.68)	.01	1.62 (0.97-2.72)	.07
Non-Hispanic White	1 [Reference]		1 [Reference]	
Other[b]	1.20 (0.81-1.76)	.35	1.35 (0.67-2.72)	.40
Below 130% of federal poverty level				
No	1 [Reference]		1 [Reference]	
Yes	1.24 (1.02-1.51)	.03	0.86 (0.60-1.21)	.37
Food insecurity				
No	1 [Reference]		1 [Reference]	
Yes	0.87 (0.70-1.09)	.22	1.50 (1.03-2.18)	.04
Menstruation status				
Premenarchal	1 [Reference]		1 [Reference]	
Menstruating	1.90 (1.12-3.12)	.02	11.21 (3.33-37.7)	<.001
Body mass index	0.98 (0.96-0.99)	.004	1.00 (0.97-1.03)	.97

Abbreviation: OR, odds ratio.

[a] Self-reported and defined by the National Health and Nutrition Examination Survey.

[b] American Indian or Alaska Native, Asian, Native Hawaiian or Pacific Islander, non-Hispanic multiracial, or other or not listed.

In multivariable analyses, non-White race, Hispanic ethnicity, and menstruation were associated with iron deficiency and iron-deficiency anemia. Lower body mass index and poverty were associated with iron deficiency. Food insecurity was associated with iron-deficiency anemia (**Table 2**). When restricting models to menstruating individuals, the number of years menstruating was not associated with iron deficiency (adjusted odds ratio, 1.05 [95% CI, 0.98-1.13]) or iron-deficiency anemia (adjusted odds ratio, 1.05 [95% CI, 0.92-1.21]).

Discussion | Among 12- to 21-year-old US females between 2003 and 2020, iron deficiency affected almost 40% and iron-deficiency anemia affected 6%, with variation by the ferritin or hemoglobin thresholds used. Menstruation was a risk factor for both, but more than one-quarter of premenarchal individuals had iron deficiency.

Limitations of this study include limited granularity of the race and ethnicity data and potential overfitting of the iron-deficiency anemia model because few premenarchal participants had iron-deficiency anemia. However, removing the menstruation variable from the model had minimal effects on other adjusted associations.

Given the high prevalence of iron deficiency found with the majority not associated with iron-deficiency anemia, current screening guidance may miss many individuals with iron deficiency. Although annual screening is recommended for higher-risk patients, risk factors (extensive menstrual blood loss,[6] low iron intake, prior diagnosis of iron deficiency) are not clearly defined and likely result in inconsistent screening.

The frequency of universal screening for iron deficiency and iron-deficiency anemia in menstruating persons and the best ferritin and hemoglobin thresholds should be evaluated. Further study is needed to identify risk factors and inform screening practices among premenarchal individuals.

Angela C. Weyand, MD
Alexander Chaitoff, MD, MPH
Gary L. Freed, MD, MPH
Michelle Sholzberg, MD, MSc
Sung Won Choi, MD, MS
Patrick T. McGann, MD, PhD

Author Affiliations: Department of Pediatrics, University of Michigan Medical School, Ann Arbor (Weyand, Choi); Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital, Boston, Massachusetts (Chaitoff); Susan B. Meister Child Health Evaluation and Research Center, University of Michigan, Ann Arbor (Freed); Department of Medicine, St Michaels Hospital, Toronto, Ontario, Canada (Sholzberg); Department of Pediatrics, Alpert Medical School of Brown University, Providence, Rhode Island (McGann).

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Corresponding Author: Angela C. Weyand, MD, Department of Pediatrics, University of Michigan Medical School, 1500 E Medical Center Dr, Ann Arbor, MI 48109 (acweyand@med.umich.edu).

Author Contributions: Drs Weyand and Chaitoff had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Weyand, Sholzberg, McGann.
Acquisition, analysis, or interpretation of data: Weyand, Chaitoff, Freed, Choi.
Drafting of the manuscript: Weyand, Chaitoff, McGann.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Weyand, Chaitoff.
Administrative, technical, or material support: Weyand, Sholzberg.
Supervision: Choi.

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COMMENT & RESPONSE

California's State Insurance Gender Nondiscrimination Act and Utilization of Gender-Affirming Surgery

To the Editor A recent study[1] investigated the association of California's 2013 Insurance Gender Nondiscrimination Act and utilization of gender-affirming surgery, with the states of Washington and Arizona serving as controls.

We believe that the largest limitation of this study was the use of inpatient databases to estimate rates and patterns in the performance of gender-affirming surgery. Between 2005 and 2019, the analysis identified only 2918 encounters for gender-affirming surgery, with 79.1% for genital surgery. However, the American Society of Plastic Surgeons reported in 2020 that chest reconstruction, which is an outpatient surgical procedure, was the most common type of gender-affirming surgery in the US.[2] Therefore, this study[1] likely underestimated gender-affirming surgery and the effect of nondiscrimination policy. Moreover, the period between 2016 and 2019 should be analyzed separately to account for the effects of Section 1557 of the Affordable Care Act (ACA), introduced in 2016, which prohibits discrimination on the basis of sex and gender identity in any health program receiving federal financial assistance. For example, a nationwide study of 21 293 encounters for gender-affirming chest reconstruction in the ambulatory surgery setting found that these procedures increased by 143.2% from 2016 to 2019, with only 5.5% of patients paying completely out of pocket.[3]

While the authors suggested that federal policy may be difficult to enforce, these study findings emphasize the importance of national legislation supporting nondiscrimination in insurance, as rates of gender-affirming surgery increased substantially after 2016. The politicization of gender-affirming care represents a more pressing driver of interstate differences in gender-affirming surgery.[4]

Rishub K. Das, BA
Brian C. Drolet, MD

Author Affiliations: Vanderbilt University School of Medicine, Nashville, Tennessee (Das); Department of Plastic Surgery, Vanderbilt University Medical Center, Nashville, Tennessee (Drolet).

Corresponding Author: Rishub K. Das, BA, Vanderbilt University School of Medicine, 1161 21st Ave S, Nashville, TN 37232 (Rishub.das@vanderbilt.edu).

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In Reply In response to our study,[1] Mr Das and Dr Drolet raise concern that the population was limited to inpatient gender-affirming surgery. Furthermore, they suggest that the period between 2016 and 2019 should be analyzed separately to account for the effects of Section 1557 of the ACA. This is an incorrect representation of the policy. Section 1557 was implemented in 2010 with the ACA.[2] The final rule issued in 2016 by the Department of Health and Human Services clarified the interpretation and enforcement of the original law to include protections based on gender identity but did not issue new language expanding protections based on gender identity.[3] The 2016 final rule was enjoined in *Franciscan Alliance v Burwell* in December 2016, prohibiting enforcement of the gender identity protections clarified in the final rule[4]; the case was not reopened until December 2018.[5] Section 1557 continues to be litigated in the courts, and its implementation has thus been too inconsistent to robustly study from a health policy standpoint.[6]

To address other trends that may have been occurring in the background of the Insurance Gender Nondiscrimination Act, we used a difference-in-differences study design, whereby we compared California with a control group (Arizona and Washington) that was experiencing the same trends except for exposure to the Insurance Gender Nondiscrimination Act policy change. Specifically, all 3 states were exposed to Medicaid expansion and the ACA, including Section 1557, as well as national trends in gender-affirming surgery. As such, the results presented in our study can be reasonably attributed to the Insurance Gender Nondiscrimination Act, as the effects of other background changes, including Section 1557, were controlled for.

In summary, health care policy must effectively address the disparities in gender-affirming care. Indubitably, any protections for vulnerable populations are better than none, and the importance of helping even one patient on the journey to access of gender-affirming care cannot be denied. However, our research indicates that federal protections, particularly in a politically divided environment, do not in isolation adequately protect this population. States such as California have demonstrated a path forward for safeguarding access to care through health policy and legislation, and as such, we believe other states should follow a similar model.