Clinical Pediatrics
51(2) 146–153

DOI: 10.1177/0009922811417290
http://cpj.sagepub.com
SAGE

# Vitamin D Insufficiency Is Associated With Diabetes Risk in Native American Children

**Phyllis A. Nsiah-Kumi, MD, MPH[1], Judi M. Erickson, BSN[1], Jennifer L. Beals, MD[1], Eric A. Ogle, BS[1], Mary Whiting[1,2], Connie Brushbreaker[2], Claudia D. Borgeson, BS[1], Fang Qiu, MS[1], Fang Yu, PhD[1], and Jennifer L. Larsen, MD[1]**

## Abstract

*Aims/Hypothesis*. Vitamin D insufficiency has not been well studied in Native American (NA) children, who are at risk for obesity and diabetes. The authors examined vitamin D insufficiency and its association with body mass index (BMI) and insulin resistance. *Methods*. In a cross-section of NA children 5 to 18 years old (N = 198), anthropometrics, biomarkers of insulin resistance, and 25-hydroxy-vitamin D concentration [25(OH) vitamin D] were measured. BMI% and homeostatic model assessment of insulin resistance (HOMA-IR) were calculated. *Results*. Mean age was 10.8 ± 0.3 years (mean ± SEM). Mean serum 25(OH) vitamin D was 17.8 ± 0.4 ng/mL and 97% had vitamin D insufficiency [25(OH) vitamin D <30 ng/mL]. After adjusting for BMI, 25(OH) vitamin D was inversely associated with HOMA-IR ($P < .0001$) and several other markers of insulin resistance. *Conclusions/Interpretation*. Vitamin D insufficiency was nearly universal in this cohort of NA children and was associated with diabetes and vascular risk markers. Whether vitamin D supplementation can improve insulin resistance must be studied further.

## Keywords

25(OH) vitamin D, 25-hydroxyvitamin D, diabetes, insulin resistance, lipids, obesity, type 2 diabetes prevention, vascular risk

## Introduction

Vitamin D has been linked to type 2 diabetes risk in youth and adults.[1,2] Vitamin D concentration is also inversely associated with body mass index (BMI) in most groups where it has been studied.[1,3] Obese children and adolescents with low vitamin D status may be at risk of developing impaired glucose metabolism, and 25-hydroxyvitamin D [serum 25(OH) D] has been independently associated with both insulin sensitivity and β-cell function among individuals at risk for type 2 diabetes.[4]

Vitamin D insufficiency is more common in people of color[4,5] and among those living at higher latitudes where sun exposure is reduced during half of the year. Native Americans (NAs) living in Great Plains states, who have darker skin color and live at higher latitudes, would be assumed to be at particular risk, although the prevalence of vitamin D insufficiency in NA youth living in the United States is as yet unknown.

We hypothesized that vitamin D insufficiency is not only common but also correlates with insulin resistance and other diabetes risk factors in NA youth. With this background, we designed a study to determine the prevalence of vitamin D insufficiency and its association with diabetes and vascular risk factors in a community sample of NA youth living in the Great Plains.

## Methods

### *Study Population*

This study was approved by the Institutional Review Boards of the Aberdeen Area Indian Health Service (IHS) and the University of Nebraska Medical Center

[1]University of Nebraska Medical Center, Omaha, NE, USA
[2]Rosebud Sioux Tribe, Rosebud, SD, USA

**Corresponding Author:**
Phyllis A. Nsiah-Kumi, Internal Medicine–Pediatrics, University of Nebraska Medical Center, 984085 Nebraska Medical Center, Omaha, NE 68198-4085, USA
Email: pnkumi@unmc.edu

(UNMC). All 5- to 18-year-old NA youth who were eligible to access IHS based on enrollment in a tribe were eligible to participate in the study. Exclusion criteria included pregnancy or delivery within 6 weeks, active infection, or illness that could affect weight such as cancer or malabsorption. No individuals were found to have exclusion criteria at the time of study. Prior diagnosis of diabetes was not considered an exclusion criterion because there was a misperception by some families that the presence of acanthosis nigricans alone was equivalent to a diagnosis of diabetes. However, no youth believed to have type 2 diabetes presented for screening.

Recruitment was performed across a reservation, located at 43° latitude, year round from April 2006 to October 2009. Brochures were distributed and educational events were held at schools, the local grocery store, the tribal exercise facility, health facilities, and community events. Interviews in the newspaper and on the radio were also used to disseminate information about the program. Youth or their parents then called the advertised number to request more information or to schedule a screening.

## Study Parameters and Study Visit

Youth were requested to fast from supper the night before until the morning of their scheduled visit. On or before the screening day, informed consent from a parent and assent from the youth were obtained. For eligible youth, height was measured to the nearest one-eighth inch using a stadiometer (Seca, Hanover, MD) and weight was measured using the clinic scale. After the child had been sitting quietly for 5 minutes, blood pressure was measured using an appropriately sized cuff with the arm at heart level. Abdominal circumference measurement was taken twice midway between the lowest rib and the superior border of the iliac crest twice without clothing, using a flexible fiberglass tape while the subject was in the standing position at the end of gentle expiration. Each of the 2 measurements was rounded to the nearest 0.5 cm, and the average of the values was used.

Body mass index (BMI) was later calculated from height and weight and BMI percentile-for-age-and-sex (BMI%) was determined using the Centers for Disease Control published growth charts. In children and adolescents, BMI varies with age and gender. A given BMI value is compared against reference charts to obtain a ranking of BMI percentile-for-age-and-sex. The BMI percentile indicates the relative position of the child's BMI compared with a historical reference population of children of the same age and gender.[6]

Blood was drawn for fasting glucose, insulin, lipid profile, high-sensitivity C-reactive protein (hsCRP), and 25-hydroxy-vitamin D [25(OH) vitamin D]. Each child was then given Glucola based on their weight (1.75 g/kg), up to a maximum of 75 g total. Two hours post–glucose load, another glucose was drawn from all participants with the exception of 10 youth who were unwilling or from whom a second sample could not be drawn.

The parent or guardian of each child was asked about family history of diabetes, and the child's birth weight, medical history, vitamin use, medications, recent infections, and dental health. Separately, youth 12 to 18 years old were asked these same questions; they were also asked about their recent physical activity, alcohol, and smoking habits.

## Laboratory Testing

Glucose was measured at the nearby IHS hospital facility laboratory. Plasma and serum were stored at −20°C for up to 1 month prior to transport on dry ice to UNMC for assay for the tests discussed below. Insulin, serum 25(OH) vitamin D, and hsCRP were assayed in the Clinical Research Center (CRC) laboratory. Plasma insulin was measured by radioimmunoassay (Millipore, St Charles, MO) in an assay with sensitivity of 2 μU/mL and <0.2% cross-reactivity with pro-insulin (intra-assay and inter-assay variation were 3.0% and 2.2%, respectively).

Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated from fasting glucose and fasting insulin using the following equation: HOMA-IR = (fasting glucose [mg/dL] × fasting insulin [mU/L])/405.[7] Serum 25(OH) vitamin D was assayed using a radioimmunoassay that positively correlates with mass spectrometry and measures both D2 and D3 (DiaSorin, Stillwater, MN; intra-assay and inter-assay variation 3.4% and 9.6%, respectively). CRP was assayed using a highly sensitive enzyme-linked immunosorbent assay (ELISA; Immundiagnostik, Bensheim, Germany; sensitivity = 0.124 ng/mL). Fasting lipids were measured in The Nebraska Medical Center Clinical laboratory using standard methodology.

## Statistical Analysis

Statistical Analysis Software (version 9.0, SAS Institute, Cary, NC) was used for all statistical analysis. Descriptive statistics were calculated for all variables. Comparisons between age groups and between boys and girls were performed with the Wilcoxon rank sum test for continuous variables. Spearman correlations were calculated between 25(OH) vitamin D, BMI%, HOMA-IR, and the other laboratory testing measurements.

Log-transformation and multiple robust regression[8] were used when necessary to satisfy the assumption of

**Table 1.** Study Population Characteristics

| Characteristic | Mean ± SEM | Median (Range) |
|---|---|---|
| N | 198 | |
| Age (years) | 10.8 ± 0.3 | 11.0 (5, 19) |
| Gender (male %/ female %) | 47/53 | 93 (47)/105 (53) |
| BMI percentile-for-age-and-sex | 77.7 ± 1.7 | 88.0 (1.0, 99.0) |
| Systolic blood pressure (mm Hg) | 103 ± 0.9 | 102 (71, 133) |
| Diastolic blood pressure (mm Hg) | 62.7 ± 0.8 | 62 (36, 92) |
| Abdominal circumference (cm) | 78.5 ± 1.4 | 76 (48, 145.5) |
| Fasting glucose (mg/dL) | 85.4 ± 0.7 | 85 (51, 157) |
| 2-hour glucose (mg/dL) | 96.1 ± 2.0 | 94 (46, 323) |
| Fasting insulin (μU/mL) | 22.6 ± 1.8 | 15 (2, 178) |
| HOMA-IR (>4 considered high) | 4.89 ± 0.42 | 3.03 (0.45, 45.66) |
| hsCRP (mg/L; <1 low, 1-3 moderate, >3 high) | 2.7 ± 0.5 | 1.24 (0.04, 70.5) |
| 25(OH) vitamin D (ng/ml) | 17.78 ± 0.4 | 17.0 (6.8, 40.0) |

Abbreviations: SEM, standard error of the mean; BMI, body mass index; HOMA-IR, homeostatic model assessment of insulin resistance; hsCRP, high-sensitivity C-reactive protein.

multiple linear regression and minimize the impact of outliers on the regression estimators. Multiple linear regression was used to assess the associations of systolic blood pressures, diastolic blood pressures, log-transformed triglycerides or log-transformed hsCRP with 25(OH) vitamin D adjusting for the effects of BMI%. Multiple robust regression was used to assess associations between log-transformed fasting glucose, log-transformed 2-hour glucose, log-transformed fasting insulin, and log-transformed HOMA-IR with 25(OH) vitamin D controlling for BMI%.

## Results

The demographic characteristics of the study population are shown in Table 1. Mean age (±SEM) was 10.8 years (±0.3). The mean BMI% was 78th percentile (±1.7), and 54.6% of participants had BMI% >85%. Mean abdominal circumference was 78.5 cm (±1.4). Vitamin D insufficiency, defined as 25(OH) vitamin D <30 ng/mL, was observed in 97%, with mean 25(OH) vitamin D of 17.8 ± 0.4 ng/mL. A significant proportion (38.9%) had more severe vitamin D deficiency, defined as 25(OH) vitamin D <16 ng/mL.

The prevalence of vitamin D insufficiency (serum 25(OH) vitamin D <30 ng/mL) was not different between warm months (April-September) and cold (October-March) months (98.7% vs 96.0%, respectively; $P = .42$), although the prevalence of vitamin D deficiency [25(OH) vitamin D <16 ng/mL] was greater in cold (58.1%) than in warm months (27.4%; $P < .0001$). As a result, median 25(OH) vitamin D was lower in cold than warm months (14.5 vs 18.9 ng/mL; $P < .0001$). Only 14/192 (7%) of the parents stated their child was taking vitamins of any kind.

25(OH) vitamin D was lower in girls than boys (median: 16.6 vs 18.4 ng/mL; $P = .02$). Levels of 25(OH) vitamin D were also lower in older participants (12- to 18-year-olds: median 15.7 ng/mL; $P = .002$) compared with younger participants (5- to 11-year-olds: median 18.0 ng/mL).

Serum levels of 25(OH) vitamin D correlated with multiple biomarkers of diabetes risk (see Figure 1). Serum 25(OH) vitamin D was negatively correlated with BMI% (Figure 1A; $P = .003$). This correlation existed in the group as a whole and was also seen in males and females (both $P$s = .02), as well as in younger (5- to 11-year-olds: $P = .02$) and older participants (12- to 18-year-olds: $P = .01$). Serum 25(OH) vitamin D concentration was also negatively correlated with fasting (Figure 1B; $P = .01$) and 2-hour glucose ($P = .0008$). Figures 1C and 1D show the negative correlation between 25(OH) vitamin D concentration and fasting insulin ($P < .0001$), and HOMA-IR ($P \leq .0001$). Level of 25(OH) vitamin D was inversely correlated with triglycerides ($P < .0001$; Figure 1E) and positively correlated with high-density lipoprotein (HDL; $P = .04$; data not shown). Serum 25(OH) vitamin D was also negatively correlated with hsCRP ($P = .007$; Figure 1F), as well as both systolic and diastolic blood pressure ($P < .0001$ for both; data not shown). There was no significant correlation between 25(OH) vitamin D and total cholesterol or low-density lipoprotein.

After adjusting for BMI%, 25(OH) vitamin D was inversely associated with log-transformed HOMA-IR ($P < .0001$), log-transformed fasting glucose ($P = .005$) and 2-hour glucose ($P = .007$), log-transformed fasting insulin ($P < .0001$), log-transformed triglycerides ($P = .0009$), systolic ($P = .002$) and diastolic ($P = .0001$) blood pressures (see Table 2).

## Discussion

Vitamin D deficiency is recognized as being common in many populations, but this is the first study to evaluate the prevalence of vitamin D insufficiency and its potential consequences in NA children. More than 95% of those we screened had a vitamin D concentration <30 ng/mL. Similarly, vitamin D concentration was <75 nmol/L (equivalent to 30 ng/mL) in >95% of French Canadian children who live at an even higher latitude.[10]

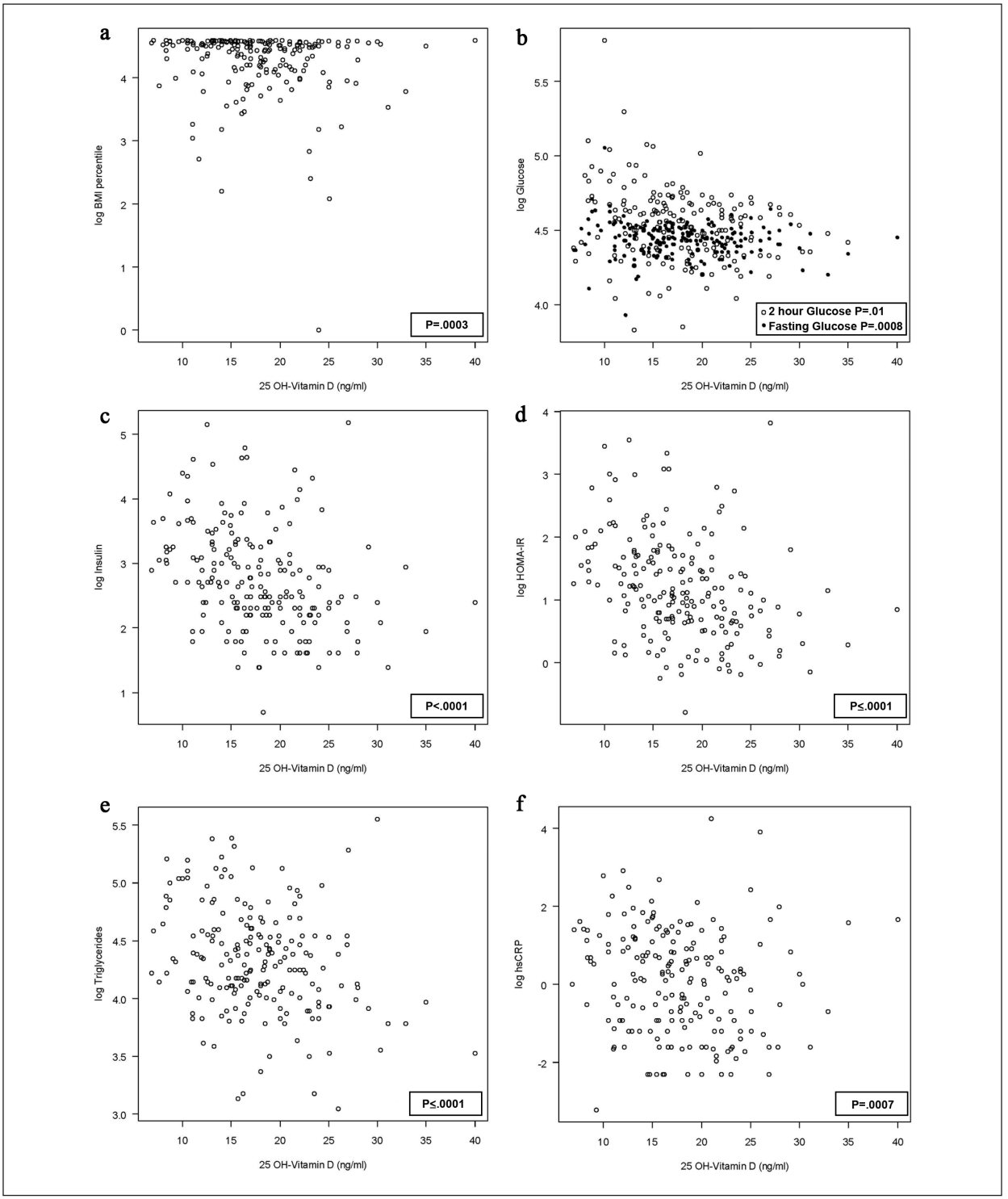


**Figure 1.** Vitamin D and diabetes and cardiovascular disease risk factors

Correlation between 25-hydroxy-vitamin D [25(OH) vitamin D] and body mass index (BMI) percentile-for-age-and-sex (BMI%) is shown in Figure 1A ($r = –0.21$, $P = .003$). Vitamin D was positively correlated with fasting and 2-hour glucose (Figure 1B; $r = 0.18$, $P = .01$ and $r = –0.24$, $P = .0008$, respectively). Figure 1C shows the correlation between 25(OH) vitamin D and fasting insulin ($r = –0.39$, $P < .0001$). Figure 1D shows a negative correlation between 25(OH) vitamin D and homeostatic model assessment of insulin resistance (HOMA-IR; $r = –0.4$, $P < .0001$). Figures 1E and 1F show the correlation between 25(OH) vitamin D and triglycerides ($r = –0.28$, $P < .0001$) and high-sensitivity C-reactive protein (hsCRP; $r = –0.19$, $P = .007$), respectively.

**Table 2.** BMI% Adjusted Association of 25(OH) Vitamin D With Biomarker Measurements[a]

| Outcome | Coefficient | 95% Confidence Limits for Coefficient | | *P* |
|---|---|---|---|---|
| | | Lower | Upper | |
| Log 0-hour glucose | –0.0036 | –0.0061 | –0.0011 | .0045 |
| Log 2-hour glucose | –0.0082 | –0.0142 | –0.0023 | .007 |
| Log fasting insulin | –0.046 | –0.063 | –0.029 | <.0001 |
| Log HOMA-IR | –0.048 | –0.066 | –0.03 | <.0001 |
| Log triglycerides | –0.02007 | –0.03179 | –0.00835 | .0009 |
| Log hsCRP | –0.01853 | –0.05174 | 0.01468 | .2725 |
| Diastolic blood pressure | –0.49792 | –0.75091 | –0.24493 | .0001 |
| Systolic blood pressure | –0.49787 | –0.80428 | –0.19147 | .0016 |
| Log HDL | 0.00421 | –0.00193 | 0.01035 | .1783 |

Abbreviations: BMI, body mass index; HOMA-IR, homeostatic model assessment of insulin resistance; hsCRP, high-sensitivity C-reactive protein; HDL, high-density lipoprotein.
[a]*P* values <.05 are considered statistically significant.

Although elevated BMI was common (53.7% of participants had a BMI% >85%), it was not as common as vitamin D insufficiency in this sample.

Although the frequency of vitamin D insufficiency was the same throughout the year, the frequency of the more severe vitamin D deficiency [25(OH) vitamin D <16 ng/mL] was higher in cold months (September-March) than in warm months (April-August). Vitamin D concentration was also lower in girls than in boys in our cohort, as reported in the third National Health and Nutrition Examination Survey (NHANES III).[9]

The causes for vitamin D insufficiency are frequently discussed. Vitamin D is acquired, in part, through exposure to the sun. As youth and adults are encouraged to use sun-blocking agents and spend more time indoors, it is not surprising that vitamin D insufficiency is common. In winter months, particularly at higher latitudes, sun exposure is even less common. Finally, dark skin pigmentation alone is recognized to result in lower vitamin D for the same amount of sun exposure. Some have postulated a role for obesity, as well.[1,4]

Whether vitamin D deficiency is a cause or an effect of obesity is still debated. In this cohort, vitamin D was not only inversely correlated with obesity (in the form of BMI%) but with many other type 2 diabetes risk factors as well: fasting and 2-hour glucose, HOMA-IR, triglycerides, hsCRP, and blood pressure. Additionally, vitamin D was positively correlated with HDL, which is also linked to insulin resistance.

Whereas this is the first study to evaluate these relationships in NA youth, others have observed similar relationships in children in other racial and ethnic groups. In 2009, Reis et al[11] demonstrated that low serum vitamin D was strongly associated with hypertension, hyperglycemia, and metabolic syndrome in a multiethnic sample of US adolescents.

While increased blood pressure can be linked to BMI alone, another mechanism may include the association between low vitamin D and elevations in parathyroid hormone, which can more directly cause elevations in blood pressure.[12] In our cohort, vitamin D was inversely associated with systolic and diastolic blood pressures, even after adjusting for BMI%. This is consistent with prior studies, which have demonstrated a relationship between vitamin D and systolic and diastolic blood pressures in adults and children.[13-15]

Inflammation, as indicated by elevations in inflammatory cytokines, is also recognized to correlate with diabetes risk and contributes to insulin resistance. However, vitamin D is known to reduce inflammation, and low vitamin D states are associated with more infections.[16] Whether vitamin D supplementation improves inflammation and, in turn, insulin resistance is as yet unknown.

The optimal dosing of vitamin D for prevention of diabetes or cardiovascular disease is currently unknown.[17,18] Current recommendations for vitamin D intake were developed with skeletal health outcomes in mind, and available evidence is inconsistent and insufficient for the development of the dietary reference intake with regards to nonskeletal outcomes. A recent Institute of Medicine report recognized the need for more studies to evaluate the optimal vitamin D concentration and the value of higher dose supplements with regard to nonskeletal outcomes.[19]

Recommendations regarding vitamin D dosing are varied. In the United States, assuming minimal sun exposure, the estimated average requirement (EAR) of vitamin D for individuals older than 1 year is 400 IU/d, and the recommended daily allowance (RDA) is 600

IU/d for those aged 1 to 70 years and 800 IU/d for those 71 years and older. These values correspond to serum 25(OH) vitamin D levels of 16 ng/mL (40 nmol/L) for EARs and 20 ng/mL (50 nmol/L) or more for RDAs.[20] The American Academy of Pediatrics currently recommends that all infants and children, including adolescents, have a daily intake of 400 IU of vitamin D beginning soon after birth.[21] The Canadian Paediatric Society recommends 400 IU/d in summer, fall, and spring and 800 IU/d of vitamin D for breastfed infants during the winter months and 800 IU/d in winter for their Native children.[22] Currently, US recommendations for vitamin D intake do not consider obesity, skin pigmentation, or the effects of season or geography.

Whereas optimal serum concentrations and dosing for nonskeletal outcomes are unknown, and vitamin D replacement is one way to improve serum vitamin D concentration, it is not recommended that healthy children and youth take a daily multivitamin unless they are at nutritional risk, for example, deprived, low-income family, obesity, or vegetarian diets.[23] Obesity and low socioeconomic status contribute to nutritional risk for many NA children, yet the national IHS formulary includes only one multivitamin, and it contains 400 IU of vitamin D3.[24]

Very few children/youth in our sample (7.7%) were taking a vitamin or any supplement on a regular basis. This low frequency of dietary supplementation is a direct contrast to a recent NHANES analysis showing that between 1999 and 2004, approximately 34% of children between the ages of 2 and 17 years had used vitamin and mineral supplements in the previous month.[25]

Although the existence of a relationship between vitamin D deficiency and obesity is apparent, the mechanism leading to it is not. Fat tissue is a storage site for vitamin D, and thus it has been hypothesized that with increasing adiposity, more vitamin D is sequestered in fat, leading to lower serum levels.[26,27] However, as vitamin D deficiency symptoms, including muscle weakness, myalgias, and arthralgias, may be gradual and vague, vitamin D deficiency may discourage physical activity and/or encourage eating behavior, as well, and thus lead to obesity.[28]

Studies suggest that vitamin D supplementation may reduce diabetes risk. In nondiabetic animal models, pharmacological doses of 1,25-dihydroxyvitamin $D_3$, or its structural analogues, have been shown to delay the onset of diabetes, mainly through immune modulation.[29,30] Additionally, in a few small, short-term human studies, vitamin D supplementation appears to improve insulin resistance and weight loss.[18,27,31] Achieving a normal vitamin D concentration may require more than twice as much vitamin D in obese preadolescent children with vitamin D deficiency as in their nonobese counterparts.[32] Thus, studies focused on individuals most at risk for diabetes, by virtue of their weight status, must consider optimal dosing of vitamin D for individuals with more adipose tissue. Additional human studies of how vitamin D impacts glucose metabolism, how vitamin D deficiency may contribute to insulin resistance and optimal dosing of vitamin D to achieve adequate levels in individuals with increased adiposity are warranted.

## Conclusions

In this first study of vitamin D in NA youth, vitamin D insufficiency was nearly universal in a sample of Great Plains NA youth. Vitamin D was also negatively correlated with multiple markers of future diabetes and vascular risk: BMI percentile, fasting and postprandial glucose, fasting insulin, triglycerides, hsCRP, systolic and diastolic blood pressure, and insulin resistance. Vitamin D was also positively associated with HDL, which protects against vascular risk.

Although there may be multiple mechanisms for vitamin D deficiency in this population, greater frequency of vitamin D supplements would be a first step in improving vitamin D concentration in NA children. Further studies are needed to determine the potential metabolic benefits and optimal dosing of vitamin D supplementation on this high-risk group.

### Acknowledgments

Special thanks to the Rosebud Diabetes Prevention Program, the Rosebud Tribal Health Board, Marlene Schafer, Tina Martinez, Duane Lamb, and Rita Broken Leg (Rosebud Sioux Tribe) for their invaluable assistance in carrying out this study. Thanks to Tanna Albin (University of Nebraska Medical Center) for her assistance with literature review.

### Authors' Note

This study was conducted through collaboration between University of Nebraska Medical Center, the Aberdeen Area Tribal Chairman's Health Board, and the Rosebud Sioux Tribe. The study sponsor played no role in the data collection, analysis, reporting, or journal selection.

### Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article:

Financial support was in the form of a Native American Research Centers for Health (NARCH) grant (No. U26IHS300002), sponsored by the Indian Health Service (IHS) and National Institute of Diabetes Digestive and Kidney Diseases (NIDDK). Dr Nsiah-Kumi supported by a National Institute for Minority Health and Health Disparities Loan Repayment Award.

## References

1. Gilbert-Diamond D, Baylin A, Mora-Plazas M, et al. Vitamin D deficiency and anthropometric indicators of adiposity in school-age children: a prospective study. *Am J Clin Nutr*. 2010;92:1446-1451.
2. Pittas AG, Dawson-Hughes B, Li T, et al. Vitamin D and calcium intake in relation to type 2 diabetes in women. *Diabetes Care*. 2006;29:650-656.
3. Elizondo-Montemayor L, Ugalde-Casas PA, Serrano-González M, Cuello-García CA, Borbolla-Escoboza JR. Serum 25-hydroxyvitamin D concentration, life factors and obesity in Mexican children. *Obesity (Silver Spring)*. 2010;18:1805-1811.
4. Alemzadeh R, Kichler J, Babar G, Calhoun M. Hypovitaminosis D in obese children and adolescents: relationship with adiposity, insulin sensitivity, ethnicity, and season. *Metabolism*. 2008;57:183-191.
5. Saintonge S, Bang H, Gerber LM. Implications of a new definition of vitamin D deficiency in a multiracial US adolescent population: the National Health and Nutrition Examination Survey III. *Pediatrics*. 2009;123:797-803.
6. Kuczmarski RJ, Ogden CL, Grummer-Strawn LM, et al. CDC growth charts: United States. *Adv Data*. 2000;314:1-27.
7. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia*. 1985;28:412-419.
8. Huber P. Robust regression: asymptotics, conjectures and Monte Carlo. *Ann Statist*. 1973;1:799-821.
9. Looker AC, Dawson-Hughes B, Calvo MS, Gunter EW, Sahyoun NR. Serum 25-hydroxyvitamin D status of adolescents and adults in two seasonal subpopulations from NHANES III. *Bone*. 2002;30:771-777.
10. Mark S, Gray-Donald K, Delvin EE, et al. Low vitamin D status in a representative sample of youth from Quebec, Canada. *Clin Chem*. 2008;54:1283-1289.
11. Reis JP, von Mühlen D, Miller ER, 3rd, Michos ED, Appel LJ. Vitamin D status and cardiometabolic risk factors in the United States adolescent population. *Pediatrics*. 2009;124:e371-e379.
12. Zhao G, Ford ES, Li C, Kris-Etherton PM, Etherton TD, Balluz LS. Independent associations of serum concentrations of 25-hydroxyvitamin D and parathyroid hormone with blood pressure among US adults. *J Hypertens*. 2010;28:1821-1828.
13. Shankar A, Sabanayagam C, Kalidindi S. Serum 25-hydroxyvitamin D levels and prediabetes among subjects free of diabetes. *Diabetes Care*. 2011;34:1114-1119.
14. Zhou P, Schechter C, Cai Z, Markowitz M. Determinants of 25(OH)D sufficiency in obese minority children: selecting outcome measures and analytic approaches. *J Pediatr*. 2011;158:930-934.
15. Smotkin-Tangorra M, Purushothaman R, Gupta A, Nejati G, Anhalt H, Ten S. Prevalence of vitamin D insufficiency in obese children and adolescents. *J Pediatr Endocrinol Metab*. 2007;20:817-823.
16. Chakarova N, Tankova T, Atanassova I, Dakovska L. Serum lipid and hsCRP levels in prediabetes—impaired fasting glucose (IFG) and impaired glucose tolerance (IGT). *Diabetes Res Clin Pract*. 2009;86:56-60.
17. Ashraf A, Alvarez J, Saenz K, Gower B, McCormick K, Franklin F. Threshold for effects of vitamin D deficiency on glucose metabolism in obese female African-American adolescents. *J Clin Endocrinol Metab*. 2009;94:3200-3206.
18. Barengolts E. Vitamin D role and use in prediabetes. *Endocr Pract*. 2010;16:476-485.
19. Institute of Medicine. *Dietary Reference Intakes for Calcium and Vitamin D*. Washington, DC: National Academies Press;2011.
20. Ross AC, Manson JE, Abrams SA, et al. The 2011 dietary reference intakes for calcium and vitamin D: What dietetics practitioners need to know. *J Am Diet Assoc*. 2011;111:524-527.
21. Wagner CL, Greer FR. Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. *Pediatrics*. 2008;122:1142-1152.
22. Canadian Paediatric Society. Vitamin D supplementation for northern native communities. Indian and Inuit Health Committee, Canadian Paediatric Society. *CMAJ*. 1988;138:229-230.
23. Barness LA, Dallman PR, Anderson H, et al. Vitamin and mineral supplement needs in normal children in the United States. *Pediatrics*. 1980;66:1015-1021.
24. Indian Health Service National Pharmacy and Therapeutics Committee. Indian Health Service National Pharmacy and Therapeutics Committee National Core Formulary. 2010. http://www.ihs.gov/MedicalPrograms/NPTC/index.cfm?module=formulary&option=core. Accessed May 3, 2011.
25. Shaikh U, Byrd RS, Auinger P. Vitamin and mineral supplement use by children and adolescents in the 1999-2004 National Health and Nutrition Examination Survey: relationship with nutrition, food security, physical activity, and health care access. *Arch Pediatr Adolesc Med*. 2009;163:150-157.

26. Osei K. 25-OH vitamin D: is it the universal panacea for metabolic syndrome and type 2 diabetes? *J Clin Endocr Metab*. 2010;95:4220-4222.
27. Tzotzas T, Papadopoulou FG, Tziomalos K, et al. Rising serum 25-hydroxy-vitamin D levels after weight loss in obese women correlate with improvement in insulin resistance. *J Clin Endocrinol Metab*. 2010;95: 4251-4257.
28. Glerup H. Hypovitaminosis D myopathy without biochemical signs of osteomalacic bone involvement. *Calcif Tissue Int*. 2000;66:419-424.
29. Mathieu C, Waer M, Laureys J, Rutgeerts O, Bouillon R.Prevention of autoimmune diabetes in NOD mice by 1,25 dihydroxyvitamin D3. *Diabetologia*. 1994;37: 552-558.
30. Overbergh L, Decallonne B, Valckx D, et al. Identification and immune regulation of 25-hydroxyvitamin D-1-alpha-hydroxylase in murine macrophages. *Clin Exp Immunol*. 2000;120:139-146.
31. Gedik O, Akalin S. Effects of vitamin D deficiency and repletion on insulin and glucagon secretion in man. *Diabetologia*. 1986;29:142-145.
32. Rajakumar K, Fernstrom JD, Holick MF, Janosky JE, Greenspan SL. Vitamin D status and response to vitamin D3 in obese vs. non-obese African American children. *Obesity (Silver Spring)*. 2007;16:90-95.