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Association of Blood Donation with Iron Deficiency among Adolescent and Adult Females in the United States: A Nationally Representative Study

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Abstract

Background: Blood donation results in a loss of iron stores, which is particularly concerning for young female blood donors. This study examines the association of blood donation and iron deficiency among adolescent and adult females in the United States.

Study design and methods: A cross-sectional analysis was performed using data from the 1999–2010 National Health and Nutrition Examination Survey. Females who reported their blood donation history in the preceding year and had serum ferritin (SF) measurements were included. Analyses were weighted and stratified by adolescents (16–19 years; n=2,419) and adults (20–49 years; n=7,228). Adjusted prevalence ratios (aPRs) were estimated by multivariable Poisson regression. Standard errors were estimated by Taylor series linearization.

Results: Geometric mean SF levels (ng/mL) were lower in blood donors compared to non-donors among adolescents (21.2 vs. 31.4; p<0.001) and among adults (26.2 vs. 43.7; p<0.001). The prevalence of absent iron stores (SF<12 ng/mL) was higher in blood donors compared to non-donors among adolescents (22.6% vs. 12.2%; aPR=2.03 [95%CI=1.45–2.85]) and among adults (18.3% vs. 9.8%; aPR=2.06 [95%CI=1.48–2.88]). Additionally, the prevalence of iron deficiency anemia (SF<26 ng/mL and hemoglobin<12.0 g/dL) was also higher in blood donors compared to non-donors among adolescents (9.5% vs. 6.1%; aPR=2.10 [95%CI=1.13–3.90]) and among adults (7.9% vs. 6.1%; aPR=1.74 [95%CI=1.06–2.85]). Similar results were observed in a sensitivity analysis restricted to adolescents aged 16–18 years.

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Conclusions: Blood donation is associated with iron deficiency among adolescent and adult females in the U.S. These national data call for further development and implementation of blood donation practices aimed toward mitigating iron deficiency.

Keywords

blood donor; blood donation; ferritin; iron deficiency; anemia; NHANES

INTRODUCTION

The blood donor profile in the United States (U.S.) is dynamic with adolescents increasingly contributing to the donor pool.^{1–3} In 2015, adolescents aged 16–18 years contributed approximately 1.5 million blood donations.² Although blood donation is largely a safe procedure, adolescents are at a higher risk for acute, adverse donation-related events (e.g., syncope-related injuries).^{4,5} Blood donation may also increase the risk of iron deficiency,⁵ as each whole blood donation removes approximately 200 to 250 mg of iron from the blood donor.⁶ Since adolescents and females typically have lower total blood volumes, a greater proportion of hemoglobin (Hb) and Hb-bound iron is lost following whole blood donation in these populations.⁷ Premenopausal females may also be at a greater risk of post-donation iron deficiency due to lower baseline iron stores (as compared to males and females 50 years) and ongoing blood loss associated with menstruation.^{6,7}

Iron deficiency can progress to anemia and manifest as pica,^{8,9} fatigue,^{10,11} restless leg syndrome,⁹ decreased exercise capacity,¹² and cognitive dysfunction.^{13–16} These issues are of particular concern for young donors who are still undergoing brain maturation.^{17–19} Iron deficiency is measured using a variety of biomarkers, such as plasma or serum ferritin (SF), which correlate relatively well with total body iron stores.²⁰ The SF threshold used to diagnose iron deficiency varies between <9 and <30 ng/mL,¹⁸ reflective of varying degrees of severity in iron deficiency. The sensitivity and specificity of a given SF threshold to diagnose iron deficiency also varies between study populations. The *AABB* Iron Deficiency Working Group recently considered the occurrence of iron deficient erythropoiesis as SF levels less than 26 ng/mL (or <20 ng/mL in females and <30 ng/mL in males) and absent iron stores as SF levels less than 12 ng/mL.¹⁸ A SF concentration less than 12 ng/mL is highly specific for depleted iron stores in the bone marrow.²¹ Iron deficient individuals who have low Hb levels (<12.0 g/dL in females and <13.5 g/dL in males) are considered to have iron deficiency anemia.¹⁸

Numerous cross-sectional and longitudinal studies have shown that younger age, female sex, and increased frequency of blood donation are factors associated with lower SF levels in blood donor populations.^{22–30} In the REDS-II Donor Iron Status Evaluation (RISE) study of adult blood donors from six U.S. blood collection centers, there was a significant association between female sex and iron deficiency, with nearly 1 in 5 female adult blood donors having absent iron stores at the time of enrollment (i.e., prior to blood donation).²⁴ More recently, the Comparison of the History of Donation and Iron Levels in Teen Blood Donors (CHILL) study of adolescent and adult blood donors from two U.S. blood collection centers confirmed that iron deficiency is more common in adolescent—as compared to—adult

donors.²⁶ The prevalence of iron deficiency and iron deficiency anemia in U.S. blood donors, however, has not been well characterized using nationally representative data.¹⁸ In addition, there are limited population-based studies comparing the prevalence of iron deficiency and iron deficiency anemia between blood donor and non-donor populations.

This study examines the association of blood donation and the prevalence of iron deficiency and iron deficiency anemia in a national probability sample of adolescent and adult females in the U.S household population.

MATERIALS AND METHODS

Study Design and Population

We performed a retrospective, cross-sectional analysis of data obtained in the continuous 1999–2010 National Health and Nutrition Examination Survey (NHANES).^{31–34} NHANES is an ongoing complex survey conducted by the National Center for Health Statistics (NCHS) of the U.S. Centers for Disease Control and Prevention (CDC). NHANES uses a stratified, multistage probability sampling design and is designed to generate estimates representative of the noninstitutionalized civilian U.S. population. In addition to a household interview, a follow-up physical examination was conducted at a local mobile examination center (MEC). At the MEC, biologic specimens were collected from consenting participants and stored for laboratory testing. On average, the follow-up physical examination at the MEC occurred approximately two weeks after the household interview.³² Data collection and study procedures were approved by the NCHS Research Ethics Board. Data were de-identified and publicly released in adjacent 2-year cycles by NCHS. This analysis of publicly available data was exempted from review by the Johns Hopkins University School of Medicine Institutional Review Board.

Between 1999 and 2010, female participants aged 16–49 years were continuously eligible to provide data on their past-year blood donation history and were eligible to have their stored sera tested for ferritin levels. The primary analytic sample for this study was restricted to female participants aged 16–49 years who had data on their past-year blood donation history and SF levels. Of note, SF was not continuously measured in older females (aged ≥ 50 years) or males across the entire study period; thus, these populations were excluded from this analysis.

Measurement of Blood Donation History in the Past 12 Months

Data on self-reported history of blood donation in the past 12 months was ascertained at the MEC via a computer-assisted personal interviewing system. Participants were first asked if they had a history of blood donation in the past 12 months and responses were coded as: “yes”, “no”, “refused”, and “don’t know” (Supplemental Table 1). Participants who reported “yes” were further questioned about their time since last blood donation (*“How long ago was [your] last blood donation?”*), providing a response in months between 1 to 12. Persons who had responses coded as “refused” or “don’t know” were considered to have missing data.

Measurement of Serum Ferritin and Hemoglobin Levels

Venous Hb and SF levels were measured using blood specimens collected at the MEC. Venous Hb values were derived using a single beam photometer (Beckman Coulter MAXM Hematology Analyzer in 1999–2006 and Beckman Coulter HmX Hematology Analyzer in 2007–2010).

SF levels were determined by three methods across study period. SF was measured by an immunoradiometric assay in 1999–2003 (Bio-Rad QuantImmune Ferritin IRMA kit), nephelometric immunoassay in 2004–2008 (Roche-Hitachi 912 clinical analyzer), and an antibody-sandwich electrochemiluminescence immunoassay (Roche-Elecys 170 system) in 2009–2010. SF levels (ng/mL) were calibrated across assays in accordance with NCHS documentation available online. In brief, NCHS performed piecewise linear regression to compare percentiles of measured SF in 2003 (Bio-Rad) and 2004 (Roche-Hitachi) in 0.1 increments, yielding the following calibration equations³⁵:

- a. SF 25: $Y_{\text{Roche-Hitachi}} = 1.2534 * X_{\text{Bio-Rad}} + 1.4683$
- b. 25<SF 65: $Y_{\text{Roche-Hitachi}} = 1.2001 * X_{\text{Bio-Rad}} + 1.4693$
- c. SF>65: $Y_{\text{Roche-Hitachi}} = 1.0791 * X_{\text{Bio-Rad}} + 4.8183$

SF levels measured in 2003 (Bio-Rad) were calibrated to the 2004 Roche-Hitachi SF levels by NCHS prior to release using equations (a), (b), and (c). We used the same regression equations to make 1999–2002 (Bio-Rad) SF data comparable to the 2004–2008 (Roche-Hitachi) SF data.

A crossover study conducted by NCHS used Deming regression to compare the 2007–2008 (Roche-Hitachi) SF data to the 2009–2010 (Roche-Elecys) SF data, yielding the following calibration equation³⁶:

- a. $Y_{\text{Roche-Elecys}} = 10^{(0.989 * \text{Log}_{10}(X_{\text{Roche-Hitachi}}) + 0.049)}$

We applied equation (d) to make the Roche-Hitachi-calibrated 1999–2003 SF data and the Roche-Hitachi 2004–2008 data comparable to the 2009–2010 Roche-Elecys SF data.

Measurement of Covariates

Potential confounding variables of the association between blood donation and SF were identified from previous studies, and were included as covariates in this analysis.^{24,28,29}

Sociodemographic data (i.e., age, race/ethnicity, birthplace, educational attainment, and annual family income to poverty level ratio) were collected during the household interview via computer-assisted personal interviewing. History of cigarette smoking was measured during the household interview via computer-assisted personal interviewing for participants aged ≥20 years, while participants aged <20 years reported their cigarette smoking history during an audio computer-assisted self-interview at the MEC. Alcohol use (drinks per week) was measured via computer-assisted personal interviewing at the MEC among participants aged ≥20 years. Data on alcohol use among participants aged <20 years was not publicly available.

Dietary supplement use in the past 30 days was obtained via computer-assisted personal interviewing during the household interview. Participants who reported taking a supplement in the past 30 days were asked to provide the name of the supplement(s) they consumed and physically provide supplement packaging, if available. The reported supplements were linked to an NHANES Dietary Supplement Database, which contains product, ingredient, and blend information for >12,000 supplements. We queried the NHANES Dietary Supplement Database to identify participants who reported taking supplement(s) that contained iron or iron-containing elements (e.g., electrolytic iron, ferrous fumarate, ferric ammonium citrate, and ferrochel) in the ingredient and/or blend fields (regardless of dose). A computer-assisted dietary interview was performed at the MEC, during which participants were asked to report their total food and beverage consumption in the past 24 hours. Reported food items were coded by NCHS to match a United States Department of Agriculture database, containing nutrient information for approximately 13,000 foods and beverages. NCHS approximated the total dietary iron intake in the 24 hours prior to the medical examination by summing the estimated iron content of each food and beverage reported by the participant.

Data on reproductive health (current hormonal contraceptive use and menstruation status in the past 12 months) were obtained at the MEC via a private face-to-face interview in 1999–2002 and a computer-assisted interviewing system in 2003–2010. The question to ascertain menstruation status in the past 12 months varied between surveys. In 1999–2002, participants were asked if they had “regular periods” in the past 12 months, whereas in 2003–2010, participants were asked if they had 1 period in the past 12 months. Pregnancy status was determined by laboratory urine testing; for those missing lab results, we used self-reported pregnancy status ascertained during the private face-to-face interview at the MEC. Data on pregnancy status was not publicly available for participants aged <20 years across the study period. Participants’ weight and height were measured during the physical examination at the MEC to allow estimation of participants’ body mass index (BMI). C-reactive protein (CRP) levels were measured in sera by latex-enhanced nephelometry.

Statistical Analysis

All analyses were stratified by adolescents (16–19 years) and adults (20–49 years). The primary exposure variable of interest was a self-reported history of blood donation in the past 12 months (i.e., blood donor status). The primary outcome was continuous SF levels (ng/mL). We also examined the prevalence of iron deficiency defined at three separate SF thresholds: <26 ng/mL, <20 ng/mL and SF<12 ng/mL. As a secondary outcome, we examined the prevalence of iron deficiency anemia using three definitions: (1) SF<26 ng/mL and Hb<12.0 g/dL; (2) SF<20 ng/mL and Hb<12.0 g/dL; (3) SF<12 ng/mL and Hb<12.0 g/dL.

The distribution of covariates was compared by blood donor status using Rao-Scott χ^2 tests and t-tests, where appropriate. SF was summarized by geometric means and corresponding 95% confidence intervals (CI) by blood donor status and time since last blood donation. Linear regression was used to examine the association of blood donor status with log-transformed SF levels. Poisson regression was used to assess the association of blood donor

status with the prevalence of iron deficiency and iron deficiency anemia. Multivariable models included all potential confounders determined *a priori*. The multivariable model for adolescents was adjusted for age group, race/ethnicity, birthplace, family income to poverty level ratio, history of cigarette smoking, estimated dietary iron intake in the past 24 hours, iron supplement use in the past 30 days, menstruation status in the past 12 months, current hormonal contraceptive use, BMI categories, and CRP quartiles. The multivariable model for adults was adjusted for age group, race/ethnicity, birthplace, educational attainment, family income to poverty level ratio, history of cigarette smoking, current alcohol use, estimated dietary iron intake in the past 24 hours, iron supplement use in the past 30 days, menstruation status in the past 12 months, current hormonal contraceptive use and pregnancy status, BMI categories, and CRP quartiles. The multivariable model for adolescents excluded adjustment for educational attainment due to collinearity with age. BMI categories and CRP quartiles were age-specific measures. Missing covariate data were handled by list-wise deletion in multivariable models.

All analyses were conducted using *svy* commands in Stata/MP, version 15.2 (Statacorp LP, College Station, TX). The medical examination weights provided by NCHS were pooled across cycles and used to account for differential probabilities of selection, unit non-response, and non-coverage of the noninstitutionalized U.S. civilian population. Taylor series linearization was used for robust variance estimation. These methods account for the complex survey design and allow findings to be nationally representative of the noninstitutionalized U.S. female population.³⁴

Sensitivity Analyses

Several sensitivity analyses were conducted to assess the robustness of our findings. First, we performed multiple imputation with chained equations to handle missing data on blood donor status, SF, and covariates (1999–2010). The imputation model included all variables in the main analysis, variables related to the complex survey design (e.g., survey weights), and several auxiliary variables. Twenty complete data sets were created and results were combined using Rubin's rules.³⁷ Second, since we calibrated SF values across multiple assays to maximize our sample size and representativeness of the national population, we performed stratified analyses by the assay used to measure SF levels. More specifically, we performed an analysis restricted to 1999–2002 data (Bio-Rad) and a separate analysis restricted to 2005–2008 data (Roche-Hitachi). Third, we reclassified adolescents as those aged 16–18 years (1999–2010).

RESULTS

The unweighted response rate for females aged 16–49 years in 1999–2010 was 79%, yielding 11,379 individuals who participated in the household interview and medical examination. The analytic sample was restricted to 9,647 participants who reported their blood donation history in the past 12 months (i.e., “no” or “yes”) and had SF measurements. Participants excluded from the primary analytic sample were more likely to be non-Hispanic black and of other/multiracial race/ethnicities than non-Hispanic white (Supplemental Table

2). There were 2,419 adolescents aged 16–19 years and 7,228 adults aged 20–49 years included in the analytic sample.

The prevalence of a self-reported history of blood donation in the past 12 months was 10.7% (95% CI: 9.1%, 12.6%) among adolescents and 6.4% (95% CI: 5.7%, 7.3%) among adults. Table 1 compares characteristics of blood donors and non-donors in the adolescent and adult populations. In both populations, blood donors were predominantly non-Hispanic white and born in the U.S., and most had family incomes above the poverty level threshold. Notably, 21.5% of adolescent blood donors were from families below the poverty level, while only 9.1% of adult blood donors were from families below the poverty level. The percentage of blood donors who reported taking a dietary supplement containing iron in the past 30 days was 21.9% among adolescents and 42.3% among adults. The estimated dietary intake of iron in the past 24 hours was higher among donors versus non-donors, particularly in the adult population.

Geometric mean SF levels (ng/mL) were lower among blood donors than among non-donors in the adolescent population (21.2 vs. 31.4; $p<0.001$) and adult population (26.2 vs. 43.7; $p<0.001$; Table 2). Similarly, the prevalence of iron deficiency was significantly higher among blood donors than among non-donors in both the adolescent and adult populations ($p<0.001$ at all SF thresholds; Table 3). In each age group, a history of blood donation in the past 12 months remained significantly associated with low SF in multivariable analyses ($p<0.001$; Tables 2, 3). Additionally, among blood donors in each age group, lower geometric mean SF levels were also associated with shorter periods since last blood donation (Figure 1).

The prevalence of iron deficiency anemia ($Hb<12$ g/dL and $SF<26$ ng/mL) was 9.5% among adolescent donors and 7.9% among adult donors (Table 4). For all three definitions examined, the prevalence of iron deficiency anemia was higher among blood donors than among non-donors in both age groups. The observed associations between a history of blood donation in the past 12 months and prevalence of iron deficiency anemia were strengthened after accounting for potential confounders in multivariable analyses.

Sensitivity Analyses

SF levels and relative effect estimates reported in the primary analysis were similar to those calculated following multiple imputation ($n=11,379$; Supplemental Table 3). Analyses restricted to data by a single SF assay also supported the primary findings (Supplemental Tables 4, 5). Among participants aged 16–18 years, the donor group had significantly lower SF levels than the non-donor group (geometric mean [ng/mL], 20.7 vs. 31.7; $p<0.001$; Supplemental Table 6). The percentage of 16–18 year olds with SF levels <26 ng/mL (62.9% vs. 36.9%; $p<0.001$), <20 ng/mL (52.9% vs. 26.3%; $p<0.001$), and <12 ng/mL (21.7% vs. 11.1%; $p=0.001$) was significantly higher among blood donors as compared to non-donors (Supplemental Table 6).

DISCUSSION

To the best of our knowledge, this is the first nationally representative study to demonstrate that iron deficiency is more prevalent in blood donors in comparison to non-donors among both adolescent and adult females. Nearly half of the female adolescents who donated blood in the preceding year had evidence of iron deficient erythropoiesis (SF<20 ng/mL). In addition, approximately 1 in 5 female adolescents who donated blood in the preceding year had evidence of absent iron stores (SF<12 ng/mL). There was also a significant association between the reported time since last blood donation and SF levels among female adolescents and adults who reported donating blood in the preceding year. Although the prevalence of iron deficiency anemia was relatively low overall, prevalence of iron deficiency anemia was higher among blood donors than among non-donors in the adolescent and adult populations.

The observed association of blood donation and low SF levels in this cross-sectional study is consistent with longitudinal studies indicating a decrease in SF levels following blood donation.^{25,27} A key strength of the present investigation is its population-based design, which allowed comparisons between blood donors and non-donors. In addition to showing differences in SF levels between blood donors and non-donors, this study showed that donors differ from non-donors in terms of sociodemographic and behavioral/lifestyle characteristics. Thus, it is difficult to directly compare the prevalences of iron deficiency observed in this population-based study to estimates derived from donor populations from blood collection centers (or blood drives). At enrollment in the CHILL study (i.e., prior to blood donation), 16–18 year old, repeat, female blood donors (32.3%) had a significantly higher prevalence of absent iron stores than 16–18 year old, first-time/reactivated, female donors (18.0%).³⁸ The effect of repeat blood donation may be underestimated in the CHILL study, an even lower prevalence of absent iron stores (11.1%) in the female, non-donor (i.e. control) population aged 16–18 years was observed in this study. Similar to the CHILL study, however, a higher prevalence of iron deficiency was observed among female adolescent donors than among female adult donors. The present study builds on the CHILL study by also demonstrating a higher prevalence of iron deficiency in female adolescent donors as compared to the non-donor female adolescent population. Furthermore, adolescent females had lower SF levels than adult females in both the donor and non-donor populations. Collectively, these data highlight the vulnerability of adolescents to blood donation-associated iron deficiency.

This study reports the first systematic estimate of iron deficiency anemia in a nationally-representative population of female blood donors in the U.S. Prevalence of iron deficiency anemia among adolescent and adult female donors was relatively low (<10%). This is likely due to the Hb-screening required for blood donation. Despite this intervention, it is notable that the prevalence of iron deficiency anemia was marginally higher among donors as compared to non-donors. The prevalence of iron deficiency anemia requires further investigation in high-risk blood donor populations (e.g., repeat blood donors). Previous studies have shown that normal Hb levels are lower among non-Hispanic blacks as compared to non-Hispanic whites.³⁹ Due to a limited number of racial/ethnic minority blood donors in the study sample, the race-specific prevalence of iron deficiency anemia could not be examined in this study.

This study has limitations that warrant consideration. The primary exposure variable of interest (history of blood donation in the past 12 months) was measured by self-report and may have been influenced by response biases, such as social desirability bias, acquiescence response bias, and recall bias. Self-reported data on history of *ever* making a blood donation has indeed been shown to have high sensitivity and suboptimal specificity compared to linked national records in Switzerland and Australia.^{40–42} However, it is unclear whether this would extend to self-reported data on history of blood donation in the past 12 months. Karki et al. recently showed that the accuracy of self-reported history of blood donation improved with time since last recorded blood donation in Australia.⁴² It is noteworthy that the prevalence of self-reported blood donation in the past 12 months observed in this study was consistent with generally reported prevalences of blood donation (<10%) in the overall U.S. population.⁴³ Furthermore, the prevalence of self-reported blood donation in the past 12 months was higher among adolescents as compared to adults in this study, consistent with other data demonstrating increasing trends in the proportion of adolescent blood donors in the donor pool.^{1–3} There may also be potential measurement error in SF levels across the primary study population (1999–2010) due to the use of multiple ferritin assays—though it is reassuring that findings were similar when stratifying the analysis by assay type.

This study is further limited by other factors. While these observational data may be subject to residual and unmeasured confounding, we were able to account for a comprehensive list of potential confounders, including oral iron supplement use and CRP levels. In fact, the observed association between history of blood donation in the past 12 months and iron deficiency was strengthened in multivariable models. Nonetheless, this study did not account for other factors related to blood donation, such as lifetime history of blood donation, frequency of blood donation, and type of blood donation, as these data were not collected. In other words, the analysis did not differentiate between first-time and repeat blood donors, or between whole blood donors, plasma donors and apheresis donors. Finally, the findings in this study may not be generalizable to a more recent time period or to other populations, particularly those not experiencing ongoing blood loss due to menstruation (males and post-menopausal females).

With the exception of capillary Hb screening, a minimum weight limit to donate, and an 8-week inter-donation interval for repeat whole blood donations, federal policies and regulations in the U.S. to protect blood donors from the risk of iron deficiency are limited.¹⁸ The *AABB* recently recommended that standard blood donor education be enhanced with additional materials on the potential risks of post-donation iron deficiency.⁴⁴ Actionable interventions beyond education must also be considered to protect blood donors from iron deficiency.⁴⁴ Possibilities include extending the inter-donation interval,⁴⁵ performing ferritin testing prior to donation,^{46–50} and providing iron supplementation.^{49,51–54} The efficacy of these interventions is well established, and there is growing evidence to support the feasibility of implementing these interventions. Age-specific efforts may also be needed to mitigate iron depletion in adolescent blood donors.⁵⁵ Currently, not all states require parental/guardian consent for blood donation.^{55,56} It may be beneficial to extend blood donor education to parents and/or guardians and require parental/guardian consent for blood donation nationwide.⁵⁶ Changes to the eligibility criteria for blood donation should also be

considered to protect adolescents, such as raising the lower age limit for blood donation and/or increasing the minimum estimated total blood volume to donate.^{55,57}

While there will likely be negative operational and economic implications for implementing interventions to protect blood donors,¹⁸ the negative long-term impact of maintaining the status quo may be greater if society does not believe the transfusion medicine community is acting in the best interest of blood donors. The comparatively higher blood donation rates observed among adolescents as compared to adults may be due in part to the prominence of blood collection activities in high schools. Although targeting adolescents may be an easy way to improve blood donation rates in the U.S., failure to address post-donation adverse events and iron deficiency in this vulnerable population may lead to restrictive regulatory requirements in the future, potentially jeopardizing the stability of the blood supply.

In summary, these national data demonstrating an association between blood donation and iron deficiency among adolescent and adult females warrant a public health response, and should be considered in the development of national regulations or accreditation standards.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Geometric mean serum ferritin levels by time since last blood donation among adolescent and adult females in the United States, NHANES, 1999–2010.

Table 1.

Characteristics of the study population by blood donor status in the past 12 months, NHANES, 1999–2010.*

Characteristic	Adolescents (16–19 years)					Adults (20–49 years)				
	Non-donor		Donor		p value	Non-donor		Donor		p value
	N	%	N	%		N	%	N	%	
Total	2236	100.0	183	100.0	-	6853	100.0	375	100.0	-
Age group, years					<.001					.130
16–17	1155	55.8	74	39.3		-	-	-	-	
18–19	1081	44.2	109	60.7		-	-	-	-	
20–29	-	-	-	-		2444	30.5	144	30.7	
30–39	-	-	-	-		2222	33.0	105	27.7	
40–49	-	-	-	-		2187	36.5	126	41.6	
Race/ethnicity					<.001					<.001
Non-Hispanic white	594	59.1	88	77.4		3012	65.9	233	77.6	
Non-Hispanic black	647	14.8	35	7.8		1360	12.6	52	7.4	
Hispanic	897	19.4	54	10.3		2163	15.7	73	10.1	
Other/multiracial	98	6.6	6	4.5		318	5.8	17	4.9	
Family income to poverty ratio					.002					<.001
< 1.0 (below poverty level)	739	24.3	57	21.5		1537	16.6	50	9.1	
1.0–3.0	819	33.3	44	21.7		2562	33.8	109	26.6	
> 3.0	495	34.9	69	51.4		2295	44.1	202	61.5	
Missing	183	7.5	13	5.3		459	5.5	14	2.8	
Educational attainment					<.001					<.001
Less than high school	1521	68.3	102	53.4		1705	16.4	35	7.3	
High school or GED	392	16.6	39	20.4		1499	22.2	63	16.5	
Some college or more	255	13.0	41	25.5		3641	61.3	277	76.2	
Missing	68	2.2	1	0.7		8	0.1	0	0.0	
Birthplace					.139					<.001
U.S. Born	1853	88.6	165	93.0		5080	83.4	339	93.8	
Foreign Born	382	11.4	18	7.0		1772	16.6	36	6.2	
Missing	1	< 0.1	0	0.0		1	< 0.1	0	0.0	
Cigarette smoking history					.214					.169
Never	1317	57.4	99	49.8		4289	58.4	239	64.5	
Ever	884	41.3	83	49.4		2561	41.5	136	35.5	
Missing	35	1.3	1	0.9		3	< 0.1	0	0.0	
Alcohol use (drinks/week)					-					.023
0	-	-	-	-		4733	63.0	215	54.9	
1–3	-	-	-	-		951	16.1	82	22.6	
>3	-	-	-	-		1152	20.7	77	22.2	
Missing	-	-	-	-		17	0.2	1	0.3	
Dietary iron intake (mg)[†]	2197	12.7 (0.9)	181	13.4 (0.6)	.256	6741	13.0 (0.7)	370	14.0 (0.6)	.025

Characteristic	Adolescents (16–19 years)					Adults (20–49 years)				
	Non-donor		Donor		p value	Non-donor		Donor		p value
	N	%	N	%		N	%	N	%	
Dietary supplement use					.659					.009
None	1596	65.7	124	60.3		3195	42.9	137	32.0	
Yes - without iron	249	15.3	25	17.0		1254	22.5	79	25.1	
Yes - with iron	380	18.7	33	21.9		2367	34.1	156	42.3	
Missing	11	0.3	1	0.7		37	0.5	3	0.7	
Menses in past 12 mo.[‡]					.377					.536
None/Irregular	367	12.2	21	8.8		1721	23.1	92	21.2	
At least one/Regular	1865	87.7	162	91.2		5120	76.7	283	78.8	
Missing	4	0.1	0	0.0		12	0.2	0	0.0	
HC use					.320					-
No	1946	81.6	157	77.6		-	-	-	-	
Yes	279	17.8	26	22.4		-	-	-	-	
Missing	11	0.6	0	0.0		-	-	-	-	
HC use / pregnancy status					-					.154
No HC/Not Pregnant	-	-	-	-		4660	74.1	245	68.7	
On HC/Not Pregnant	-	-	-	-		708	13.7	59	18.5	
Pregnant	-	-	-	-		1002	5.3	48	5.5	
Missing	-	-	-	-		483	6.9	23	7.3	
Body mass index (kg/m²)[§]					.039					.455
Underweight	62	3.3	1	0.6		168	3.0	5	1.9	
Normal weight	1339	65.4	101	58.2		2213	37.8	127	35.9	
Overweight	389	14.5	38	21.0		1910	25.6	114	30.8	
Obese	412	14.7	41	19.6		2510	32.8	128	30.9	
Missing	34	2.2	2	0.7		52	0.7	1	0.5	
CRP quartiles					.140					.609
Quartile 1	621	32.5	41	23.0		1799	31.3	109	31.4	
Quartile 2	509	23.7	47	24.3		1656	24.7	84	25.6	
Quartile 3	546	23.2	48	26.6		1677	22.8	95	25.2	
Quartile 4	555	20.4	46	25.2		1719	21.3	87	17.7	
Missing	5	0.2	1	1.0		2	< 0.1	0	0.0	

* Data are unweighted sample sizes (N), weighted column percentages (%), and p values calculated from Rao-Scott chi-square tests, unless specified otherwise.

[‡] Data on dietary iron intake in the past 24 hours were expressed as weighted geometric means (standard deviation). Data were missing for 41 study participants in the adolescent population and 117 study participants in the adult population. P values were calculated from t-tests.

[‡] In 1999–2002, participants were asked if their menstrual cycles were regular in the past 12 months. In 2003–2010, participants were asked if they had at least one menstrual cycle in the past 12 months.

[§] Adult BMI categories were defined as < 18.5 (Underweight), 18.5–24.9 (Normal), 25–29.9 (Overweight), and 30+ (Obese). Cut off levels for defining BMI categories in adolescents were chosen based on NCHS BMI-for-age percentile growth charts.

Abbreviations: GED = general education development; HC = hormonal contraceptive; CRP = C-reactive protein.

Table 2.

Association of blood donation in the past 12 months with serum ferritin levels among adolescent and adult females in the United States, NHANES, 1999–2010.*

SF (ng/mL)	N [†]	Geometric Mean (95% CI)	Univariable		Multivariable ^{§//}	
			β (95% CI) [‡]	p value	β (95% CI) [‡]	p value
Adolescents (16–19 y)						
Non-donor	2236	31.4 (30.1, 32.9)	Ref.	-	Ref.	-
Donor	183	21.2 (18.3, 24.6)	-0.39 (-0.54, -0.25)	<.001	-0.45 (-0.58, -0.31)	<.001
Adults (20–49 y)						
Non-donor	6853	43.7 (42.6, 44.8)	Ref.	-	Ref.	-
Donor	375	26.2 (23.6, 29.2)	-0.51 (-0.63, -0.40)	<.001	-0.54 (-0.66, -0.41)	<.001

*Data are weighted estimates, unless specified otherwise.

[†]N represents the unweighted sample size.

[‡] β represents the absolute difference in natural log-transformed serum ferritin levels estimated by linear regression.

[§]The multivariable linear regression model for adolescents included adjustment for age group, race/ethnicity, birthplace, family income to poverty level ratio, smoking history, dietary iron intake in the past 24 hours, iron supplement use in the past 30 days, menses/regular menses in the past 12 months, hormonal contraceptive use, body mass index, and C-reactive protein levels. Of the 2,419 adolescent participants, 2,105 (87%) had complete information and were included in the multivariable model.

//The multivariable linear regression model for adults included adjustment for age group, race/ethnicity, educational attainment birthplace, family income to poverty level ratio, cigarette smoking history, dietary iron intake in the past 24 hours, iron supplement use in the past 30 days, alcohol use, menses/regular menses in the past 12 months, hormonal contraceptive use and pregnancy status, body mass index, and C-reactive protein levels. Of the 7,228 adult study participants, 6,098 (84%) had complete information and were included in the multivariable model.

Abbreviations: SF = serum ferritin; CI = confidence interval

Table 3.

Association of blood donation in the past 12 months with the prevalence of iron deficiency among adolescent and adult females in the United States, NHANES, 1999–2010.*

Outcome	N [†]	Prevalence (95% CI)	Univariable		Multivariable ^{‡§}		
			PR (95% CI)	p value	PR (95% CI)	p value	
SF<26 ng/mL							
Adolescents (16–19 y)							
Non-donor	2236	37.4 (34.5, 40.3)	Ref.	-	Ref.	-	
Donor	183	60.8 (51.2, 69.6)	1.63 (1.40, 1.89)	<.001	1.80 (1.57, 2.06)	<.001	
Adults (20–49 y)							
Non-donor	6853	25.3 (24.2, 26.5)	Ref.	-	Ref.	-	
Donor	375	48.7 (43.1, 54.4)	1.93 (1.68, 2.20)	<.001	2.05 (1.77, 2.37)	<.001	
SF<20 ng/mL							
Adolescents (16–19 y)							
Non-donor	2236	27.0 (24.5, 29.7)	Ref.	-	Ref.	-	
Donor	183	48.0 (38.4, 57.9)	1.78 (1.47, 2.14)	<.001	1.99 (1.66, 2.38)	<.001	
Adults (20–49 y)							
Non-donor	6853	17.9 (17.0, 18.9)	Ref.	-	Ref.	-	
Donor	375	35.0 (29.4, 41.0)	1.95 (1.63, 2.34)	<.001	2.12 (1.75, 2.58)	<.001	
SF<12 ng/mL							
Adolescents (16–19 y)							
Non-donor	2236	12.2 (10.3, 14.4)	Ref.	-	Ref.	-	
Donor	183	22.6 (15.9, 31.0)	1.85 (1.33, 2.59)	<.001	2.03 (1.45, 2.85)	<.001	
Adults (20–49 y)							
Non-donor	6853	9.8 (9.1, 10.6)	Ref.	-	Ref.	-	
Donor	375	18.3 (13.9, 23.7)	1.86 (1.38, 2.50)	<.001	2.06 (1.48, 2.88)	<.001	

* Data are weighted estimates, unless specified otherwise.

[†]N represents the unweighted sample size.

[‡]The multivariable Poisson regression models for adolescents were adjusted for age group, race/ethnicity, birthplace, family income to poverty level ratio, cigarette smoking history, dietary iron intake in the past 24 hours, iron supplement use in the past 30 days, menses/regular menses in the past 12 months, hormonal contraceptive use, body mass index, and C-reactive protein levels. Of the 2,419 adolescent participants, 2,105 (87%) had complete information and were included in the multivariable analyses.

[§]The multivariable Poisson regression models for adults were adjusted for age group, race/ethnicity, educational attainment birthplace, family income to poverty level ratio, cigarette smoking history, dietary iron intake in the past 24 hours, iron supplement use in the past 30 days, alcohol use, menses/regular menses in the past 12 months, hormonal contraceptive use and pregnancy status, body mass index, and C-reactive protein levels. Of the 7,228 adult study participants, 6,098 (84%) had complete information and were included in the multivariable analyses.

Abbreviations: SF = serum ferritin; PR = prevalence ratio; CI = confidence interval

Table 4.

Association of blood donation in the past 12 months with iron deficiency anemia among adolescent and adult females in the United States, NHANES 1999–2010.*

Outcome	N [†]	Prevalence (95% CI)	Univariable		Multivariable ^{‡§}	
			PR (95% CI)	p value	PR (95% CI)	p value
Hb<12 g/dL and SF<26 ng/mL						
Adolescents (16–19 y)						
Non-donor	2234	6.1 (5.0, 7.5)	Ref.	-	Ref.	-
Donor	182	9.5 (5.5, 15.8)	1.55 (0.89, 2.70)	.119	2.10 (1.13, 3.90)	.019
Adults (20–49 y)						
Non-donor	6841	6.1 (5.5, 6.7)	Ref.	-	Ref.	-
Donor	375	7.9 (5.0, 12.3)	1.30 (0.81, 2.09)	.274	1.74 (1.06, 2.85)	.030
Hb<12 g/dL and SF<20 ng/mL						
Adolescents (16–19 y)						
Non-donor	2234	5.5 (4.4, 6.9)	Ref.	-	Ref.	-
Donor	182	8.3 (4.7, 14.2)	1.50 (0.83, 2.71)	.176	1.96 (1.00, 3.84)	.050
Adults (20–49 y)						
Non-donor	6841	5.5 (5.0, 6.1)	Ref.	-	Ref.	-
Donor	375	7.3 (4.6, 11.5)	1.33 (0.82, 2.14)	.241	1.76 (1.05, 2.97)	.033
Hb<12 g/dL and SF<12 ng/mL						
Adolescents (16–19 y)						
Non-donor	2234	4.1 (3.1, 5.3)	Ref.	-	Ref.	-
Donor	182	6.5 (3.4, 12.3)	1.59 (0.79, 3.22)	.193	2.07 (0.91, 4.75)	.084
Adults (20–49 y)						
Non-donor	6841	4.4 (3.9, 4.9)	Ref.	-	Ref.	-
Donor	375	6.7 (4.0, 10.8)	1.52 (0.91, 2.54)	.108	1.97 (1.13, 3.45)	.018

* Data are weighted estimates, unless specified otherwise.

[†]N represents the unweighted sample size.

[‡]The multivariable Poisson regression models for adolescents were adjusted for age group, race/ethnicity, birthplace, family income to poverty level ratio, cigarette smoking history, dietary iron intake in the past 24 hours, iron supplement use in the past 30 days, menses/regular menses in the past 12 months, hormonal contraceptive use, body mass index, and C-reactive protein levels. Of the 2,416 adolescent participants, 2,103 (87%) had complete information and were included in the multivariable analyses.

[§]The multivariable Poisson regression models for adults were adjusted for age group, race/ethnicity, educational attainment, birthplace, family income to poverty level ratio, cigarette smoking history, dietary iron intake in the past 24 hours, iron supplement use in the past 30 days, alcohol use, menses/regular menses in the past 12 months, hormonal contraceptive use and pregnancy status, body mass index, and C-reactive protein levels. Of the 7,216 adult study participants, 6,091 (84%) had complete information and were included in the multivariable analyses.

Abbreviations: Hb = hemoglobin; SF = serum ferritin; PR = prevalence ratio; CI = confidence interval