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

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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 ≤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).

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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 ≥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 ≥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 ≥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 ≥140/90 mmHg) were 67.9 (1.4), 61.5 (1.2), and 62.4 (2.1) nmol/L, respectively. Compared

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

		Sex		Age (years)				BMI category (kg/m^2)			
	Total	Male	Female	20–39	40–59	60–69	70+	<18.5	18.5–<25	25–<30	30+
Sample size	1,711	898	813	726	637	162	186	35	634	622	420
Mean	65	64.4	65.7	66.3	64	63.5	63.1	66.0	69.5	65.2	58.0
(95% CI)	(62.7–67.3)	(62.1–66.6)	(62.7–68.6)	(63.7–68.9)	(61.3–66.7)	(59.0–68.1)	(59.3–66.9)	(57.8–74.2)	(66.5–72.6)	(62.7–67.8)	(55.0–60.9)
	n	PreHTN (ref = normotension)		PreDM (ref = normoglycemia)				PreHTN and PreDM (ref = normotension/normoglycemia)			
Model 1*											
Vitamin D											
≤76.3 nmol/L	1,272	1.83	(1.45–2.31)	1.50		(1.19–1.89)		2.71		(1.84–3.99)	
P value			<0.0001			0.0006				<0.0001	
>76.3 nmol/L	439		1.00			1.00				1.00	
Model 2											
Vitamin D											
≤76.3 nmol/L	1,272	1.61	(1.23–2.10)	1.33		(1.01–1.75)		2.41		(1.36–4.25)	
P value			0.0004			0.0431				0.0024	
>76.3 nmol/L	439		1.00			1.00				1.00	
Age											
20–39	726		1.00			1.00				1.00	
40–59	637	1.77	(1.41–2.22)	2.28		(1.72–3.01)		2.55		(1.68–3.87)	
P value			<0.0001			<0.0001				<0.0001	
60–69	162	4.90	(3.28–7.32)	4.55		(3.08–6.73)		10.21		(5.02–20.77)	
P value			<0.0001			<0.0001				<0.0001	
70+	186	3.49	(1.98–6.15)	5.21		(3.49–7.78)		12.28		(4.61–32.71)	
P value			<0.0001			<0.0001				<0.0001	
Sex											
Female	813	1.00				1.00				1.00	
Male	898	2.41	(1.86–3.13)	3.00		(2.54–3.54)		4.80		(3.25–7.08)	
P value			<0.0001			<0.0001				<0.0001	
BMI category											
<18.5	35	0.68	(0.21–2.2)	1.31		(0.42–4.10)		1.73		(0.49–6.14)	
			0.5198			0.6464				0.3983	
18.5–<25	634		1.00			1.00				1.00	
25–<30	622	1.26	(0.97–1.65)	2.04		(1.62–2.56)		2.35		(1.55–3.57)	
P value			0.0808			<0.0001				<0.0001	
30+	420	2.87	(2.14–3.84)	3.15		(2.42–4.11)		7.88		(5.10–12.2)	
P value			<0.0001			<0.0001				<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 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 <75th 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.

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