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The Longitudinal Association of Vitamin D Serum Concentrations & Adiposity Phenotype

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Abstract

Several *cross-sectional* studies have reported on the association between serum 25-hydroxy vitamin D concentrations (25(OH)D) and body mass index (BMI). We examined the longitudinal effect of BMI on serum 25(OH)D concentrations among 866 Puerto Rican adults living in the Greater Boston area: 246 men and 620 women, aged 45–75 years at baseline and 2 year. Our analyses showed negative correlations at two time points between BMI and serum 25(OH)D concentrations. The multivariate analysis showed that when predicting the change of serum 25(OH)D concentrations, baseline-BMI had significant inverse association ($P<0.04$) controlling for age, sex, and baseline-25 (OH)D). This association remained significant after adjusting for vitamin D supplement use, smoking, miles walking/day and alcohol intake ($P<0.01$). In conclusion, the major findings of the present study are obesity 1) was inversely associated with 25(OH)D at baseline; 2) with the change in serum 25(OH)D at 2-year in this population of older Puerto Rican adults living in the Boston area.

Keywords

vitamin D; serum 25(OH)D; obesity; BMI; Puerto Rican

1. Introduction

The prevalence of overweight and obesity has increased among all socioeconomic classes, thus leading to an increased risk of associated mortality and morbidity [1]. A recent report indicated that vitamin D (vitD) deficiency is another re-emerging global health problem that might lead to an increase in the prevalence of related-chronic diseases [2]. Several factors are known to influence 25-hydroxy vitamin D [25(OH)D] concentrations, including age, sun exposure, skin pigmentation, ethnicity, obesity, and physical activity [3, 4]. Ethnic minorities, *generally*, and Puerto Ricans (PRs), *specifically*, shoulder great burden of health disparities, which might results in a greater risk of chronic disease [5–7]. In the US, obesity is prevalent, among minorities such as Hispanics, i.e. 39.1% [8, 9]. In a review by Renzaho

and colleagues, they have reported that ethnic minorities have significantly higher risk of vitD deficiency along with higher obesity rate, nevertheless due to the nature of the available data, the link between vitD deficiency and obesity-related chronic disease could not be affirmed [10]. The association between vitD deficiency and obesity is consistently documented, indicating that obesity is inversely associated with lower serum 25(OH)D [11–14]. The aim of this study is to determine the baseline and longitudinal associations for body mass index (BMI) on serum 25(OH)D among participants of the Boston Puerto Rican Health Study (BPRHS) and its ancillary study Boston Puerto Rican Osteoporosis Study (BPROS).

2. Materials and Methods

2.1. Study Population and Data Collection

Briefly, self-identified Puerto Rican adults, aged between 45–75 years, were recruited in the Greater Boston area as participants in the BPRHS to examine the role of social and psychological stress on physiological dysfunction and related health outcomes. Study design, sampling, and recruitment methods have been described in detail elsewhere [15]. Once the 2-yr follow up was complete, participants were re-consented for the osteoporosis study, BPROS and had bone density and body composition measurements, additional blood samples and completed further questionnaires; more detailed information are described elsewhere [15]. All protocols were approved by the Institutional Review Boards at Tufts Medical Center and Northeastern University, and each participant provided written informed consent.

2.2. Laboratory assays

At each time point, fasting blood samples (12-h) were drawn by a certified phlebotomist at the participant's home on the morning after the home interview, or as soon thereafter as possible. Aliquots were saved and stored at −80°C until processed. Serum 25(OH)D concentration were measured by extraction followed by 25I radioimmunoassay Packard COBRA II Gamma Counter (DiaSorin Inc., Stillwater, MN 55082) catalog # 68100E with intra-assay and inter-assay coefficients of variation of 10.8% and 9.4%, respectively.

2.3. Covariates Assessments and Definition

BMI was calculated as weight (kg) divided by height $(m)^2$ and categorized using the class III obesity BMI (BMI<25 kg/m^2, 25–29.9 kg/m^2, 30–34.5 kg/m^2, 35–39.9 kg/m^2, ≥ 40 kg/m^2) [16]. Smoking was categorized into yes and no for the current behavior.

2.4. Statistical analyses

All statistical analyses were conducted with SAS 9.1.3 (SAS Institute Inc., Cary, NC). All tests were 2-sided with $P < 0.05$ considered statistically significant. We used student *t*-test to compare continuous variables and chi square for categorical variables. Paired *t*-test was used to compare variables across time points. The least-square means and linear trends of 25(OH)D across the BMI categories were tested using the PROC GLM and adjusted for multiple comparisons using Dunnett's adjustment, with the lowest group as the reference group. We constructed three general linear models (PROC GLM) to model the longitudinal associations baseline-BMI and the change in 25(OH)D concentration. Model-1 was adjusted

for age (y), baseline-25(OH)D (nmol/L), serum creatinine (μmol/L), follow-up time (months), and sex. In addition to model-1 covariates, model-2 included seasonality, dietary vitD & supplements intake. Model-3 was adjusted for model-1 and 2 covariates plus miles walking/day, alcohol intake (g), current smoking status (y/n), poverty level and education.

3. Results

Complete data of study participants was available for 620 women and 246 men for both baseline and 2-year. Table 1 shows the characteristics of the study participants at both time points. Among all, the mean of 25(OH)D at 2-year was 5.5 nmol/L higher compared to baseline (P<0.0001).

3.1 Cross-sectional analyses

The Pearson correlation coefficients of BMI and serum 25(OH)D at both time points, showed significant negative correlation (data not shown), baseline (r = –0.1, P =0.006) and 2-year (r = –0.1, P =0.01). Figure 1 shows that the cross-sectional adjusted-means of serum 25(OH)D among our participants at both time points across BMI categories. At both time points, there was significantly lower trend with increased obesity, P-trend <0.01 and <0.002, respectively, adjusting for sex, age seasonality, miles/day, vitD supplements and dietary intake, and smoking.

3.2 Longitudinal analyses

The longitudinal linear regression model (Table 2) showed that baseline-BMI had a significant inverse association on the change in serum 25(OH)D (regression coefficient (β) = –0.17, P =0.04) controlling for age, sex, creatinine baseline-25(OH)D, and f/up time. All three models showed similar significant results.

4. Discussion

We believe that the results of our longitudinal analysis confirm an inverse longitudinal association between BMI and serum 25(OH)D among the older PR adults living in the Greater Boston area. The cross-sectional analysis showed that obese, severely obese and morbidly obese participants of our study exhibited significantly lower adjusted-mean serum 25(OH)D concentrations, which is in agreement with many studies [12, 13, 17, 18]. The longitudinal multivariate linear regression showed that the change in BMI over time was negatively associated with the change in serum 25(OH)D concentrations (P =0.01), independent of known factors including age, sex, serum creatinine, miles walking/day, smoking, alcohol, seasonality, poverty and education.

There is no clear mechanism that can fully explain the phenomena of how increased obesity affects serum 25(OH)D or vice versa. A recent review by Earthman and colleague discusses a number of proposed theories that link obesity to serum 25(OH)D [19]. They discussed one potential explanation is that because vitD is fat-soluble; thus, it might be sequestered within the adipose tissue resulting in lower circulating concentrations. One group suggested that the adipose tissue of obese individuals might have higher 25(OH)D uptake and storage relative to lean individuals [20]. Another theory suggests that due to the fact that obesity, especially

visceral adiposity, contributes to a high inflammatory state [21], this in turn, might contributes to lower serum 25(OH)D concentration [21, 22]. One last the hypothesis suggests that because of increased obesity, there may possibly be an increase of the action of 24-hydroxylase, leading to amplified catabolism of vitD within the adipose tissue, thus, lowering circulating 25(OH)D [23]. Consequently, further research is needed to elucidate our understanding of how vitD may be affected by obesity.

Our findings should be interpreted within the context of a few limitations. First, our population is primarily Puerto Ricans, therefore our findings could be very specific to this particular admixture population, with genetic variation interacting not only with the environment, but social factors as well [24–27]; thus, generalizability may not be an option. Additionally, even though we have controlled for all the known potential covariates, residual confounding is still be a possibility. However, our study has substantial strengths: a total large sample size with low attrition rate (35%) and the use of a detailed questionnaire with an FFQ that allowed detailed information. In summary, 2.5-yr change in obesity, i.e. BMI was inversely associated with serum 25(OH)D concentrations. In addition, the adjusted-means of serum 25(OH)D concentrations showed declining trend, at both time points, with the increase in BMI especially when reaching class III obesity.

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- Our analysis provide confirmation to the inverse association and low serum 25(OH)D and obesity
- We observed lower adjusted mean serum 25(OH)D in obese, severe and morbidly
- Adjusted for all covariates in 3 models, all showed significant negative association

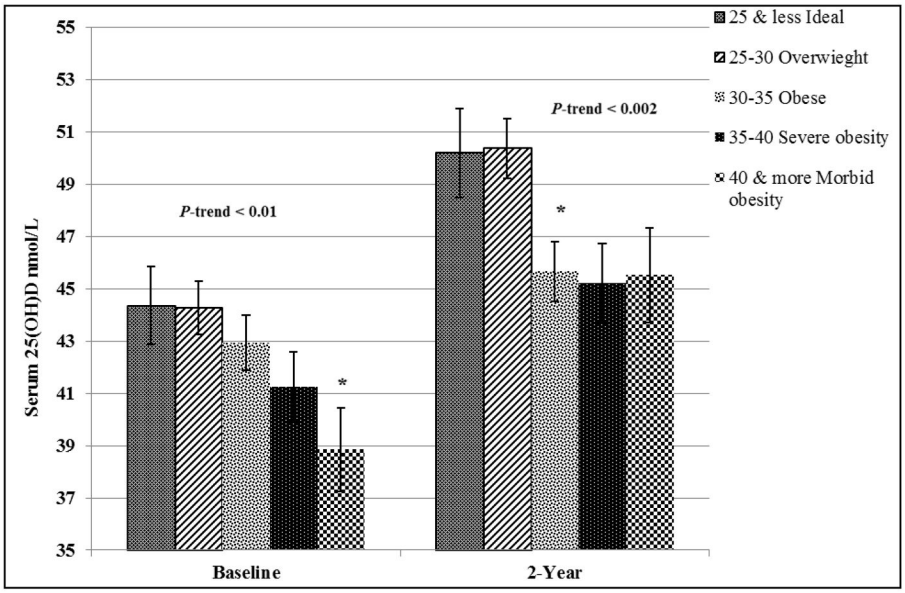

FIGURE 1.

The adjusted means of serum 25(OH)D concentrations within the categories of class III obesity. LS-Means adjusted for sex, age seasonality, miles/day, vitD supplements and dietary intake, and smoking.

*Different from referent group (BMI ≥ 25) (Dunnett adjustment for multiple comparisons; $P < 0.05$)

TABLE 1

Descriptive characteristic of men and women in the Boston Puerto Rican Health Study (BPRHS) & Boston Puerto Rican Osteoporosis Study (BPROS)

	Baseline (BPRHS)		Two Year (BPROS)	
	Women (n=620)	**Men (n=246)**	**Women (n=620)**	**Men (n=246)**
Age (y)	57.0 ± 7.3	56.0 ± 8.0	60.3 ± 7.5	59.5 ± 8.0
Education (>8th grade %)	51.5	55.5	--	--
Poverty (%)	60.0	49.0$^{\$\$}$	59.0	48.5$^{\$\$}$
Serum 25(OH)D (nmol/L) §§§	44.0± 17.4	43.0 ± 16.5	50.1 ± 19.0	47.0 ± 17.5*
Follow-up time (months)	--	--	33.3 ± 12	30.5 ± 49
BMI (kg/m^2)	33.0 ± 7.0	30.1 ±5.5***	33.0 ± 7.0	30.2 ± 5.5***
Miles walking/day §§§	1.0 ± 1.5	1.4 ± 2.0***	1.4 ± 2.0	2.0 ± 2.4 ***
Current- smoking (%)	20.1	32.5$^{\$\$\$}$	--	--
Current- alcohol drinking (%)	36.0	51.0$^{\$\$\$}$	--	--
VitD Supplement (>200IU/day) (%)	30.0	24.1	30.2	18.5$^{\$\$}$
Total vitD intake (IU/day)	290.5 ± 172.0	280.0 ±178.0	287.5 ± 152.0	257.0 ± 123.0**

BMI, body mass index; 25(OH)D, 25-hydroxyvitamin D.

[1] Data are presented as mean ± SD for continuous variables or as % for categorical variables

Means were compared using t-test for between gender (within each time points): *P -value <0.05, ** P -value <0.001, ***P-value <0.0001

Means were compared using paired t-test for between time points: $^{\S}P$ -value <0.05, $^{\S\S}P$ -value <0.001, $^{\S\S\S}P$-value <0.0001

Percentages were compared using Chi-square test for between sex (within each time points): $^{\$}P$ -value <0.05, $^{\$\$}P$ -value <0.001, $^{\$\$\$}$ P-value <0.0001

TABLE 2

Regression coefficients (± SE) from longitudinal linear regression analysis of BMI on plasma 25(OH)D concentrations.

Change in 25(OH)D (nmol/L)	Baseline-BMI		
	Regression coefficient	**Standard Error**	***P*-value**
Model 1	–0.17	± 0.1	0.04
Model 2	–0.22	± 0.1	0.01
Model 3	–0.22	± 0.1	0.01

Model 1: adjusted for age, baseline 25(OH)D, serum creatinine, time f/up (mos), & sex

Model 2: adjusted for model 1 variables plus seasonality, dietary VD & supplements.

Model 3: adjusted for model 1 variables plus miles-walking/day, alcohol, smoking, poverty level, & education.