

# Prediabetes and Prehypertension in Healthy Adults Are Associated With Low Vitamin D Levels

ALOK K. GUPTA, MD  
MEGHAN M. BRASHEAR, MPH  
WILLIAM D. JOHNSON, PHD

**OBJECTIVE**—To determine whether modest elevations of fasting serum glucose (FSG) and resting blood pressure (BP) in healthy adults are associated with differential serum vitamin D concentrations.

**RESEARCH DESIGN AND METHODS**—Disease-free adults in the National Health and Nutrition Examination Survey 2001–2006 were assessed. Prediabetes (PreDM) and prehypertension (PreHTN) were diagnosed using American Diabetes Association and Seventh Report of the Joint National Committee on Prevention, Detection, and Treatment of High Blood Pressure criteria: FSG 100–125 mg/dL and systolic BP 120–139 mmHg and/or diastolic BP 80–89 mmHg. Logistic regression was used to assess the effects of low vitamin D levels on the odds for PreDM and PreHTN in asymptomatic adults ( $n = 1,711$ ).

**RESULTS**—The odds ratio for comorbid PreDM and PreHTN in Caucasian men ( $n = 898$ ) and women ( $n = 813$ ) was 2.41 ( $P < 0.0001$ ) with vitamin D levels  $\leq 76.3$  versus  $> 76.3$  nmol/L after adjusting for age, sex, and BMI.

**CONCLUSIONS**—This study strengthens the plausibility that low serum vitamin D levels elevate the risk for early-stage diabetes (PreDM) and hypertension (PreHTN).

*Diabetes Care* 34:658–660, 2011

The link between low serum vitamin D concentrations and abnormal bone and calcium metabolism has been known for many years. The adverse associations between low vitamin D concentrations and metabolic syndrome (1), diabetes mellitus (2), hypertension (3), cardiovascular health (4), cardiovascular, and all-cause mortality (5) have also been identified. Vitamin D concentrations have an inverse relationship with circulating renin and angiotensin II, suggesting a mechanism for elevation of blood pressure (BP) (6). Moreover, dietary supplementation with vitamin D seems to reduce blood glucose and BP. The relationship between serum vitamin D and fasting serum glucose (FSG) and resting BP, specifically prediabetes (PreDM) and prehypertension (PreHTN), in healthy disease-free adults, however, is unknown.

## RESEARCH DESIGN AND METHODS

Analyses were conducted using data from the United States National Health and Nutrition Examination Survey, 2001–2006. Trained personnel collected demographic, socioeconomic, dietary, and health-related information. A mobile exam center obtained anthropometric measurements and BP data, and secured a fasting blood draw for laboratory measurements (7).

The 2001–2006 National Health and Nutrition Examination Survey samples included 15,431 adults aged  $\geq 20$  years. Those with an ongoing pregnancy ( $n = 886$ ), who had participated in the interview portion only ( $n = 843$ ), who were missing data ( $n = 8,247$ ), who had a chronic disease ( $n = 2,065$ ), or who were of race/ethnicity other than non-Hispanic white ( $n = 1,679$ ) were excluded. Because

serum vitamin D concentrations differ substantially in various races, only healthy disease-free Caucasians ( $n = 1,711$ , men [ $n = 898$ ] and women [ $n = 813$ ]) were included.

The American Diabetes Association criteria for impaired fasting glucose were used to define PreDM: FSG level 100–125 mg/dL. The Seventh Report of the Joint National Committee on Prevention, Detection, and Treatment of High Blood Pressure criteria for PreHTN (systolic BP: 120–139 mmHg and/or diastolic BP: 80–89 mmHg) provided the diagnosis for PreHTN. Serum vitamin D (25-hydroxyvitamin D) concentration at the 75th percentile ( $> 76.3$  nmol/L and  $< 76.3$  nmol/L) was used to create differential categories for assessments.

Calculations were performed using the statistical software SAS version 9.1 (SAS Institute, Inc., Cary, NC).

## RESULTS

Table 1 depicts the summary statistics for serum 25-hydroxyvitamin D (nmol/L). In 1,711 disease-free adult Caucasians, the mean serum vitamin D concentration (mean [SEM]) was 65.0 [1.1] nmol/L. The mean concentration was slightly lower in men (64.4 [1.1] nmol/L) compared with women (65.7 [1.5] nmol/L) and was incrementally lower with increasing age and across BMI categories 18.5–24.9, 25–29.9, and  $\geq 30$  kg/m<sup>2</sup>. Although not presented in Table 1, average serum vitamin D concentration decreased steadily across the range of FSG: normoglycemia (FSG  $< 100$  mg/dL), PreDM (FSG 100–125 mg/dL), and undiagnosed diabetes (FSG  $\geq 126$  mg/dL), with mean concentrations of 66.2 (1.2), 62.3 (1.4), and 54.2 (2.7) nmol/L, respectively. Mean vitamin D concentration was significantly lower in adults with PreDM and undiagnosed diabetes compared with those with normoglycemia ( $P = 0.004$  and  $P = 0.0002$ , respectively). Mean serum vitamin D concentrations in those with desirable BP ( $< 120/80$  mmHg), PreHTN (systolic BP 120–139 mmHg and/or diastolic BP 80–89 mmHg), and untreated hypertension (BP  $\geq 140/90$  mmHg) were 67.9 (1.4), 61.5 (1.2), and 62.4 (2.1) nmol/L, respectively. Compared

From the Pennington Biomedical Research Center, Louisiana State University System, Baton Rouge, Louisiana. Corresponding author: Alok K. Gupta, alok.gupta@pbrc.edu. Received 24 September 2010 and accepted 6 November 2010.

DOI: 10.2337/dc10-1829

© 2011 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See <http://creativecommons.org/licenses/by-nc-nd/3.0/> for details.



with those with desirable BP, adults with PreHTN had significantly lower mean vitamin D concentration ( $P < 0.0001$ ). Compared with those with both normal fasting glucose and desirable resting BP, who average 68.8 (1.4) nmol/L serum vitamin D concentration, adults with coexisting PreDM and PreHTN averaged 61.0 (1.5) nmol/L ( $P = 0.0002$ ). Similarly, those with undiagnosed diabetes and untreated hypertension averaged even lower at 49.3 (3.5) nmol/L ( $P < 0.0001$ ).

Disease-free Caucasian adults with serum vitamin D concentrations  $< 76.3$  nmol/L displayed (both unadjusted and adjusted) odds ratios for PreDM, PreHTN, and coexisting PreDM and PreHTN that were significantly greater than unity (Table 1).

**CONCLUSIONS**—The prevalence of PreDM, PreHTN, and coexisting PreDM and PreHTN in disease-free healthy adults is on the rise. One in four disease-free adults has PreDM, one in three disease-free adults has PreHTN, and one in 10 disease-free adults has coexisting PreHTN and PreDM (8). The risk for adverse cardiovascular outcomes in these disease-free adults is elevated independently of the enhanced risk for subsequent conversion to recognized high-risk states of diabetes and hypertension (8,9). Recognition of the enhanced risk for untoward events along with the modification or reversal of risk is a goal that all physicians aspire to.

This study alludes to the merits of serum vitamin D testing in seemingly healthy adults at risk for (or exhibiting) PreDM, PreHTN, or coexisting PreDM and PreHTN. These healthy disease-free men and women also tended to have a substantially larger waist circumference, higher serum triglycerides, and lower HDL cholesterol concentrations (all appropriately

more than or less than the desirable range) attesting to an increased cardiovascular disease risk (data not shown) (10). Although in this cross-sectional study, the mechanistic sequence of events leading to low vitamin D in healthy Caucasian men and women with aging and increasing BMI, or in the development of PreDM and PreHTN cannot be identified, low vitamin D levels in otherwise healthy Caucasian men and women are associated with PreDM, PreHTN, and coexisting PreDM and PreHTN. Both the unadjusted and adjusted odds ratios were significantly greater than unity for PreDM, PreHTN, and coexisting PreDM and PreHTN with serum vitamin D concentrations  $< 75$ th percentile. It is therefore plausible that among those with the above conditions and low serum vitamin D concentrations, exogenous vitamin D supplementation and increasing the serum 25-hydroxyvitamin D concentration may reverse subtle changes in FSG and resting BP. Disease-free adults with PreDM, PreHTN, and coexisting PreDM and PreHTN are on an accelerated pathway for adverse cardiovascular events (8,10). This simple measure, combined with individually tailored intervention/s targeted toward the reduction of other risk factors, may then also prevent subsequent conversion from PreDM to diabetes and PreHTN to hypertension.

**Acknowledgments**—No potential conflicts of interest relevant to this article were reported.

A.K.G. conceived the study, initiated the article, and compiled the final version for submission. M.M.B. performed the data analyses and participated in editing the article. W.D.J. directed the statistical analyses and participated in editing the article. All authors have read and are in agreement with the publication of this article.

## References

1. Florentin M, Elisaf MS, Mikhailidis DP, Liberopoulos EN. Vitamin D and metabolic syndrome: is there a link? *Curr Pharm Des* 2010;16:3417–3434
2. Boucher BJ. Vitamin D insufficiency and diabetes risks. *Curr Drug Targets* 2011; 12:61–87
3. Pilz S, Tomaschitz A, Ritz E, Pieber TR; Medscape. Vitamin D status and arterial hypertension: a systematic review. *Nat Rev Cardiol* 2009;6:621–630
4. Forman JP, Williams JS, Fisher ND. Plasma 25-hydroxyvitamin D and regulation of the renin-angiotensin system in humans. *Hypertension* 2010;55:1283–1288
5. Dobnig H, Pilz S, Scharnagl H, et al. Independent association of low serum 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D levels with all-cause and cardiovascular mortality. *Arch Intern Med* 2008; 168:1340–1349
6. Reddy Vanga S, Good M, Howard PA, Vacek JL. Role of vitamin D in cardiovascular health. *Am J Cardiol* 2010;106:798–805
7. United States Department of Health and Human Services. The National Health and Nutrition Examination Survey. Available at <http://www.cdc.gov/nchs/nhanes.htm>. Accessed 18 August 2009
8. Gupta AK, Brashear MM, Johnson WD. Coexisting prehypertension and prediabetes in healthy adults: a pathway for accelerated cardiovascular events. *Hypertens Res*. 13 January 2011 [Epub ahead of print]
9. Gupta AK, McGlone MM, Greenway FL, Johnson WD. Prehypertension in disease-free adults: a marker for an adverse cardiometabolic risk profile. *Hypertens Res* 2010;33:905–910
10. Gupta AK, Johnson WD. Prediabetes and prehypertension in disease free obese adults correlate with an exacerbated systemic proinflammatory milieu. *J Inflamm (Lond)* 2010;7:36