Associations Between Concentrations of Vitamin D and Concentrations of Insulin, Glucose, and HbA_{1c} Among Adolescents in the United States

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OBJECTIVE—Our objective was to examine the associations between concentrations of vitamin D and concentrations of insulin, glucose, and HbA_{1c} in a nationally representative sample of adolescents in the U.S.

RESEARCH DESIGN AND METHODS—We used data for 1,941 adolescents, aged 12–17 years, who participated in the National Health and Nutrition Examination Survey between 2001 and 2006.

RESULTS—Adjusted concentrations of insulin were ~24% lower among male subjects with a concentration of vitamin D ≥75 nmol/L than among male subjects with a concentration of vitamin D <50 nmol/L ($P = 0.003$). Concentrations of vitamin D were inversely associated with concentrations of glucose only among Mexican American male subjects ($P = 0.007$). No significant associations between concentrations of vitamin D and HbA_{1c} were detected.

CONCLUSIONS—Our results support an inverse association between concentrations of vitamin D and insulin primarily in adolescent male subjects.

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In recent years, the relationships between vitamin D and factors involved in glucose homeostasis have received a great deal of attention. Few studies have been conducted using pediatric samples (1–3). Because the prevalence of deficient or insufficient vitamin D status is high among children and adolescents in the U.S. and is possibly increasing (4,5), any deleterious effect of suboptimal vitamin D status on glucose homeostasis is of interest, especially in light of concerns about increases in diabetes among youth in the U.S. (6). Most previous studies have used small, selected samples of adolescents. To provide additional insights into the associations between circulating concentrations of vitamin D and concentrations of insulin and glucose, we examined data from a large, representative sample of adolescents that included African Americans and Mexican Americans in the U.S.

RESEARCH DESIGN AND METHODS

We used data from the National Health and Nutrition Examination Survey (NHANES) 2001–2006 (7). The participants were recruited using a multistage, stratified sampling design, which is an efficient approach to obtaining a sample representative of the civilian noninstitutionalized population. The participants were interviewed at home and were invited to attend a mobile examination center, where they were asked to complete additional questionnaires, to undergo various examinations, and to provide a blood sample. The study received approval from the NHANES Institutional Review Board, and participants were asked to sign an informed consent form. Details about the survey can be found elsewhere (7).

Serum concentrations of vitamin D (25-hydroxyvitamin D) were measured using the Diasorin 25-OH-vitamin D assay (Diasorin, Stillwater, MN), a radioimmunoassay (8). We created three categories of vitamin D concentrations: deficiency, <50 nmol/L; insufficiency, 50 to <75 nmol/L; and sufficiency, ≥75 nmol/L (9). The methods used to measure insulin (a Pharmacia insulin radioimmunoassay kit, a Tosoh AIA-PACK IRI, and a Merocodia insulin enzyme-linked immunosorbent assay), glucose (a Cobas Mira chemistry system and a Roche/Hitachi 911 analyzer), and HbA_{1c} (Primus automated high-performance liquid chromatography models CLC330 and CLC385 and an HbA_{1c} 2.2 Plus glycohemoglobin analyzer) are described elsewhere (7).

Covariates included age, sex, race, or ethnicity (white, African American, Mexican American, other Hispanic, or mixed race), leisure-time physical activity, BMI percentiles, supplement use during the past months (yes or no), concentrations of HDL cholesterol and non-HDL cholesterol, and a 6-month sampling period. To estimate physical activity, we calculated an average daily metabolic equivalent task hours index. BMI percentiles were calculated from measured weight and height using the Centers for Disease Control and Prevention's growth charts.

We limited our analyses to participants aged 12–17 years who attended the morning examination and who had fasted at least 8 h. We excluded participants who had been diagnosed with diabetes. Adjusted mean concentrations of insulin (after log transformation), glucose, and HbA_{1c} were calculated using ANCOVA. The statistical significance of the tests for linear trend of means conducted by using general linear contrasts was assessed with an adjusted Wald F statistic that adjusts for the denominator degrees of freedom. The statistical software SUDAAN was used for the analyses to account for the multistage, stratified sampling design.

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Table 1—*Unadjusted and adjusted geometric means for concentrations of insulin and means for glucose and HbA_{1c} by levels of concentrations of vitamin D among participants aged 12–17 years, NHANES 2001–2006*

		Unadjusted vitamin D (nmol/L)				Vitamin D adjusted for sampling period (nmol/L)				Vitamin D adjusted for multiple covariates (nmol/L)*			
	n	<50	50 to <75	≥75	*P*†	<50	50 to <75	≥75	*P*†	<50	50 to <75	≥75	*P*†
Insulin (pmol/L)													
Total	1,941	60.1	50.4	44.7	<0.001	60.3	50.4	44.5	<0.001	56.3	51.2	47.7	0.004
Male subjects	1,000	60.4	48.2	40.7	<0.001	60.3	48.2	40.7	<0.001	56.7	48.5	43.3	0.003
Female subjects	941	59.8	53.0	50.8	0.040	60.3	52.8	50.2	0.021	55.7	54.4	54.7	0.818
White subjects	531	57.5	51.8	44.7	0.013	57.6	51.8	44.7	0.012	52.8	51.5	47.4	0.172
African American subjects	620	59.7	46.1	43.3	0.053	60.1	45.3	42.8	0.033	57.4	51.7	48.1	0.080
Mexican American subjects	632	68.4	51.3	44.9	<0.001	68.0	51.5	45.4	<0.001	62.8	54.0	52.3	0.008
Male subjects													
White	268	72.5	50.2	40.7	0.001	71.8	50.1	41.0	0.001	58.8	50.2	44.6	0.043
African American	343	50.2	40.2	37.7	0.075	50.4	39.9	37.3	0.053	48.2	44.5	37.4	0.033
Mexican American	313	67.7	49.2	40.3	<0.001	67.4	49.3	40.6	<0.001	60.9	51.5	46.3	0.005
Female subjects													
White	263	48.3	53.5	50.5	0.701	48.5	53.6	50.1	0.776	46.9	53.0	52.7	0.236
African American	277	69.3	57.3	78.6	0.773	69.7	55.9	77.1	0.808	68.9	58.6	78.4	0.677
Mexican American	319	69.1	54.2	58.9	0.301	68.5	54.7	60.1	0.349	65.5	57.5	63.3	0.726
Glucose (mmol/L)													
Total	1,941	5.1	5.1	5.1	0.469	5.1	5.1	5.1	0.806	5.1	5.1	5.1	0.457
Male subjects	1,000	5.2	5.2	5.2	0.847	5.2	5.2	5.2	0.993	5.2	5.2	5.2	0.710
Female subjects	941	4.9	5.0	4.9	0.862	5.0	5.0	4.9	0.503	5.0	5.0	4.9	0.401
White subjects	531	5.1	5.1	5.1	0.812	5.1	5.1	5.1	0.982	5.1	5.1	5.1	0.728
African American subjects	620	5.0	4.9	4.9	0.397	5.0	4.9	4.9	0.321	5.0	4.9	4.8	0.095
Mexican American subjects	632	5.2	5.1	5.1	0.119	5.2	5.1	5.1	0.072	5.2	5.1	5.0	0.012
Male subjects													
White	268	5.3	5.2	5.2	0.916	5.3	5.2	5.2	0.841	5.2	5.2	5.2	0.973
African American	343	5.1	5.0	4.9	0.072	5.1	5.0	4.9	0.071	5.1	5.0	4.9	0.098
Mexican American	313	5.4	5.2	5.2	0.009	5.4	5.2	5.2	0.003	5.4	5.2	5.2	0.007
Female subjects													
White	263	4.9	5.0	4.9	0.730	5.0	5.0	4.9	0.591	5.0	5.0	4.9	0.584
African American	277	4.9	4.8	4.8	0.907	4.9	4.8	4.8	0.789	4.9	4.8	4.8	0.706
Mexican American	319	5.1	5.0	4.9	0.150	5.1	5.0	4.9	0.159	5.1	5.0	4.9	0.258
HbA_{1c} (%)													
Total	1,941	5.2	5.2	5.2	0.471	5.2	5.2	5.2	0.286	5.2	5.2	5.2	0.626
Male subjects	1,000	5.2	5.2	5.2	0.803	5.2	5.2	5.2	1.000	5.2	5.2	5.2	0.187
Female subjects	941	5.2	5.2	5.1	0.227	5.2	5.1	5.1	0.086	5.2	5.2	5.2	0.694
White subjects	531	5.1	5.2	5.2	0.282	5.1	5.2	5.2	0.364	5.1	5.2	5.2	0.487
African American subjects	620	5.3	5.3	5.2	0.578	5.3	5.3	5.2	0.552	5.3	5.3	5.2	0.427
Mexican American subjects	632	5.2	5.2	5.2	0.562	5.2	5.2	5.2	0.832	5.2	5.2	5.2	0.621
Male subjects													
White	268	5.1	5.2	5.2	0.287	5.1	5.2	5.2	0.208	5.1	5.2	5.2	0.182
African American	343	5.3	5.3	5.2	0.587	5.3	5.3	5.2	0.575	5.3	5.4	5.2	0.596
Mexican American	313	5.2	5.2	5.2	0.815	5.2	5.2	5.2	0.676	5.2	5.2	5.2	0.600
Female subjects													
White	263	5.1	5.1	5.1	0.906	5.1	5.2	5.1	0.910	5.1	5.1	5.1	0.899
African American	277	5.3	5.2	5.1	0.493	5.3	5.2	5.1	0.443	5.3	5.2	5.1	0.298
Mexican American	319	5.1	5.2	5.1	0.891	5.1	5.2	5.1	0.905	5.1	5.2	5.2	0.851

*Adjusted for age; sex; race, or ethnicity; leisure-time physical activity; 30-day use of vitamins, minerals, or other dietary supplements; BMI percentile; HDL cholesterol; non-HDL cholesterol; and examination period. Examination period was a dichotomous variable representing the two 6-month periods of 1 November through 30 April and 1 May through 31 October. †*P* value for adjusted Wald *F* test for linear contrast.

RESULTS—During the 6-year study period, 2,070 adolescents, aged 12–17 years, attended the morning examination of the mobile examination center. Data for concentrations of glucose, insulin, and vitamin D were available for 2,028 subjects. After excluding records with missing data for covariates, the final analytic sample comprised 1,941 participants, including 531 whites, 620 African Americans, 632 Mexican Americans, and 158 participants of another race or ethnicity.

The means were 65.9 pmol/L (geometric mean: 50.3 pmol/L), 5.1 mmol/L, 5.2%, and 59 nmol/L for concentrations of

insulin, glucose, HbA_{1c}, and vitamin D, respectively. Furthermore, 31.5 ± 2.1% (means ± SE; male subjects 27.4%, female subjects 35.7%) had a concentration of vitamin D <50 nmol/L, 48.3 ± 2.0% (male subjects 49.8%, female subjects 46.6%) had a concentration 50 to <75 nmol/L, and 20.3 ± 1.6% (male subjects 22.7%, female subjects 17.7%) had a concentration ≥75 nmol/L.

Adjusted concentrations of insulin were approximately 24% lower among male subjects with a concentration of vitamin D ≥75 nmol/L than among male subjects with a concentration of vitamin D <50 nmol/L ($P = 0.003$) (Table 1). Concentrations of vitamin D were inversely associated with concentrations of glucose among Mexican American male subjects ($P = 0.007$). No significant associations between concentrations of vitamin D and HbA_{1c} were detected.

CONCLUSIONS—After adjusting for covariates, we found significant inverse associations between concentrations of vitamin D and insulin among adolescent male subjects but not female subjects. Several previous reports have noted inverse relationships between concentrations of vitamin D and surrogate measures of insulin resistance in samples of obese adolescents (1,2) and in a population-based sample of children and adolescents (3). Studies in animals and humans suggest that vitamin D status affects insulin secretion (10), vitamin D receptor expression (11), and tyrosine phosphorylation of insulin receptor substrate 1 (12).

The large, nationally representative sample of adolescents represents an important strength of our study. Several limitations deserve to be acknowledged. The cross-sectional study design precludes establishing causality. The possible effect of the use of different methods to measure concentrations of insulin, glucose, and HbA_{1c} during the various survey cycles on our results is unclear. Concern has been expressed about possible assay variability for the vitamin D assay in the NHANES (13). However, the apparent impact on vitamin D parameters for the period of 2000–2004 was small (14). We were unable to adjust for Tanner stage because this information was not collected.

Prospective studies and clinical trials are needed to clarify the relationships between concentrations of vitamin D and factors involved in glucose homeostasis. Studies using gold-standard techniques to assess insulin resistance also would yield valuable insights. The possibility that vitamin D may affect insulin resistance has potential implications for testing vitamin D concentrations in children and adolescents; recommendations regarding the use of vitamin D supplements and sun exposure, especially in populations at risk for insulin resistance; and fortification of foods. The prevalence of vitamin D deficiency and insufficiency is substantial among adolescents in the U.S.; ~2% of adolescents had concentrations of vitamin D <27 nmol/L, 14% had concentrations <50 nmol/L, and 33% had a concentration ≥75 nmol/L during 2001–2004 (4,5).

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E.S.F. researched data and wrote the manuscript. G.Z. researched data, contributed to the discussion, and reviewed and edited the manuscript. J.T. contributed to the discussion and reviewed and edited the manuscript. C.L. contributed to the discussion and reviewed and edited the manuscript.

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