Concentrations of Serum Vitamin D and the Metabolic Syndrome Among U.S. Adults

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Accumulating research suggests that circulating concentrations of vitamin D may be inversely related to the prevalence of diabetes (1–4), to the concentration of glucose (4–8), and to insulin resistance (4,5,8,9). In addition, vitamin D deficiency may be a risk factor for the metabolic syndrome (8,10), a highly prevalent condition among U.S. adults (11). Much remains to be learned, however, about the relationship between vitamin D status and metabolic syndrome. Because this topic has received scant attention and the available information was derived from a small clinically based sample, we sought to examine the nature and strength of the association between serum concentrations of vitamin D and the metabolic syndrome in a large nationally representative sample of the U.S. population.

RESEARCH DESIGN AND METHODS

— Between 1988 and 1994, a representative sample of the noninstitutionalized civilian U.S. population, selected using a multistage stratified sampling design, participated in the NHANES III (Third National Health and Nutrition Examination Survey). Survey participants were interviewed and invited for a clinical examination (12–14).

The metabolic syndrome was defined according to National Cholesterol Education Program criteria (11,15). Serum concentrations of vitamin D {25-hydroxyvitamin D [25(OH)D]} were measured using a radioimmunoassay method (DiaSorin, Stillwater, MN) (16). Detailed information about procedures for this assay was published in the NHANES III laboratory manual (14).

The analyses included the following variables: age, sex, race or ethnicity (white, African American, Mexican American, and other), education, smoking status (current, former, and never), serum cotinine concentration, concentration of C-reactive protein, total cholesterol concentration, leisure time physical activity, vitamin or mineral use during the previous 24 h (yes/no), alcohol use (times per month), intake of fruits and vegetables (times per day), and season of study participation.

We limited our analyses to 8,421 men and nonpregnant women who were ≥20 years and had fasted ≥8 h. Based on the final analytic sample, we created quintiles of concentration of 25(OH)D from its distribution determined using the sampling weights. To compare proportions across quintiles of serum concentrations of 25(OH)D, we used a test for linear trend. In addition, the associations between the metabolic syndrome and its components and concentrations of 25(OH)D were examined by multiple logistic regression analysis. To account for the complex survey design, we used SUDAAN and the medical examination clinic sampling weights to produce our weighted estimates and standard errors (17).

RESULTS

— Among the 8,421 participants, the unadjusted prevalence of the metabolic syndrome was 21.9%. Concentrations of 25(OH)D ranged from 8.7 to 227.9 nmol/l. The mean, median, and geometric mean concentrations were 74.0, 71.0, and 68.1 nmol/l, respectively. The mean concentration of 25(OH)D was 67.1 nmol/l (median 64.1 [range 12.5–192.2]) among those with the metabolic syndrome and 75.9 nmol/l (73.1 [8.7–227.9]) among those without the metabolic syndrome ($P < 0.001$).

After multiple adjustment, the odds of having the metabolic syndrome decreased progressively across increasing quintiles of concentration of 25(OH)D (Table 1). The associations between 25(OH)D and the metabolic syndrome did not differ between men and women ($P = 0.726$) or among the three major racial or ethnic groups ($P = 0.377$). After splitting the lowest quintile into two categories, <25.0 nmol/l (presumed hypovitaminosis D as the new reference category) and 25.0–48.4 nmol/l, while leaving the other quintiles unchanged, the odds ratios for increasing categories of concentration of 25(OH)D were 0.81 (95% CI 0.48–1.39), 0.67 (0.37–1.23), 0.62 (0.33–1.15), 0.50 (0.26–0.93), and 0.38 (0.20–0.72). After excluding people with diagnosed diabetes ($n = 7,904$), the adjusted odds ratios for having the metabolic syndrome relative to the 1st quintile for the 2nd through 5th quintiles of concentration of 25(OH)D were 0.85 (95% confidence limits 0.61, 1.17), 0.75 (0.54, 1.03), 0.62 (0.46, 0.86), and 0.46 (0.32, 0.66) ($P < 0.001$ by Wald χ^2). Among the components, significant inverse associations were present for quintiles of concentration of 25(OH)D and abdominal adiposity, hypertriglyceridemia, and hyperglycemia.

CONCLUSIONS

— Studies showing an inverse association between concen-

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Abbreviations: 25(OH-D), 25-hydroxyvitamin D.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1 —*Unadjusted prevalence and adjusted odds ratios and 95% confidence limits of having the metabolic syndrome by quintiles of serum vitamin D concentration among 8,421 U.S. adults aged ≥20 years, NHANES III, 1988–1994*

	Quintiles of vitamin D (nmol/l)					
	1 (≤48.4)	2 (48.5–63.4)	3 (63.5–78.1)	4 (78.2–96.3)	5 (≥96.4)	*P**
Metabolic syndrome						
Unadjusted prevalence†	27.5 (1.7)	26.6 (1.4)	23.3 (1.5)	18.7 (1.3)	13.5 (1.7)	<0.001
Model 1‡	1.00	0.91 (0.72, 1.17)	0.80 (0.62, 1.03)	0.65 (0.51, 0.83)	0.49 (0.37, 0.66)	<0.001
Model 2§	1.00	0.82 (0.60, 1.10)	0.75 (0.55, 1.02)	0.60 (0.44, 0.83)	0.46 (0.32, 0.67)	<0.001
Components of the metabolic syndrome						
Abdominal obesity						
Unadjusted prevalence†	49.9 (1.9)	43.7 (1.9)	37.2 (1.5)	31.0 (1.5)	19.3 (1.5)	<0.001
Model 1‡	1.00	0.74 (0.60, 0.91)	0.58 (0.49, 0.70)	0.47 (0.37, 0.59)	0.27 (0.21, 0.33)	<0.001
Model 2§	1.00	0.78 (0.61, 0.98)	0.65 (0.52, 0.81)	0.55 (0.41, 0.72)	0.30 (0.21, 0.42)	<0.001
Model 3‖	1.00	0.79 (0.63, 0.98)	0.68 (0.55, 0.85)	0.58 (0.44, 0.76)	0.32 (0.23, 0.45)	<0.001
Hypertriglyceridemia						
Unadjusted prevalence†	29.3 (1.5)	32.8 (1.4)	32.0 (2.0)	24.4 (1.8)	24.2 (2.6)	<0.001
Model 1‡	1.00	1.16 (0.96, 1.41)	1.17 (0.93, 1.47)	0.83 (0.66, 1.06)	0.90 (0.70, 1.14)	0.016
Model 2§	1.00	0.89 (0.69, 1.15)	0.88 (0.67, 1.16)	0.58 (0.45, 0.75)	0.59 (0.44, 0.80)	<0.001
Model 3‖	1.00	0.98 (0.75, 1.27)	1.03 (0.78, 1.37)	0.66 (0.50, 0.86)	0.76 (0.57, 1.01)	0.002
Model 4¶	1.00	1.00 (0.80, 1.24)	1.02 (0.80, 1.31)	0.67 (0.52, 0.85)	0.84 (0.64, 1.10)	0.005
Low HDL cholesterol						
Unadjusted prevalence†	39.8 (1.9)	37.9 (1.8)	38.4 (2.3)	36.6 (2.1)	33.3 (2.3)	0.031
Model 1‡	1.00	0.92 (0.75, 1.12)	0.94 (0.73, 1.22)	0.88 (0.69, 1.10)	0.77 (0.60, 0.97)	0.172
Model 2§	1.00	0.84 (0.69, 1.04)	0.89 (0.69, 1.16)	0.81 (0.64, 1.03)	0.71 (0.56, 0.90)	0.050
Model 3‖	1.00	0.88 (0.71, 1.09)	0.99 (0.76, 1.29)	1.03 (0.80, 1.31)	0.96 (0.76, 1.22)	0.636
Model 4¶	1.00	0.88 (0.71, 1.08)	0.99 (0.76, 1.29)	1.03 (0.82, 1.30)	0.92 (0.72, 1.17)	0.567
High blood pressure						
Unadjusted prevalence†	34.4 (1.5)	36.5 (1.7)	30.7 (2.1)	29.5 (1.8)	23.9 (1.9)	<0.001
Model 1‡	1.00	1.06 (0.89, 1.26)	0.84 (0.67, 1.05)	0.91 (0.69, 1.20)	0.79 (0.61, 1.02)	0.067
Model 2§	1.00	1.10 (0.89, 1.37)	0.91 (0.71, 1.18)	1.00 (0.73, 1.37)	0.88 (0.63, 1.21)	0.416
Model 3‖	1.00	1.17 (0.95, 1.44)	1.00 (0.77, 1.30)	1.16 (0.85, 1.59)	1.07 (0.77, 1.50)	0.489
Hyperglycemia						
Unadjusted prevalence†	14.6 (1.0)	15.1 (1.2)	9.9 (1.2)	10.8 (1.1)	6.3 (1.0)	<0.001
Model 1‡	1.00	1.01 (0.78, 1.31)	0.63 (0.44, 0.90)	0.78 (0.58, 1.05)	0.50 (0.34, 0.73)	<0.001
Model 2§	1.00	0.92 (0.69, 1.23)	0.59 (0.40, 0.87)	0.71 (0.50, 1.01)	0.44 (0.29, 0.68)	<0.001
Model 3‖	1.00	0.98 (0.74, 1.29)	0.61 (0.42, 0.89)	0.83 (0.59, 1.18)	0.54 (0.35, 0.84)	0.005

*For prevalence, *P* value is for a test for linear trend; for odds ratio, *P* value is for the Wald χ^2 test. †Data represent % (SE). ‡Model 1: adjusted for age. §Model 2: adjusted for age, sex, race or ethnicity, education, smoking status, cotinine concentration, total cholesterol concentration, C-reactive protein concentration, alcohol use, physical activity, intake of fruits and vegetables, vitamin or supplement use, and season of study participation. ‖Model 3: adjusted for all variables in model 2 plus other components of the metabolic syndrome. ¶Model 4: adjusted for all variables in model 3 minus concentration of total cholesterol.

trations of vitamin D and insulin resistance provide a possible explanation for our findings of an inverse association between serum concentrations of vitamin D and the prevalence of the metabolic syndrome (4,5,8,9). Insulin resistance is considered a likely mechanism underlying the metabolic syndrome (18). An inverse association between various anthropometric measures and intake of vitamin D or circulating concentrations of vitamin D has been reported by a number of studies (19,20). Because excess weight is a major component of the metabolic syndrome, the associations noted in our analyses may largely reflect an association between concentrations of vitamin D and excess weight.

The principal limitation of our study was its cross-sectional design, and thus the causative nature of the association cannot be established. In addition, this study was based on a single measurement of vitamin D. Finally, parathyroid hormone was not measured in this survey.

Further investigation into whether vitamin D may play a role in the prevention of diabetes and pre-diabetic states appears warranted. Because of the close interrelationships between vitamin D, parathyroid hormone, calcium, and phosphate, untangling the contributions of each of these factors on insulin resistance and glucose homeostasis is important in developing possible future approaches to the prevention of insulin resistance, the metabolic syndrome, and diabetes.

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