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

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$^2$. 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
Table 1 — Summary statistics and odds ratios (95% CI) for serum 25-hydroxyvitamin D (nmol/L) in unadjusted and adjusted models

| BMI category (kg/m²) | Sample size | Mean (95% CI) | Model 1* | Model 2 | PreHTN (ref = normotension) | PreDM (ref = normoglycemia) | PreHTN and PreDM (ref = normotension/normoglycemia) |
|---------------------|-------------|---------------|----------|---------|-----------------------------|-----------------------------|--------------------------------------------------|
| 18.5–25              | 1,711       | 64.4 (62.7–66.6) | 1.83 (1.45–2.31) | 1.50 (1.19–1.89) | 2.71 (1.84–3.99) | 0.0001 | 0.0006 |
| 25–30+               | 898         | 63.5 (61.3–66.7) | 1.61 (1.23–2.10) | 1.33 (1.01–1.75) | 2.41 (1.36–4.25) | 0.0004 | 0.0431 |
| 20–39                | 813         | 63.1 (59.0–68.1) | 1.77 (1.41–2.22) | 2.28 (1.72–3.01) | 2.55 (1.68–3.87) | 0.0001 | 0.0001 |
| 40–59                | 637         | 63.0 (59.3–66.9) | 4.90 (3.28–7.32) | 4.55 (3.08–6.73) | 10.21 (5.02–20.77) | 0.0001 | 0.0001 |
| 60–69                | 162         | 62.3 (59.3–66.3) | 2.55 (1.98–3.13) | 3.00 (2.54–3.54) | 4.80 (3.25–7.08) | 0.0001 | 0.0001 |
| >70                  | 186         | 58.0 (55.0–60.9) | 3.49 (1.98–6.15) | 5.21 (3.49–7.78) | 12.28 (4.61–32.71) | 0.0001 | 0.0001 |

Sex

| Sex             | Sample size | Mean (95% CI) | Model 1* | Model 2 | PreHTN (ref = normotension) | PreDM (ref = normoglycemia) | PreHTN and PreDM (ref = normotension/normoglycemia) |
|-----------------|-------------|---------------|----------|---------|-----------------------------|-----------------------------|--------------------------------------------------|
| Female          | 813         | 63.1 (59.0–68.1) | 1.00     | 1.00    | 1.00                        | 0.5198                      | 0.6464 0.3983                                       |
| Male            | 898         | 2.41 (1.86–3.13) | 1.26 (0.97–1.65) | 2.04 (1.62–2.56) | 2.35 (1.55–3.57) | 0.0808 | 0.0001 |

Model 1 is unadjusted. Model 2 is adjusted for age categories, sex, and BMI category.
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 screening for and treating young adults correlated with an exacerbated systemic proinflammatory milieu. J Inflamm (Lond) 2010;7:36

**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, Eliaf MS, Mikhalidis 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.