Serum 25-Hydroxy Vitamin D and Insulin Resistance, Metabolic Syndrome, and Glucose Intolerance among Arab Americans

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Submitted 1 December 2009 and accepted 11 March 2010.

This is an uncopyedited electronic version of an article accepted for publication in Diabetes Care. The American Diabetes Association, publisher of Diabetes Care, is not responsible for any errors or omissions in this version of the manuscript or any version derived from it by third parties. The definitive publisher-authenticated version will be available in a future issue of Diabetes Care in print and online at http://care.diabetesjournals.org.
Objective-To describe 25-hydroxy Vitamin D (25-OH-D) levels and examine associations between 25-OH-D levels and insulin resistance (IR), metabolic syndrome (MS), and glucose intolerance in Arab Americans (AA).

Research design and methods-Serum 25-OH-D levels were measured in a representative, cross-sectional sample of 542 AA with IR (46%), MS (33%), and glucose intolerance (42%).

Results-Vitamin D insufficiency (5 to <20ng/mL) was present in 75% and hypovitaminosis D (20 to <40ng/mL) in 24% of participants. In men, 25-OH-D levels were lower in those with glucose intolerance than normoglycemia (p=0.01). No such difference was found in women. In men, 25-OH-D was negatively correlated with HOMA-IR (r=-0.19; P=0.0043), triglycerides (r=-0.18; P=0.0069), FPG (r=-0.15; P=0.027), and A1C (r=-0.14; P=0.038). In women, 25-OH-D was positively correlated with HDL (r=0.19; P=0.0008).

Conclusions- Vitamin D insufficiency and hypovitaminosis D are extremely common among AA, and in men are associated with IR, components of the MS, and glucose intolerance.
Altered calcium and vitamin D homeostasis are associated with insulin resistance (IR), reduced β-cell function, metabolic syndrome (MS), glucose intolerance, and diabetes (1-4). We have previously shown that the age- and sex-standardized prevalence of diabetes is 18% among Arab Americans (AA) (5-6). Although previous studies have documented an association between 25-hydroxy vitamin D (25-OH-D) levels and glucose intolerance, few have focused on the Arab American community, a culturally unique, understudied, and medically underserved community in which traditional dress may limit sun exposure and dietary preferences may further contribute to 25-OH-D deficiency. The purpose of this study was to describe levels of 25-OH-D and examine associations between 25-OH-D levels and IR, MS, and glucose intolerance among AA adults.

**RESEARCH DESIGN AND METHODS**

The methods have been described in detail elsewhere (5-7). Briefly, we studied 542 randomly selected AAs 20-75 years of age. Demographic, anthropometric, and behavioral characteristics were measured. To examine food preferences, we calculated the ratio of Arab meals to total meals consumed in 1-week; a higher ratio indicates consumption of more Middle Eastern foods (diet rich in meat, yogurt, grains, and vegetables, and low in food fortified with vitamin D such as milk and breakfast cereals). Subjects performed strenuous physical activity if, ≥3 times weekly, they engaged in exercise for ≥20 minutes that made them breathe hard and sweat. Those engaging in strenuous activity <3 times weekly performed moderate physical activity and all others were considered inactive. Smoking status was self-reported and verified by serum cotinine (Siemens Healthcare Diagnostics Inc., Deerfield, IL).

Acculturation was assessed with a validated 4-item survey.

Fasting glucose, insulin, lipids, and hemoglobin A1c (A1C) were measured and glucose tolerance assessed with 75-g oral glucose tolerance tests. IR was defined as HOMA-IR≥3.8 (8). Subjects meeting the revised NCEP ATP III criteria were defined as having the MS (9). Glucose intolerance was defined as impaired fasting glucose, impaired glucose tolerance, or diabetes (10).

Serum 25-OH-D samples were coded, centrifuged, and stored at -70°C. In 2009, serum 25-OH-D was measured using the 125I Radioimmunoassay kit (DiaSorin, Stillwater, MN) and quality control materials provided by the manufacturer. The inter-assay coefficients of variation are 7.3% at 13.7ng/mL and 9.6% at 53.4ng/mL. 25-OH-D status was classified as: Deficiency: <5ng/mL; Insufficiency: 5-<20ng/mL; Hypovitaminosis D: 20-<40ng/mL; Sufficiency: 40-<100ng/mL; and Toxicity: ≥100ng/mL (11).

All analyses were performed separately by sex. Data are expressed as mean±standard deviation or percentage. Continuous or categorical data were analyzed utilizing ANOVA or chi-square tests. 25-OH-D levels were described by demographic, anthropometric, behavioral characteristics, and by measures of disease status. Spearman correlation coefficients were calculated to examine association between 25-OH-D levels and measures of disease status. Analyses were performed using SAS, version 9.1 (SAS Institute, Cary, North Carolina).

**RESULTS**

The mean age was 38±13 years and 39% were men. The mean BMI was 28.4±5.5 kg/m². Subjects consumed mostly traditional Middle Eastern foods. The majority were inactive or only moderately physically active (52%). One-third reported smoking cigarettes. Acculturation was low. IR was present in
Vitamin D insufficiency was present in 75% and hypovitaminosis D in 24%; only 4 subjects had 25-OH-D levels in the normal range. Serum 25-OH-D levels were lower in women (14.1±7.1) than men (18.1±6.4) (p<0.0001). Only two subjects reported taking vitamin D supplements.

Vitamin D levels as a function of glucose tolerance status and other factors is shown in Table 1. In men, 25-OH-D levels were lower in those with glucose intolerance than in those who were normoglycemic (p=0.005). No such difference was found in women. 25-OH-D levels also varied by season (p<0.0001) and by level of cotinine (p=0.04) in men. Men with IR, hypertriglyceridemia, and glucose intolerance had lower serum 25-OH-D levels than men who were insulin sensitive (p=0.01), had triglycerides <150mg/dL (p=0.0016), and FPG <100mg/dL (p=0.023). Decreased 25-OH-D levels were present in women with the MS compared to those without the MS (p=0.0086). Women with low HDL levels had low 25-OH-D levels compared to those with HDL levels ≥50mg/dL (p=0.0016).

In men, serum 25-OH-D was negatively correlated with HOMA-IR (r=-0.19; p=0.0043), triglycerides (r=-0.18; P=0.0069), FPG (r=-0.15; P=0.027) and A1C (r=-0.14; p=0.038). In women, 25-OH-D was positively correlated with HDL (r=0.19; p=0.0008).

**CONCLUSIONS**

This study provides population-based estimates of vitamin D status among AA and reports associations between 25-OH-D levels and IR, MS, and glucose intolerance. Our findings are similar to those reported from a convenience sample of 87 AA women and a representative sample of 6,228 people in the U.S. (12-13) in whom vitamin D levels were not adequate. 25-OH-D levels have been inversely associated with diabetes in non-Hispanic whites and Mexican Americans, but not in non-Hispanic blacks despite their high prevalence of diabetes and inadequate vitamin D levels (14-15). Our findings in AA males are similar to those reported in Hispanic whites and Mexican Americans.

There are several potential limitations to our study. First, factors influencing skin synthesis of vitamin D such as traditional Islamic dress, ultraviolet exposure, and sunscreen utilization were not assessed nor was dietary consumption of vitamin D. In addition, the cross-sectional design of our study limited our ability to examine causal relationships between levels of 25-OH-D and IR, MS, and glucose intolerance.

In summary, the prevalence of inadequate vitamin D levels is high among AA men and women. Very few subjects reported taking supplements. In men, lower 25-OH-D levels were associated with IR, components of the metabolic syndrome, and glucose intolerance. In women, lower 25-OH-D was associated with lower HDL cholesterol levels. Greater public awareness and interventions to encourage vitamin D consumption are needed in the AA community.

**ACKNOWLEDGEMENTS**

This study was funded by the American Diabetes Association and through a Clinical and Translational Science Award from the Michigan Institute for Clinical & Health Research by grant UL1RR024986 from the National Institutes of Health. Statistical support was provided by the Biostatistics and Economic Modeling Core and laboratory analysis was conducted by the Chemistry Laboratory Core of the Michigan Diabetes Research and Training Center funded by DK020572 from the National Institute of Diabetes and Digestive and Kidney Diseases. The authors have no conflicts of interest to disclose.

**Conflict of Interest:** Nicole R. Pinelli-Nothing to disclose; Morton B. Brown-Nothing to disclose; Linda A. Jaber-Nothing to disclose.
to disclose; William H. Herman-Nothing to disclose.
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## Table 1: Vitamin D levels as a function of glucose tolerance status and other factors.

|                | Men                          | Women                        |
|----------------|------------------------------|------------------------------|
|                | Normoglycemia | Glucose | p-value* | Total | Normoglycemia | Glucose | p-value* | Total |
|                | Intolerance | Men      |          |       | Intolerance | Men      |          |       |
| Sample size   | 103          | 111      | 214      | 204   | 113          | 317      | 14.1±7.1 |
| All           | 19.4±7.0     | 16.9±5.5 | 0.005    | 18.1±6.4 | 14.1±7.6 | 14.0±6.2 | 0.95     | 14.1±7.1 |
| Age (years)*  | 0.94         | 0.92     |          | 0.31  | 0.16         |          |          | 0.16  |
| 20-29         | 20.1±6.2     | 16.1±4.5 |          | 18.6±5.9 | 13.8±6.8 | 15.7±9.5 | 14.0±7.1 |
| 30-39         | 19.3±8       | 16.8±7   |          | 18.3±7.7 | 15±9.3  | 13.2±5.9 | 14.8±8.9 |
| 40-49         | 20.6±7.2     | 16.8±5.2 |          | 18.2±6.2 | 13.8±7.3 | 11.9±3.5 | 13.1±6.2 |
| 50-59         | 17.5±5.7     | 17.4±5.9 |          | 17.4±5.7 | 12.5±4.3 | 15.2±7   | 14.3±6.3 |
| ≥ 60          | 17.6±5.1     | 17.4±4.7 |          | 17.5±4.7 | 13.2±4.3 | 14.4±6.1 | 14.1±5.7 |
| BMI (kg/m²)*  | 0.31         | 0.16     |          |       |             |          |          |       |
| <30           | 19.1±7.2     | 17.6±5.9 |          | 18.4±6.6 | 14.3±8.5 | 16.3±6.8 | 14.8±8.1 |
| 30-<35        | 20.8±6.3     | 15.9±4.5 |          | 18±5.8  | 12.8±5   | 12.7±5.5 | 12.8±5.2 |
| ≥35           | 18.8±8.2     | 13.3±4.1 |          | 15.8±6.7 | 14.2±5.2 | 12.9±5.7 | 13.4±5.5 |
| Food Preference+* | 0.15         | 0.50     |          |       |             |          |          |       |
| <0.5          | 20.7±6.1     | §         |          | 21.6±6.3 | 18.6±7.6 | §         | 18±7.4  |
| 0.5-<0.8      | 18.7±6.5     | 16.5±6   |          | 17.9±6.4 | 15.1±7.3 | 13.7±5.2 | 14.6±6.7 |
| 0.8+          | 18.1±6.2     | 16.7±5.5 |          | 17.2±5.8 | 12.8±5.9 | 13.9±5.9 | 13.2±5.9 |
| Physical Activity* | 0.22         | 0.98     |          |       |             |          |          |       |
| Strenuous/Moderate | 19.7±7.6     | 17.5±5.3 |          | 18.6±6.6 | 14.6±9.2 | 14.1±7.2 | 14.4±8.6 |
| Light/Inactive | 19±6.2       | 16.1±5.8 |          | 17.4±6.1 | 13.7±6  | 14.2±5.6 | 13.8±5.8 |
| Smoking Status* | 0.44         | 0.27     |          |       |             |          |          |       |
| Current Smoker | 18.6±6.3     | 16.6±5.6 |          | 17.7±6.1 | 14.5±7.5 | 12.9±4.8 | 14±6.9  |
| Ex Smoker     | 19.9±6.4     | 17.9±3.3 |          | 18.7±4.7 | 17.5±7.5 | 15.3±5.3 | 16.5±6.5 |
| Never Smoker  | 20.4±7.9     | 16.9±6   |          | 18.4±7  | 13.7±7.6 | 14.3±6.7 | 13.9±7.2 |
### Vitamin D and Arab Americans

| Cotinine Status±* | Normal | Abnormal | p-value | Normal | Abnormal | p-value |
|-------------------|--------|----------|---------|--------|----------|---------|
| <10               | 20.2±7.5 | 16.8±5.6 | 0.04 | 18.2±6.7 | 14.2±7.7 | 0.78 |
| 10 – 99           | 21.3±6.2 | 19.6±4.9 |       | 20.5±5.6 | 12.7±3.8 |       |
| 100-199           | 17.3±6.5 | 16.9±7.1 |       | 17.1±6.5 | 12±6 |       |
| 200-299           | 20.9±7.6 | 16.8±4.2 |       | 19.5±6.9 | 17.9±11 |       |
| 300+              | 15.3±4.2 | 15.7±5.5 |       | 15.5±4.8 | 14.5±4.9 |       |
| Acculturation*    | 0.52 | 0.50 |       |       |       |       |
| <2                | 18.3±5.9 | 17.1±5.6 |       | 17.6±5.7 | 13.8±7.3 |       |
| 2+                | 23±9.2 | 15.4±5.5 |       | 20.8±9 | 15.2±8.7 |       |
| Season*           | <0.0001 | 0.20 |       |       |       |       |
| Jan-March         | 13.3±5.2 | 13.7±4.7 |       | 13.6±4.8 | 11.4±4.5 |       |
| Apr-June          | 18.3±6.4 | 17.1±5.1 |       | 17.7±5.7 | 12.1±4.5 |       |
| July-Sept         | 21.6±6.9 | 18.2±4.7 |       | 20±6.2 | 15±8.6 |       |
| Oct-Dec           | 19.3±7 | 16.7±6.7 |       | 17.8±6.8 | 16.2±8.4 |       |

### Normal Abnormal p-value Normal Abnormal p-value

| HOMA-IR        | 19.4±6.9 | 16.9±5.7 | 0.01 | 14.8±8.2 | 13.1±5.2 | 0.1 |
| Metabolic syndrome | 18.5±6.6 | 17.1±5.8 | 0.16 | 14.9±7.9 | 12.6±5.1 | 0.0086 |
| Waist circumference | 18.3±6.5 | 17.4±5.9 | 0.45 | 15±8.4 | 13.1±5.3 | 0.093 |
| Hypertension    | 18.1±6.7 | 18.3±5.8 | 0.62 | 14±7.3 | 14.3±6.8 | 0.56 |
| Triglycerides   | 19.2±6.7 | 16.5±5.6 | 0.0016 | 14.3±7.4 | 13.4±6 | 0.37 |
| HDL             | 18.4±6.7 | 17.8±6.1 | 0.52 | 15.4±8.4 | 12.9±5.4 | 0.0016 |
| Fasting plasma glucose | 19.6±7 | 17.4±6 | 0.023 | 14.4±8 | 13.7±6.1 | 0.69 |

### HbA1c

| <7 | 7-<9 | 9+ | <7 | 7-<9 | 9+ |
|----|------|----|----|------|----|
| 18.3±6.5 | 14.4±4.4 | 16.6±4.4 | 0.2 | 14±7.2 | 15.4±6.1 | 14.6±5 | 0.41 |

* P-value: of factor adjusted for glycemic status
+ Ratio of Arabic meals to total meals consumed in a 1-week period with a higher ratio indicating consumption of more Middle Eastern foods.
± Cotinine levels <10 ng/mL are considered to be consistent with no active smoking.
§Insufficient data