Vitamin D, Race, and Risk for Anemia in Children

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Objective To examine the association between 25-hydroxyvitamin D [25(OH)D] deficiency and anemia in a cohort of otherwise-healthy children and to determine whether race modifies the association between 25(OH)D status and hemoglobin (Hgb).

Study design Cross-sectional study of 10 410 children and adolescents ages 1-21 years from the 2001-2006 National Health and Nutrition Examination Survey. Anemia was defined as Hgb less than the 5th percentile for age and sex based on National Health and Nutrition Examination Survey III (1988-1994) data.

Results Lower 25(OH)D levels were associated with increased risk for anemia; <30 ng/mL, adjusted OR 1.93, 95% CI 1.21-3.08, $P = .006$, and <20 ng/mL, OR 1.47, 95% CI 1.14-1.89, $P = .004$. In linear regression, small but significant increases in Hgb were noted in the upper quartiles of 25(OH)D compared with the lowest quartile (<20 ng/mL) in the full cohort. Results of race-stratified linear regression by 25(OH)D quartile in white children were similar to those observed in the full cohort, but in black children, an increase in Hgb in the upper 25(OH)D quartiles was only apparent compared with the lowest black race−specific quartile (<12 ng/mL).

Conclusion 25(OH)D deficiency is associated with increased risk of anemia in healthy US children, but the 25(OH)D threshold levels for lower Hgb are lower in black children in comparison with white children. *(J Pediatr 2014;164:153-8)*.

Seen in 70% of those ≤21 years, deficiency of 25-hydroxyvitamin D [25(OH)D], is highly prevalent in US children and adolescents.[1,2] Non-Hispanic black children and adults have a greater prevalence of 25(OH)D deficiency than non-Hispanic white children.[1,3,4] 25(OH)D is known for its crucial role in bone and mineral metabolism and is increasingly recognized to have extraskeletal effects on immune function, cell proliferation and differentiation, and cardiovascular function.[5,6] An increasing body of evidence suggests that 25(OH)D deficiency also is associated with increased risk for anemia, a common condition experienced by up to 20% of children.[7] Lower levels of 25(OH)D have been independently associated with lower hemoglobin (Hgb) levels and anemia in adults with heart failure, diabetes, and chronic kidney disease (CKD, including dialysis-dependent CKD).[8-12] This association also has been observed in otherwise-healthy adults[13] and in adults ages 60 years and older in the National Health and Nutrition Examination Survey (NHANES) III (1988-1994) and 2001-2006 cohorts.[14] However, this association has not been explored in healthy children.

The objective of this study was to examine the association of 25(OH)D levels with Hgb levels and anemia status in a nationally representative sample of US children. In addition, given the differences in 25(OH)D deficiency by race, we sought to examine whether race modifies the association between 25(OH)D status and Hgb.

Methods

NHANES 2001-2006 is a nationally representative cross-sectional survey of the civilian, noninstitutionalized US population ages 2 months and older performed by the National Center for Health Statistics, which is located within the Centers for Disease Control and Prevention (CDC). NHANES 2001-2006 consisted of an in-home interview followed by a medical evaluation and blood sample collection at a mobile examination center. Within NHANES, Hgb was measured in all chil-

25(OH)D	25-Hydroxyvitamin D
BMI	Body mass index
CDC	Centers for Disease Control and Prevention
CKD	Chronic kidney disease
CRP	C-reactive protein
ESA	Erythropoiesis-stimulating agent
GFR	Glomerular filtration rate
Hgb	Hemoglobin
NHANES	National Health and Nutrition Examination Survey
TIBC	Total iron-binding capacity

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M.A. was supported by the National Institutes of Health (NIH)/National Institute of Diabetes and Digestive and Kidney Diseases [NIDDK] (K23-DK-084116). M.M. was supported by NIDDK (K23-DK-078774), NIH (R01 DK087783), and the American Society of Nephrology (Carl W. Gottschalk Research Scholar grant). The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the National Center for Health Statistics, Centers for Disease Control and Prevention. The authors declare no conflicts of interest.

Portions of this study were presented as a poster at the Pediatric Academic Societies' Meeting, Denver, CO, April 30 - May 3, 2011.

 http://dx.doi.org/10.1016/j.jpeds.2013.08.060

dren >1 year of age in each study year, and 25(OH)D levels were measured in those ages ≥6 years from 2001 to 2002 and in those aged ≥1 year from 2003 to 2006. Of 14 815 children 1 to <21 years included in NHANES 2001-2006, children and adolescents missing data on 25(OH)D levels (n = 1172), Hgb (n = 2612), C-reactive protein (CRP; n = 163), serum folate (n = 33), vitamin B12 (n = 119), or body mass index (BMI; n = 134) were excluded from this analysis. NHANES 2001-2006 was approved by the National Center for Health Statistics Institutional Review Board, and all participants ≥18 years of age provided written informed consent. Consent was obtained from guardians of children <18 years of age, with assent obtained from those 12-17 years.

Demographic variables in the current analysis included age, sex, and race/ethnicity, categorized as non-Hispanic white, non-Hispanic black, Mexican-American, Hispanic non-Mexican, and other. Race/ethnicity data were collected by self-report or, for those <12 years of age, by parent/guardian report. Each participant's height and weight was measured during the examination, and BMI was calculated. BMI percentiles were determined by the CDC's BMI-for-age sex-specific growth charts.[15] Obesity was defined as BMI >95th percentile for age and sex or BMI >30 in those aged ≥18 years.

Hgb was determined with a Coulter Counter Model S-Plus JR (Beckman Coulter, Brea, California). Anemia was defined as Hgb value less than the age- and sex-specific fifth percentile values established in NHANES III (http://www.kidney.org/professionals/KDOQI/guidelines_anemia/images/tables/table39.jpg).[16] In the 25(OH)D quartile analysis, we elected to focus on the association of 25(OH)D levels with Hgb specifically, rather than the risk for anemia, because the definition of "anemia" in individuals of black vs white race is the subject of some debate.[17-24] 25(OH)D was measured at the National Center for Environmental Health, CDC, Atlanta, Georgia, using the DiaSorin radioimmunoassay kit (DiaSorin, Stillwater, Minnesota). To account for observed drifts in the 25(OH)D assay performance (secondary to reagent and calibration lot changes) observed during the period of 2003-2006 compared with 2001-2002, the 2003-2006 data were adjusted by NHANES.[25] A statistical adjustment model based on quality control pool data that encompassed the period of method drift was used as the results would be independent of any empirical trend in the sample participant data, and the new 2003-2006 adjusted 25(OH)D data files replaced the unadjusted 25(OH)D files in November 2010.[25] As a result, 2003-2004 25(OH)D data were adjusted to lower values and 2005-2006 data to greater values than initially observed.[25] 25(OH)D values of <20 and <30 ng/mL defined the thresholds of deficiency and insufficiency, respectively.[2] High-sensitivity CRP was measured by latex-enhanced nephelometry, with normal values defined as ≤0.5 mg/dL.[26] Serum folate (normal values ≥3 ng/dL) and vitamin B12 (normal values ≥200 pg/mL) were measured with the Quantaphase Folate radioassay kit (Bio-Rad Laboratories, Hercules, California).[26] Serum B12 in the 2001-2002 cohort was available only for children ages >3 years but for all ages in 2003-2006.

Variables used in secondary analyses included serum ferritin, measured with the Quantimmune Ferritin IRMA kit (Bio-Rad Laboratories) in 2001-2004, and with the Roche Tina-quant kit on the Hitachi 912 clinical analyzer (Roche Diagnostics Corporation Inc, Indianapolis, Indiana) in 2005-2006, and serum iron and total iron-binding capacity (TIBC), measured colorimetrically (RFA Analyzer; Alpkem Corporation, Clackamas, Oregon) in 2001-2002, and and by a timed-endpoint method using the Beckman Synchron LX20 (Beckman Coulter) in 2003-2006. Transferrin saturation was calculated as the serum iron divided by the TIBC. Serum ferritin, iron, and TIBC were measured in all subjects in NHANES 2001-2002 and limited to those ages 3-5 years and female subjects ≥12 years in 2003-2006. Estimated glomerular filtration rate (GFR) was estimated via use of the bedside equation from the Chronic Kidney Disease in Children Study for those <18 years of age and the Chronic Kidney Disease Epidemiology Collaboration equation for those ≥18 years of age.[27,28] Serum creatinine was not measured in NHANES participants <12 years of age. Family poverty income ratio was calculated by NHANES as a ratio of reported family income to poverty threshold according to family size, state of residence, and year as defined by the US Census Bureau and was included as a socioeconomic indicator.

Statistical Analyses

All statistical analyses were performed with Stata statistical software, version 11.0 (StataCorp, College Station, Texas). Survey commands were used to account for the NHANES complex sampling design. The statistical significance level was set at $\alpha = 0.05$. All statistical analyses were 2-sided. Descriptive statistics are reported as mean and SE, median, and IQR, or proportions as noted. Mean 25(OH)D concentrations according to subgroups were compared by independent sample t tests. Logistic regression was used to examine the association of 25(OH)D deficiency or insufficiency with anemia with adjustment for age, sex, race, obesity, CRP, and serum B12 and folate. Linear regression was used to examine the association of 25(OH)D quartiles (whole population and race-specific) with Hgb. In secondary analyses, we performed logistic regressions as described previously in only those subjects with available markers of iron stores and in those with available creatinine data to calculate estimated GFR.

Results

There were 10 410 children included in the analysis. Demographic and clinical characteristics of the cohort overall and by race are presented in **Table I**. Mean (SE) weighted age of participants was 11.8 (0.13) years, 51.7% were male, 60.8% white, and 14.8% black. Seventeen percent were obese, with a significantly greater proportion of black children meeting criteria for obesity compared with white children (21.5% vs 15.5%, $P < .001$). The median (IQR) 25(OH)D level in the overall cohort was 25 (20, 30).

Table I. Demographic characteristics, 25(OH)D levels, and anemia status in US children 1 to <21 years of age, NHANES 2001-2006

	Total (n = 10 410)	Black (n = 3364)	White (n = 2894)	*P* value (black vs white)
Age, years (mean, SE)	11.8 (0.13)	11.8 (0.19)	12.0 (0.19)	.40
Male, %	51.7 (0.67)	50.9 (1.18)	52.1 (1.04)	.47
Race/ethnicity, %				
Mexican-American	12.9 (1.26)			
Hispanic, non-Mexican	5.4 (0.76)			
White (non-Hispanic)	60.8 (2.17)			
Black (non-Hispanic)	14.8 (1.40)			
Other race	6.0 (0.73)			
Obese, %	17.0 (0.76)	21.5 (0.98)	15.5 (1.04)	<.001
25(OH)D, ng/mL (mean, SE)	25.4 (0.33)	17.6 (0.39)	28.2 (0.36)	<.001
25(OH)D, ng/mL (median, IQR)	25 (20, 30)	17 (12, 22)	27 (23, 33)	
Hgb, g/dL (mean, SE)	13.9 (0.04)	13.2 (0.03)	14.0 (0.05)	<.001
Hgb, g/dL (median, IQR)	13.7 (12.9, 14.7)	13.0 (12.3, 13.9)	13.9 (13.1, 14.9)	
% anemic*	4.2 (0.39)	14.3 (0.77)	2.1 (0.36)	<.001
CRP, mg/dL (mean, SE)	0.17 (0.01)	0.18 (0.01)	0.16 (0.01)	.25
% CRP >0.5 mg/dL	7.4 (0.38)	8.3 (0.49)	6.8 (0.51)	.04
Vitamin B12, pg/mL (mean, SE)	662.8 (6.23)	750.3 (8.29)	632.1 (7.63)	<.001
% Vitamin B12 <200 pg/mL	0.36 (0.066)	0.30 (0.075)	0.38 (0.091)	.41
Folate, ng/mL (mean, SE)	14.91 (0.18)	13.45 (0.21)	15.56 (0.25)	<.001
% folate <3 ng/mL	0.063 (0.029)	0.022 (0.022)	0.056 (0.041)	.46
Iron markers†		(n = 911)	(n = 736)	
Ferritin, ng/mL (mean, SE)	37.05 (0.96)	39.98 (2.47)	36.45 (1.16)	.20
% low ferritin	15.62 (0.0086)	16.35 (0.011)	15.23 (0.013)	.52
Iron, mcg/dL (mean, SE)	79.88 (1.17)	72.14 (1.01)	82.54 (1.72)	.0001
% low iron	22.24 (0.012)	25.67 (0.016)	21.04 (0.017)	.070
TSAT, % (mean, SE)	22.27 (0.30)	20.37 (0.33)	23.04 (0.43)	.0002
% low TSAT	22.65 (0.010)	26.07 (0.016)	21.17 (0.015)	.045

TSAT, transferrin saturation.
*Anemia defined as Hgb less than fifth percentile for age and sex.
†Subcohort, n = 2763 (911 black, 736 white).

Median (IQR) 25(OH)D was 27 (23, 33) in white subjects vs 17 (12, 22) in black subjects. The overall prevalence of anemia was 4.2%, but this also differed by race, with 2.1% of white children meeting criteria for anemia vs 14.3% of black children ($P < .001$). There was no difference in mean CRP by racial group, although a slightly greater proportion of black children demonstrated CRP >0.5 mg/dL ($P = .04$).

Figure 1 demonstrates mean 25(OH)D levels by race/ethnicity and anemia status in the cohort. There was a trend for mean 25(OH)D levels to be consistently lower in the anemic children compared with the nonanemic children across racial/ethnic groups. The difference in mean 25(OH)D levels by anemia status reached statistical significance in the overall cohort ($P < .001$) and in the non-Hispanic white subjects ($P = .02$).

The associations between 25(OH)D level, modeled categorically and linearly, and anemia are summarized in **Table II**. The OR for anemia for those with 25(OH)D levels <30 ng/mL, compared with ≥30, was 1.93 (95% CI 1.21-3.08, $P = .006$) in fully adjusted analyses. For those with 25(OH)D levels <20 ng/mL, compared with ≥20, the adjusted OR for anemia was 1.47 (95% CI 1.14-1.89, $P = .004$). The OR for anemia for each 1-ng/mL increase in 25(OH)D was 0.97 (95% CI 0.95-0.99, $P = .009$).

In a secondary logistic regression analysis that included subjects with available ferritin, iron and transferrin saturation levels (n = 2763), those with 25(OH)D <30 ng/mL compared with ≥30 continued to have an increased risk for anemia (OR 3.51, 95% CI 1.28-9.62, $P = .016$). The trend was similar for those with 25(OH)D levels <20 ng/mL, although statistical significance was not reached (OR 1.47, 95% CI 0.87-2.48, $P = .14$). Among those subjects with estimated GFR available (n = 6154), very few demonstrated values consistent with CKD; only 0.004% had estimated

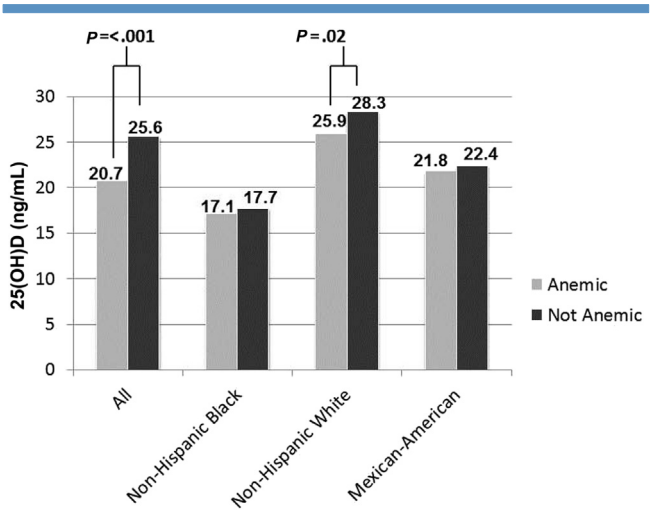

Figure 1. Mean 25(OH)D levels in otherwise-healthy children ages 1 to <21 years by anemia status and race/ethnicity (n = 10 410).

Table II. Logistic regression models demonstrating association between 25(OH)D and anemia* in US children 1 to <21 years (n = 10 410)

Risk for anemia	OR (95% CI)	*P* value
In children with 25(OH)D <30 ng/mL (vs ≥30)		
Unadjusted	3.33 (2.12-5.22)	<.001
Adjusted†	1.97 (1.23-3.16)	.006
Fully adjusted‡	1.93 (1.21-3.08)	.006
In children with 25(OH)D <20 ng/mL (vs ≥20)		
Unadjusted	3.25 (2.5-4.17)	<.001
Adjusted†	1.53 (1.20-1.96)	.001
Fully adjusted‡	1.47 (1.14-1.89)	.004
By increasing 25(OH)D level‡		
Per 1-ng/mL increase in 25(OH)D	0.97 (0.95-0.99)	.009
Per doubling of 25(OH)D, ng/mL	0.74 (0.58-0.93)	.013

*Anemia defined as Hgb less than fifth percentile for age and sex.
†Model adjusted for age, sex, race, and obesity.
‡Model adjusted for age, sex, race, obesity, CRP, B12, and folate.

GFR <60 mL/min per 1.73 m^2, a GFR cut-off most often used to define CKD in adults and below which anemia related to CKD becomes prevalent.[29] In this subgroup, logistic regression modeling continued to demonstrate increased risk for anemia in those with 25(OH)D <30 ng/mL compared with ≥30 (OR 2.68, 95% CI 1.31-5.50, P = .008) and with 25(OH)D levels <20 ng/mL vs ≥20 (OR 1.55, 95% CI 1.10-2.20, P = .014). Further adjustment for family poverty income ratio as an indicator of socioeconomic status (n = 9926) did not change the results significantly; increased risk for anemia was still demonstrated in those with 25(OH)D <30 ng/mL compared with ≥30 (OR 1.87, 95% CI 1.16-2.99, P = .011) and with 25(OH)D levels <20 ng/mL vs ≥20 (OR 1.47, 95% CI 1.14-1.90, P = .004).

A strikingly lower distribution of 25(OH)D values was noted among black (50th percentile 17 ng/mL, 95th percentile 30 ng/mL) compared with white (50th percentile 27 ng/mL, 95th percentile 42 ng/mL) children in the cohort (**Figure 2**; available at www.jpeds.com). To examine the extent to which race modifies the observed association between 25(OH)D level and Hgb, we performed a linear regression by 25(OH)D quartile stratified by race (**Table III**). Using whole population quartile values in the full cohort, we noted significant increases in Hgb in each of the upper 25(OH)D quartiles compared with the first quartile of 25(OH)D <20 ng/mL. In a race-stratified analysis, the magnitude and significance of the increase in Hgb seen in the upper 25(OH)D quartiles in the white children was consistent with increases observed in the whole population. However, in the black children, no significant change in Hgb was observed in the greater quartiles compared with lowest 25(OH)D quartile.

Table III. Change in Hgb associated with 25(OH)D whole population quartiles (ng/mL) in all children, and in children of white and black race (first quartile <20 referent)*

25(OH)D quartile (ng/mL) (first quartile referent)	Hgb, g/dL (95% CI)	*P* value
All children (n = 10 410), ng/mL		
Second (20-25)	0.196 (0.114-0.278)	<.001
Third (25-30)	0.168 (0.076-0.260)	.001
Fourth (>30)	0.179 (0.071-0.286)	.002
White children (n = 2894), ng/mL		
Second (20-25)	0.194 (0.051-0.338)	.009
Third (25-30)	0.179 (0.032-0.326)	.018
Fourth (>30)	0.160 (0.011-0.309)	.036
Black children (n = 3364), ng/mL		
Second (20-25)	−0.013 (−0.109 to 0.083)	.788
Third (25-30)	−0.013 (−0.120 to 0.095)	.815
Fourth (>30)	0.032 (−0.170 to 0.234)	.751

*Models adjusted for age, sex, obesity, CRP, B12, and folate.

We then conducted a regression analysis in the black children by using the non-Hispanic-black race-specific 25(OH)D quartiles (**Table IV**; available at www.jpeds.com). This demonstrated increases in Hgb in greater 25(OH)D quartiles compared with the lowest quartile, which were of similar magnitude to the increases observed in the quartile analysis for white children: second vs first (<12 ng/mL) quartile, Hgb increased by 0.240 (95% CI 0.096-0.384) g/dL, P = .002; third vs first quartile, Hgb increased by 0.116 (95% CI −0.019 to 0.251) g/dL, P = .091; and fourth vs first quartile, Hgb increased by 0.146 (95% CI 0.025-0.267) g/dL, P = .019.

Discussion

This study demonstrates that in a large, population-based cohort of healthy US children, lower 25(OH)D levels were associated with increased risk for anemia. The observed association between vitamin D status and anemia was independent of other factors that may contribute to anemia risk, including obesity, inflammation, socioeconomic status, and nutritional status, including B12, folate, and iron deficiency. Furthermore, an association between 25(OH)D level and Hgb was observed in children of both black and white race, but the 25(OH)D levels at which this association becomes apparent differed by race and were lower in black children. Among white subjects, 25(OH)D levels in the upper quartiles (≥20 ng/mL) were associated with a nearly 0.2 g/dL greater Hgb compared with those <20 ng/mL, and in black children, Hgb was greater among those with 25(OH)D levels >11 ng/mL.

Vitamin D has long been recognized for its role in regulating calcium, phosphorus, and bone metabolism, but in recent years it has received attention as a regulator of a variety of biological functions, including immune function, cellular proliferation, and cardiovascular function.[5,30,31] An accumulating body of evidence suggests that 25(OH)D deficiency may also play a role in the pathogenesis of anemia. Lower 25(OH)D levels have been associated with anemia/lower Hgb values in population-based samples of US adults[13,14] and in adults with nondialysis CKD and end-stage kidney disease,[9,10,32-34] end-stage heart failure,[12] and type 2 diabetes.[11] Furthermore, retrospective cohort studies in adults with CKD have demonstrated that vitamin D supplementation may improve the management of anemia and decrease dose requirements for erythropoiesis-stimulating agents (ESAs), suggesting that vitamin D plays a role in

erythropoiesis.[32,33] Among anemic patients with nondialysis CKD treated with ESAs, ergocalciferol supplementation to normalize 25(OH)D values to ≥30 ng/mL was associated with a 24% decrease in the ESA dose required to maintain Hgb in the range of 11-12 g/dL.[32] In a study of >100 adults on chronic hemodialysis, ergocalciferol supplementation to normalize 25(OH)D was associated with a decrease in the ESA dose required to maintain Hgb targets in the majority of subjects.[33]

There are several possible mechanisms to explain the association of vitamin D deficiency with anemia. Vitamin D deficiency in children has been shown to be associated with lifestyle and nutritional factors such as obesity and decreased milk intake.[1] However, in the present study, the association between 25(OH)D status and anemia remained after we adjusted for obesity and additional markers of nutritional status, including B12 and folate levels and, in a subcohort of children, iron markers, suggesting that there are other explanatory mechanisms. Vitamin D and its metabolites are present in many tissues, as are the receptors for the active form of vitamin D, calcitriol. Although calcitriol production for the regulation of bone mineral metabolism takes place via the action of the 1-α-hydroxylase enzyme in renal tissue, there are multiple extrarenal sites at which locally produced calcitriol regulates host-cell DNA, and from which the extra-skeletal actions of vitamin D are controlled.[5,35] There are data to suggest that inadequate levels of 25(OH)D leading to decreased local calcitriol production in the bone marrow may limit erythropoiesis; calcitriol has a direct proliferative effect on erythroid burst-forming units that is synergistic with endogenously produced erythropoietin, and it also up-regulates expression of the erythropoietin receptor on erythroid progenitor cells.[33,36,37]

Calcitriol also plays a key role in the regulation of immune function by inhibiting the expression of proinflammatory cytokines by a variety of immune cells, thus providing negative feedback to prevent excessive inflammation.[5] The immunomodulatory effects of vitamin D may be central to its role in preventing anemia via modulation of systemic cytokine production, which may in turn suppress specific inflammatory pathways which contribute to the development of anemia. In a study of adults ages ≥60 years in NHANES, Perlstein et al[14] demonstrated an association between vitamin D deficiency and anemia that became statistically significant at a 25(OH)D level of 24 ng/mL. They also found a strong association between vitamin D deficiency and anemia of inflammation compared with both nonanemic subjects and subjects with other anemia subtypes. Interestingly, they also found that among subjects with anemia of inflammation, non-Hispanic blacks were overrepresented, comprising nearly 44% of the group.[14]

Although we controlled for CRP in our multivariate models, it may not be the most sensitive marker of inflammation in children who could have a variety of infectious stimuli causing transient decreases in Hgb, including viral infections. It is possible that there are other inflammatory mediators, unmeasured in the pediatric NHANES cohort, which are associated with lower levels of 25(OH)D. The role of inflammation in the etiology of anemia has been further clarified through study of the iron-regulatory protein hepcidin, an inflammation-induced negative regulator of erythropoiesis.[38,39] Low levels of calcitriol have been found to be associated with increased hepcidin levels in adults with CKD.[40]

Our finding that the 25(OH)D threshold above which Hgb increases differs by race suggests a possible differential sensitivity to the effects of vitamin D by race. This finding is not unique to Hgb, as recently published NHANES studies also have demonstrated racial variation in 25(OH)D threshold for other adverse health effects. In a study of adults in NHANES 2003-2006, bone mineral density was significantly decreased in those with lower levels of 25(OH)D among non-Hispanic whites but not in non-Hispanic blacks,[41] and in another community-based study researchers found that black women have increased serum parathyroid hormone levels at lower 25(OH)D levels compared with white women.[42] In adults in NHANES III, 25(OH)D deficiency (defined as level <15 ng/mL) was associated with an increased risk of fatal stroke in non-Hispanic whites but not in blacks.[43] Total 25(OH)D levels have not been consistently correlated with bone mineral density in the literature, and bioavailable vitamin D, which is the fraction of circulating 25(OH)D that is unbound to either vitamin D binding protein or albumin and is thus available to effect biologic actions, is strongly correlated with bone mineral density.[44] A recent study performed in a small cohort of healthy young adults revealed that mean levels of the vitamin D binding protein were significantly lower in nonwhite subjects compared with white subjects, with a trend towards increased bioavailable vitamin D among the nonwhite subjects.[44] Thus, the variation by race in total 25(OH)D levels at which certain adverse health effects are observed may be explained by racial differences in bioavailability of vitamin D.

Our study has several strengths, including a nationally representative, population-based sample of children and adolescents and standardized data collection and quality control procedures. This was a cross-sectional study, and thus the association between vitamin D deficiency and lower Hgb cannot be assumed to be causal. We did not have access to data on iron deficiency, one of the most common causes of anemia in children, in the majority of subjects, but sensitivity analyses conducted among subjects with iron data showed similar direction and magnitude of associations between 25(OH)D deficiency and anemia. Hereditary hemoglobinopathies may be associated with lower Hgb levels, particularly in black children, but we did not have access to data to estimate the prevalence of these traits. NHANES does not analyze vitamin D binding protein, preventing the determination of bioavailable 25(OH)D. ■

Submitted for publication Jun 13, 2013; last revision received Jul 24, 2013; accepted Aug 26, 2013.

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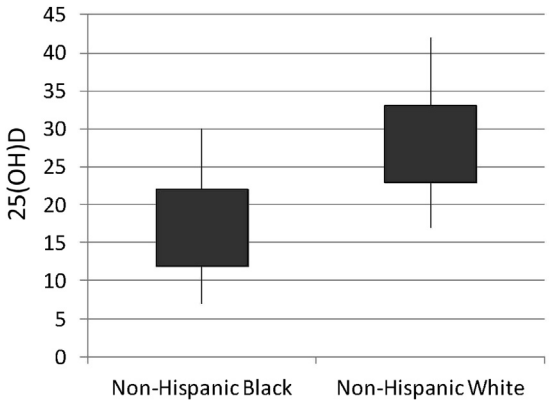

25(OH)D Percentiles by Race		
	Non-Hispanic Black	Non-Hispanic White
5th	7	17
50th	17	27
95th	30	42

Figure 2. Frequency and percentile distributions of 25(OH)D (ng/mL) levels in black and white US children 1 to <21 years of age, NHANES 2001-2006 (n = 6258).

Table IV. Change in Hgb associated with 25(OH)D black population-specific quartiles (ng/mL) in black children (first quartile <12 referent)*

25(OH)D quartile (ng/mL) (first quartile referent), black children (n = 3364)	Hgb, g/dL (95% CI)	*P* value
Second (12-17)	0.240 (0.096-0.384)	.002
Third (17-22)	0.116 (−0.019 to 0.251)	.091
Fourth (>22)	0.146 (0.025-0.267)	.019

*Model adjusted for age, sex, obesity, CRP, B12, and folate.