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ORIGINAL ARTICLE

Relationship of vitamin D and parathyroid hormone with obesity and body composition in African Americans

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Summary

Background Obesity disproportionately affects African Americans (AA) (especially women), and is linked to depressed 25-hydroxyvitamin D (25-OH D) and elevated parathyroid hormone (PTH). The relationship of 25-OH D and PTH with body composition and size in AA is not well known.

Objective To determine the relationship of 25-OH D and PTH levels with body composition and anthropometric measures.

Design A cross-sectional study was conducted in 98 healthy, overweight, adult AA enrolled in an NIH/NIEHS-sponsored weight loss/salt-sensitivity trial.

Measurements Multivariable linear regression analyses were used to explore the relationship of 25-OH D and PTH with body composition, determined by dual-energy X-ray absorptiometry, and anthropometric measures. Body composition and size were contrasted across vitamin D/PTH groups using general linear models: (i) normal (25-OH D >50 nmol/l, PTH ≤65 pg/ml), (ii) low 25-OH D and normal PTH and (iii) low 25-OH D and high PTH.

Results Age, gender and season-adjusted regression analyses showed that PTH was directly correlated with total ($P = 0{\cdot}02$), truncal ($P = 0{\cdot}03$) and extremity ($P = 0{\cdot}03$) fat mass, while 25-OH D was inversely related to truncal fat mass ($P = 0{\cdot}02$). Total fat mass in groups 1–3, respectively, was 30·0, 34·0 and 37·4 kg ($P = 0{\cdot}008$); truncal fat mass was 13·4, 15·9 and 17·6 kg ($P = 0{\cdot}006$) and extremity fat mass was 15·8, 16·9 and 19·7 kg ($P = 0{\cdot}02$). Lean mass did not differ across the three groups.

Conclusions Our findings show that lower 25-OH D and raised PTH are both correlated, though in opposite directions, with fat mass, fat distribution and anthropometric measures in adult AA.

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Introduction

Obesity is a risk factor for a multiplicity of cardiovascular diseases.[1] The prevalence of overweight and obesity is significantly more common in adult African Americans (AA) than whites.[2] This is particularly true amongst women who are less physically active and have elevated hypertension, and diabetes mellitus, two obesity-related conditions, relative to white women than is observed in AA men relative to white men.[2,3] Several epidemiological studies have linked vitamin D deficiency to obesity.[4–15] Data from the Third National Health and Nutrition Examination Survey (1988–1994) showed that serum 25-hydroxycholecalciferol (25-OH D) was lower in non-Hispanic blacks in comparison with that in both Mexican Americans and non-Hispanic whites.[4] Furthermore, vitamin D deficiency is strikingly more prevalent in AA women than in white women.[5] Epidemiological studies document that both hypovitaminosis D and secondary hyperparathyroidism are highly prevalent in AA compared with that in whites, particularly in obese AA.[6,7]

To date, most studies have correlated circulating 25-OH D and/or parathyroid hormone (PTH) levels with crude body size measures, such as body mass index (BMI), and markers of body composition, such as percent body fat. Several cross-sectional studies have reported a strong inverse association between 25-OH D and obesity (BMI, waist circumference, waist to hip ratio, total body fat percentage and total body fat mass), as well as a direct association between PTH and obesity.[6,8–15] However, other studies have shown a weaker inverse correlation between 25-OH D and percent body fat in AA compared with that in whites of the same age,[16] and no correlation between serum 25-OH D and BMI[17,18] or between PTH and body weight.[19] However, little is known in AA or any other racial/ethnic group about the relationship of body composition and lean and fat mass distribution in relation to the levels of vitamin D and PTH.

Thus, we undertook these analyses to determine the relationship between 25-OH D and PTH with body composition, lean and fat mass distribution and body size in healthy AA. The healthy cohort of AA in this work provides a unique opportunity to study these relationships before the development of hypertension, diabetes and other obesity-related morbidities.

Methods

A cross-sectional design was used in an all AA cohort recruited in Detroit, Michigan, for a salt-sensitivity/weight loss study. Data were collected between February 2004 and March 2008. Personal identifiers were removed prior to importing the data into a research database for analysis. This study was reviewed and approved by the Wayne State University, Institutional Review Board. Signed informed consent was obtained from all participants prior to their participation.

Study population

The study population was comprised of 98 healthy, normotensive (blood pressure <140/90 mmHg), overweight (BMI = 25–39·9 kg/m^2) AA men and women aged 35 years and older who were enrolled in an NIH/NIEHS-sponsored clinical trial – 'Obesity, Nitric Oxide and Salt Sensitivity'. Participants were excluded for the following reasons: medical illness, those consuming >3 alcoholic drinks per day, eating >6 restaurant meals per week, taking oral steroids or nitrates, nonsteroidal antiinflammatory drugs >4 days/week, using supplemental vitamins/herbs, working night shift, actively dieting or losing weight and/or planning to move >50 miles or travel extensively from the area during the next 12 months. They were also excluded for refusing to give informed consent, refusing venipuncture and/or having a positive pregnancy test (given to premenopausal women who have not had a hysterectomy and have not been surgically sterilized).

Study measures

Venous blood sampling was performed in all participants to measure circulating 25-OH D and PTH in serum. To minimize variations, both 25-OH D and PTH were processed in batches.

25-OH vitamin D

25-Hydroxyvitamin D was measured using liquid chromatography-tandem spectrometry at Mayo Medical Laboratories, MN. Functional sensitivity (FS) of the assay was <10 nmol/l and the mean interassay coefficient of variation (CV) was 3·8%.

Intact PTH

Intact PTH was measured using immunochemiluminometric assay and electrochemiluminescence method at Mayo Medical Laboratories, MN. FS of the assays was <5 pg/ml and <6 pg/ml, respectively, and mean interassay CV was 8% and 6–7%, respectively. Validation using least square linear regression analysis by Mayo Laboratories resulted in a good linear fit (R^2 = 0·99) between the assays and produced a linear equation [electrochemiluminescent = (0·7721 × immunometric) + 2·9337]. To be consistent, this equation was used to convert PTH values obtained from immunometric assay into values from electrochemiluminescent assay. Converted PTH values (N = 48) and PTH values from electrochemiluminescent assay (N = 50) were used for statistical analysis.

Dietary data

Block 98 Food Frequency Questionnaire (FFQ) was completed by each participant to capture usual eating patterns over the last 12 months.[20] Daily vitamin D, caloric, calcium and magnesium intakes were estimated from FFQ records that were analysed with the Nutrition Data System, research version of the software (University of Minnesota, Nutrition Coordinating Center). Calcium and magnesium intakes were from dietary and supplemental sources, whereas vitamin D intake was solely from diet.

Physical activity

Physical activity was assessed using the MESA Typical Week Physical Activity Survey (MESA-TWPAS). The survey is designed to capture typical activity patterns in one's daily life by identifying the time and frequency spent in various physical activities during a typical week in the past month. The survey consisted of 28 questions that covered household chores, lawn/yard/garden/farm work, care of children/adults, transportation, walking (not at work), dancing/sport activities, conditioning activities, leisure activities, occupational activities and volunteer activities. Minutes spent per activity were converted into hours. The total hours spent per week for the nine physical activity categories were multiplied by the metabolic equivalent (MET) level[21] to obtain an estimated score for the self-reported physical activity in units of MET-h/week. Light (mostly comprised of indoor activities), moderate and vigorous (mostly comprised of outdoor activities) physical activity scores were also calculated. We excluded three participants who did not complete the survey and 15 who reported an average physical activity per day of more than 24 h.

Body mass index

Height was measured using a stadiometer to the nearest 0·001 m. Body weight was measured using a standard balance beam scale to the nearest 0·1 kg. BMI was calculated as body weight divided by the square of their height (kg/m^2).

Waist and hip circumference

Waist circumference was measured to the nearest 0·1 cm by applying the measuring tape horizontally midway between the lowest rib and the iliac crest after a normal expiration. Hip circumference was measured at the point yielding the maximum circumference over the greater trochanter.

Body composition

Dual-energy X-ray absorptiometry (DEXA) measurements were performed in all participants using a total body scanner (QDR 4500 Acclaim Series Elite, Hologic Inc., Bedford, MA, USA). DEXA is a noninvasive method of assessing bone mineral, fat and bone-free lean mass, requiring the participant to lie supine for 5–10 min.[22]

Repeatability errors (CV) obtained with DEXA are: fat, in grams (and percent total mass), CV = 2·6%; lean, in grams, CV = 0·9%. Total, truncal and extremity fat mass and corresponding lean mass were evaluated. Extremity fat mass and lean mass were comprised of both upper and lower limbs. Truncal fat mass and lean mass were comprised of thoracic, abdominal and pelvic regions.

Statistical analysis

Continuous data were summarized as mean values, medians, standard deviations and 95% confidence intervals (CI), while categorical variables were summarized as frequencies and counts. The distributions of all continuous variables were examined for skewness/normality using Shapiro-Wilk statistic. Continuous data that deviate significantly from normality were transformed to the natural logarithm to approximate a normal distribution prior to analysis. The independent sample t-test and the Wilcoxon signed-rank test were utilized to compare mean values of continuous variables. Pearson correlation coefficient (r) and Spearman's rank correlation coefficient (r_s) were used to display the univariate strength and direction of the relationship between selected study variables. Wilcoxon test and Spearman correlation were used for the physical activity variables because these variables were skewed. As the data for the vigorous physical activity score had many zero values, the distribution showed over-dispersion. Thus, an over-dispersed generalized linear model (GLM) using generalized estimation equation was used to compare the mean value of vigorous physical activity score between men and women.

Primary analyses utilized multivariable regression models adjusted for age, gender and season to characterize the relationship of 25-OH D and PTH with fat mass and body size. Three dummy variables were used for seasonal adjustment where the months of the year were stratified into four groups: January–March (used as the reference group), April–June, July–September and October–December. To allow for considerations of the joint effects of 25-OH D and PTH, a secondary analytical approach was performed utilizing age, gender and season-adjusted GLM to contrast body composition (fat mass and lean mass) and anthropometric measures (BMI, weight and hip circumference) across three mutually exclusive vitamin D/PTH groups: (i) normal [25-OH D = 51–249 nmol/l (1 nmol/l = 0·4 ng/ml), PTH ≤ 65 pg/ml (1 pg/ml = 1 ng/l)]; (ii) LN or low 25-OH D and normal PTH and (iii) secondary hyperparathyroidism (SHPT) or low 25-OH D and high PTH. Dietary intakes (caloric, vitamin D, calcium and magnesium) were also contrasted across the three groups using age and gender-adjusted GLM. If a difference is detected among the vitamin D/PTH groups, Bonferroni's correction, a multiple comparisons procedure, was utilized to determine which vitamin D/PTH groups were significantly different. Adjusted GLM was also applied to determine statistical significance of between-group differences comparing study variables between the normal and the combined abnormal (LN + SHPT) groups. Statistical analyses were performed using SAS statistical software (SAS, version 9.1, SAS Institute Inc., Cary, NC, USA). Statistical significance was set at $P < 0·05$.

Imputation of missing data

Only 77 participants had complete dietary data. As deletion of incomplete cases may result in severe bias as well as loss of power, multiple imputation (MI) was utilized to fill in the missing values. MI is a Markov-chain Monte Carlo technique[23] in which the missing values are replaced by more than one simulated versions using R statistical software (R, version 2.7.0, Vienna, Austria). The rate of our missing information was not high (21%); therefore, three imputations were used to analyse multivariable regression models. Results from the three imputed data sets were very similar. We reported results from both the original data set ($n = 77$) and from one imputed data set ($n = 98$). Imputation was also applied for the physical activity data.

Results

Study subjects characteristics

The majority of participants were women. There were no gender differences in average 25-OH D and average PTH levels (Table 1). The average 25-OH D level was in the range considered to represent vitamin D deficiency (25-OH D ≤50 nmol/l).[24] However, the average PTH level was within the normal range. Average BMI was in the obese range (BMI ≥30 kg/m^2). On average, women had greater fat body mass, BMI and hip circumference than men. The average lean body mass was greater in men than women. The average total physical activity did not differ between men and women. Men had higher mean caloric intake but lower mean calcium and mean magnesium intakes than women. However, average calcium, magnesium and vitamin D intakes were all below daily recommended intakes.

About 5% of the participants had optimal vitamin D level of ≥75 nmol/l.[24,25] The highest serum 25-OH D level was 95 nmol/l, a level below the vitamin D toxicity level of >250 nmol/l.[25] Nearly one-fifth of the participants had vitamin D insufficiency (25-OH D = 51–74 nmol/l).[24] The remaining three quarters of the study cohort had vitamin D deficiency (25-OH D ≤50 nmol/l)[24] in which a third had vitamin D levels ≤25 nmol/l.

Correlation of 25-hydroxyvitamin D with physical activity and dietary vitamin D

25-hydroxyvitamin D was positively correlated with vigorous physical activity score (original: $r_s = 0·25$, $P = 0·02$; imputed: $r_s = 0·22$, $P = 0·03$) and with dietary vitamin D intake that was borderline significant (original: $r = 0·09$, $P = 0·42$; imputed: $r = 0·19$, $P = 0·05$).

Relationships of 25-hydroxyvitamin D and parathyroid hormone levels with fat mass and anthropometric measures

Parathyroid hormone and 25-OH D were regressed on fat mass and anthropometric measures using age, gender and season-adjusted multivariable regression models (Table 2). There were no interactions between either PTH or 25-OH D with gender in these

Table 1. Characteristics of all study subjects and gender stratification.

Characteristic	All *N* = 98	Female *N* = 82	Male *N* = 16	*P*-value
Age (years)	49·0 (7·0)	49·5 (7·2)	46·6 (5·6)	0·13
25-OH D (nmol/l)	40·4 (18·9)	40·6 (19·1)	39·3 (18·8)	0·80
PTH (pg/ml)	42·7 (26·0)	43·6 (27·2)	38·3 (19·1)	0·45
Fat distribution (kg)	*N* = 98	*N* = 82	*N* = 16	
Total fat mass	33·5 (8·6)	35·3 (7·6)	24·2 (7·4)	<0·0001
Truncal fat mass	15·5 (4·3)	16·1 (4·1)	12·5 (4·2)	0·002
Extremity fat mass	17·0 (4·9)	18·2 (4·1)	10·5 (3·4)	<0·0001
Lean distribution (kg)	*N* = 98	*N* = 82	*N* = 16	
Total lean mass	52·5 (9·5)	47·0 (5·6)	66·0 (7·3)	<0·0001
Truncal lean mass	24·0 (4·3)	22·1 (2·8)	30·1 (3·6)	<0·0001
Extremity lean mass	24·3 (5·0)	21·4 (2·8)	31·5 (3·8)	<0·0001
Anthropometric Measures	*N* = 98	*N* = 82	*N* = 16	
BMI (kg/m^2)	31·8 (3·6)	32·1 (3·6)	30·1 (3·3)	0·04
Hip circumference (cm)	115·4 (9·0)	116·2 (9·0)	110·9 (7·9)	0·03
Waist circumference (cm)	98·6 (10·5)	98·0 (10·6)	101·3 (9·4)	0·25
Waist:Hip ratio	0·86 (0·08)	0·84 (0·07)	0·91 (0·06)	0·0007
Physical activity score – original	*N* = 80	*N* = 67	*N* = 13	
$^{\gamma}$Total (MET-h/week)	215·3 (109·6)	208·8 (112·2)	249·1 (91·9)	0·13
$^{\gamma}$Light (MET-h/week)	83·9 (52·2)	87·6 (54·4)	64·5 (34·6)	0·15
$^{\gamma}$Moderate (MET-h/week)	57·5 (63·6)	53·8 (30·5)	76·6 (55·9)	0·05
Vigorous (MET-h/week)†	12·9 (29·7)	9·8 (22·5)	28·9 (52·1)	0·02
Physical activity score – imputed	*N* = 98	*N* = 82	*N* = 16	
Total (MET-h/week)*	220·3 (121·5)	219·1 (125·3)	226·2 (103·1)	0·54
Light (MET-h/week)*	86·6 (58·5)	91·8 (61·0)	59·9 (33·7)	0·05
Moderate (MET-h/week)*	67·4 (67·1)	64·7 (69·3)	81·5 (54·6)	0·09
Vigorous (MET-h/week)†	17·3 (31·0)	14·7 (25·7)	30·8 (49·3)	0·03
Dietary intake – original	*N* = 77	*N* = 70	*N* = 7	
Calorie (kcal/day)	2159 (1346)	1946 (863)	4280 (2938)	0·08
Calcium (mg/1000 kcal/day)	479 (265)	498 (270)	291 (66)	<0·0001
Magnesium (mg/1000 kcal/day)	168 (54)	172 (55)	124 (17)	<0·0001
Vitamin D (IU/day)	257 (200)	248 (192)	350 (269)	0·19
Dietary intake – imputed	*N* = 98	*N* = 82	*N* = 16	
Calorie (kcal/day)	2404 (1536)	1962 (890)	4670 (2106)	0·0001
Calcium (mg/1000 kcal/day)	420 (287)	460 (290)	217 (159)	<0·0001
Magnesium (mg/1000 kcal/day)	162 (154)	176 (164)	90 (49)	0·0002
Vitamin D (IU/day)	277 (192)	264 (191)	340 (195)	0·14

Values are expressed as mean, with corresponding standard deviations (SD) in parentheses. Comparison between male and female groups using the independent sample *t*-test or otherwise indicated – *Wilcoxon signed-rank test or †over-dispersed generalized linear model using generalized estimation equation. 25-OH D, 25-hydroxyvitamin D; PTH, parathyroid hormone; BMI, body mass index; MET, metabolic equivalent; IU, international unit.

analyses. Table 2 shows the 25-OH D and PTH regression coefficients from three different linear regression models using total, truncal and extremity fat mass, BMI, hip and waist circumferences as dependent variables. Linear regression models 1 and 2 display the association of 25-OH D and PTH with dependent variables, respectively, and model 3 displays the association of both 25-OH D and PTH with dependent variables.

Total body fat mass. PTH was directly related to total fat mass ($P = 0{\cdot}02$, model 2). However, the strength of the association

Table 2. Regression coefficients for the regression of fat distribution and body size on 25-hydroxyvitamin D and parathyroid hormone levels ($N = 98$)

Dependent variable	Model	Independent variable	Coefficient (P-value)	1-SD higher
Total body fat mass (g)	1	25-OH D	−65·2 (0·10)	
	2	PTH	69·2 (0·02)	+1·8 kg
	3	25-OH D	−39·3 (0·34)	
		PTH	59·5 (0·06)	+1·5 kg
Truncal fat mass (g)	1	25-OH D	−49·0 (0·02)	−0·9 kg
	2	PTH	34·2 (0·03)	+0·9 kg
	3	25-OH D	−38·2 (0·09)	−0·7 kg
		PTH	24·9 (0·14)	
Extremity fat mass (g)	1	25-OH D	−15·8 (0·46)	
	2	PTH	34·4 (0·03)	+0·9 kg
	3	25-OH D	−10·0 (0·96)	
		PTH	34·1 (0·04)	+0·9 kg
Body mass index (kg/m^2)	1	25-OH D	−0·04 (0·01)	−0·76 kg/m^2
	2	PTH	0·02 (0·17)	
	3	25-OH D	−0·04 (0·04)	−0·76 kg/m^2
		PTH	0·01 (0·51)	
Hip circumference (cm)	1	25-OH D	−0·09 (0·07)	−1·70 cm
	2	PTH	0·07 (0·06)	+1·82 cm
	3	25-OH D	−0·06 (0·21)	
		PTH	0·05 (0·17)	
Waist circumference (cm)	1	25-OH D	−0·14 (0·01)	−2·65 cm
	2	PTH	0·03 (0·47)	
	3	25-OH D	−0·14 (0·01)	−2·65 cm
		PTH	−0·004 (0·92)	

Multivariable linear regression models adjusted for age, gender and seasons. Values are expressed as regression coefficients and P-values are in parentheses. Values for one-standard deviation (1-SD) higher indicate measurable amounts of dependent variables that correspond to 1-SD higher PTH or 25-OH D levels. 1-SD higher is calculated by multiplying regression coefficient by 1-SD value of either PTH or 25-OH D. 1-SD 25-OH D = 18·9 nmol/l; 1-SD PTH = 26·0 pg/ml. For example, a 1-SD higher PTH level corresponded to: 1·8 kg higher total fat mass ($P = 0·02$, model 2), 0·9 kg higher truncal fat mass ($P = 0·03$, model 2) and 0·9 kg higher extremity fat mass ($P = 0·03$, model 2) and 1·82 cm greater hip circumference ($P = 0·06$, model 2). A 1-SD lower 25-OH D level corresponded to: 0·9 kg greater truncal fat mass ($P = 0·02$, model 1), 0·76 kg/m^2 higher BMI ($P = 0·02$, model 1), 1·70 cm greater hip circumference ($P = 0·07$, model 1) and 2·65 cm greater waist circumference ($P = 0·01$, model 1).

between PTH and total fat mass became borderline significant after adjustment for 25-OH D levels ($P = 0·06$, model 3). 25-OH D showed a trend towards a negative correlation that did not quite attain statistical significance before (model 1) and after adjustment for PTH levels (model 3).

Truncal fat mass. Truncal fat mass demonstrated an inverse relationship with 25-OH D ($P = 0·02$, model 1) and a direct relationship with PTH ($P = 0·03$, model 2). The inverse association between 25-OH D and truncal fat mass became borderline significant ($P = 0·09$, model 3) after adjustment for PTH levels. However, PTH lost its significant direct relationship with truncal fat mass after adjustment for 25-OH D levels.

Extremity fat mass. Parathyroid hormone was directly related to extremity fat mass ($P = 0·03$, model 2). The direct association between PTH and extremity fat mass remained statistically significant after adjustment for 25-OH D levels ($P = 0·04$, model 3). 25-OH D was unrelated to extremity fat mass even after adjustment for PTH levels.

Body mass index. 25-Hydroxyvitamin D was inversely associated with BMI ($P = 0·01$, model 1), although PTH was not. The relationship between 25-OH D and BMI remained significant even after adjustment for PTH levels ($P = 0·04$, model 3).

Hip circumference. The inverse association of 25-OH D ($P = 0·07$, model 1) and the direct association of PTH ($P = 0·06$, model 2) with hip circumference were both borderline significant. The strength of the associations of 25-OH D and PTH with hip circumference was not significantly influenced when PTH or 25-OH D, respectively, was considered simultaneously in the regression models.

Waist circumference. 25-Hydroxyvitamin D was inversely related to waist circumference both before ($P = 0·01$, model 1) and after ($P = 0·01$, model 3) adjustment for PTH levels. PTH, on the other hand, was unrelated to waist circumference.

Body composition, body size and dietary intakes across the vitamin D/PTH categories

25-hydroxyvitamin D and PTH. 25-Hydroxyvitamin D trended lower when progressing from the normal to the most abnormal vitamin D/PTH groups ($P < 0·0001$). The normal group had significantly greater 25-OH D level (67·7 (95% CI: 63·2–72·2) nmol/l) that was more than two times the 25-OH D levels of the LN (32·4 (29·6–35·2) nmol/l) and SHPT (26·4 (19·6–33·3) nmol/l) groups. 25-OH D levels for the LN and SHPT groups were within the range of vitamin D deficiency of ≤50 nmol/l,[24] with the lowest levels in the latter group. PTH trended higher towards the most abnormal vitamin D/PTH group ($P < 0·0001$). PTH level in SHPT group (97·6 (87·1–108·2) pg/ml) was approximately three times greater than PTH levels in both the normal (32·0 (25·1–39·0) pg/ml) and LN (37·2 (32·9–41·5) pg/ml) groups. Both the normal and LN groups had comparable normal PTH levels.

Body composition. Total body fat mass ($P = 0·008$), truncal fat mass ($P = 0·006$) and extremity fat mass ($P = 0·02$) were incrementally higher from the normal group to the most abnormal vitamin D/PTH group (Fig. 1). The differences (all statistically significant) in total body fat mass, truncal fat mass and extremity fat mass between the normal and SHPT groups were 27%, 31% and 25%, respectively. However, the difference between the normal and LN group was statistically significant only for truncal fat mass. Furthermore, total fat mass ($P = 0·01$) and truncal fat mass ($P = 0·003$) were greater in the combined abnormal groups relative to the normal group. Extremity fat mass was also greater in the combined abnormal groups compared with that in the normal group, which was of borderline significance ($P = 0·08$). Total body, truncal and extremity lean mass did not differ across the vitamin D/PTH groups.

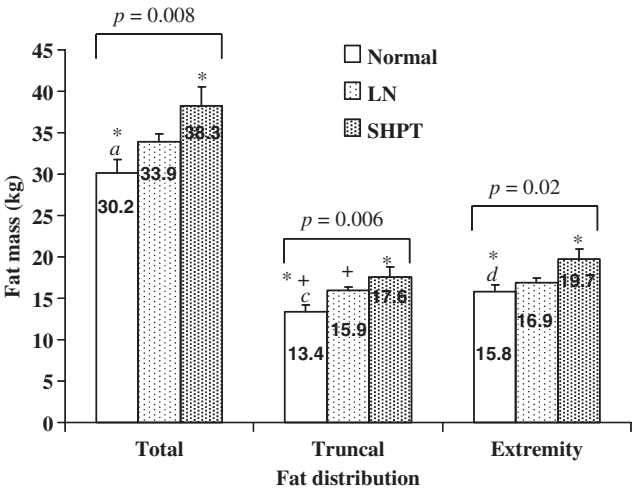

Fig. 1 Fat distribution across the vitamin D/PTH Groups. Least square means with corresponding standard errors of fat mass across the vitamin D/PTH groups using general linear models adjusted for age, gender and season. Total, truncal and extremity fat mass were incrementally higher from the normal to the most abnormal vitamin D/PTH groups to a significant degree. Bonferroni's correction detected significant differences between (*) the normal and SHPT groups and between (+) the normal and LN groups. (a) $P = 0{\cdot}01$ *vs.* LN + SHPT; (b) $P = 0{\cdot}003$ *vs.* LN + SHPT; (c) $P = 0{\cdot}08$ *vs.* LN + SHPT. Normal, normal 25-OH D and normal PTH ($n = 24$); LN, low 25-OH D and normal PTH ($n = 63$); SHPT, secondary hyperparathyroidism group or low 25-OH D and high PTH ($n = 11$). Normal 25-OH D >50 nmol/l; Normal PTH ≤65 pg/ml.

Anthropometric measures. Body mass index ($P = 0{\cdot}002$), waist ($P = 0{\cdot}02$) and hip ($P = 0{\cdot}03$) circumferences were monotonically higher across the three vitamin D/PTH groups (Table 3). The differences in BMI, waist and hip circumferences between the normal and SHPT groups were 12%, 7% and 7%, respectively. The difference between the normal and SHPT groups for BMI and hip circumference and the difference between the normal and LN groups for BMI and waist circumference were statistically significant. In addition, BMI ($P = 0{\cdot}0007$), waist circumference ($P = 0{\cdot}007$) and hip circumference ($P = 0{\cdot}02$) were greater in the combined abnormal groups *vs.* the normal group. There was no significant difference in weight and height across the vitamin D/PTH groups.

Dietary intake. The incrementally lower daily caloric, vitamin D, calcium and magnesium intakes across the vitamin D/PTH groups were not statistically significant (Table 3). Magnesium intake was borderline higher in the normal group compared with that in the combined abnormal groups ($P = 0{\cdot}06$).

Discussion

Our cross-sectional study in overweight adult AA demonstrated that depressed 25-OH D and raised PTH levels were both linked to body composition, fat distribution and anthropometric measures. Surprisingly, lean body mass, which was expected to increase with increasing physical load of higher fat mass, did not differ across the vitamin D/PTH groups. Currently published data predicting hormonal correlates for body fat and body size are not well-documented. We reported new observations in an overweight AA cohort linking 25-OH D closely to truncal fat mass, BMI and waist circumference, and linking PTH closely to total fat mass and extremity fat mass.

Most studies have correlated obesity with vitamin D and PTH separately.[6,8–10,12–15,26] A recent work by Rejnmark and colleagues further showed the relationship of PTH with the two locations of fat mass – trunk and extremity, in vitamin D insufficient postmenopausal women.[11] We extended these observations by assessing the

Table 3. Anthropometric measures and dietary intakes across the vitamin D/PTH groups

Dependent Variable Characteristics† ($N = 98$)	Normal $N = 24$	LN $N = 63$	SHPT $N = 11$	*P*-value
Age (years)	50·3 (47·5–53·2)	48·5 (46·7–50·2)	49·3 (45·1–53·5)	0·52
Gender (% female)	20 (83)	52 (83)	10 (91)	0·79
Anthropometric measures‡ ($N = 98$)				
Body mass index (kg/m^2)	29·7 (28·3–31·0)[ab]	32·3 (31·5–33·2)[a]	33·3 (31·3–35·4)[b]	0·002
Waist circumference (cm)	93·7 (89·6–97·8)[a]	100·2 (97·6–102·8)[a]	100·0 (93·7–106·2)	0·02
Hip circumference (cm)	111·7 (108·2–115·3)[b]	116·0 (113·8–118·2)	119·5 (114·1–124·9)[b]	0·03
Waist:Hip ratio	0·84 (0·81–0·87)	0·86 (0·85–0·88)	0·84 (0·80–0·89)	0·31
Dietary Intake – imputed* ($N = 98$)				
Vitamin D (IU/day)	317 (241–394)	278 (231–325)	177 (65–290)	0·12
Calorie (kcal/day)	2448 (1972–2924)	2421 (2128–2714)	2208 (1506–2910)	0·83
Magnesium (mg/1000 kcal/day)	207 (151–264)	150 (116–185)	128 (44–211)	0·17
Calcium (mg/1000 kcal/day)	451 (339–564)	420 (351–489)	354 (189–520)	0·63

Values are expressed as least square mean values with corresponding 95% confidence intervals in parentheses, unless otherwise indicated. *General linear models adjusted for age and gender only. †Unadjusted general linear models. ‡General linear models adjusted for age, gender and season. Bonferroni's correction detecting a difference that was statistically significant between [a]the normal and LN groups and between [b]the normal and SHPT groups. Normal, normal 25-hydroxyvitamin D (25-OH D) and normal parathyroid hormone (PTH); LN, low 25-OH D and normal PTH; SHPT, secondary hyperparathyroidism group or low 25-OH D and high PTH. Normal 25-OH D >50 nmol/l; Normal PTH ≤65 pg/ml.

combined effect of 25-OH D and PTH on body composition and body size. Our findings show that total, truncal and extremity fat mass were incrementally higher when moving from the normal to the most abnormal vitamin D/PTH group.

Our study supports a positive association of serum 25-OH D levels with both dietary vitamin D intake and vigorous physical activity,[17,18,27] which is mostly comprised of outdoor activities. However, vitamin D deficiency is highly prevalent in our study cohort. Approximately three quarters of the participants were vitamin D deficient (25-OH D ≤50 nmol/l).[24] Thus, we chose a lower 25-OH D threshold of normalcy of 50 nmol/l in combination with a threshold PTH value of 65 pg/ml[7,25] for the secondary analyses. Previous studies on elderly and other population with limited sunlight exposure and susceptibility to low vitamin D levels have utilized a 25-OH D cut-off value of 50 nmol/l.[11,28] A recent epidemiological study in AA utilized a much lower 25-OH D threshold of 37·5 nmol/l.[6] We performed sensitivity analyses contrasting fat mass and anthropometric measures utilizing age, gender and season-adjusted GLM across the vitamin D/PTH groups using a lower 25-OH D threshold value of 37·5 nmol/l in combination with a PTH threshold value of 65 pg/ml and also using a lower PTH threshold value of 45 pg/ml in combination with a 25-OH D threshold value of 50 nmol/l; the findings were in agreement with the trends observed using a combination of a 25-OH D threshold value of 50 nmol/l and a PTH threshold value of 65 pg/ml.

It has long been accepted that both depressed 25-OH D and reactive rises in PTH were *consequences* of obesity. Both the level and conversion of 7-dehydrocholesterol to vitamin D_3 in the skin are normal in obese persons. However, the increase in circulating vitamin D_3 after UV light exposure is lower in obese than that in non-obese subjects.[14] Thus, the reduced serum vitamin D_3 level is probably attributable to sequestration of fat-soluble vitamin D_3 in adipocytes.[10] However, it is also plausible that depressed 25-OH D and elevated PTH levels might play a role in the development of obesity, as there are known physiological mechanisms through which depressed 25-OH D and/or PTH elevations promote the accumulation of adipose tissue.

Elevated PTH augments renal 25-hydroxyvitamin D_3-1alpha-hydroxylase (1α-hydroxylase) activity, producing an increase in circulating 1,25-$(OH)_2$ D.[29] Production of 1,25-$(OH)_2$ D from kidneys is the only pathway that is, however, tightly regulated by negative calcitriol feedback on 1α-hydroxylase activity. The enzyme 1α-hydroxylase, which is expressed predominantly in the kidney, is also expressed in a number of extra-renal sites, such as skin, gastrointestinal tract, vasculature, immune cells, bones and adipocytes.[30,31] Activation of extra-renal 1α-hydroxylase is shown to be independent of PTH and the extra-renal 1,25-$(OH)_2$ D production is dependent on the availability of its substrate, 25-OH D.[32,33] Currently, the involvement of extra-renal 1α-hydroxylase in fat accumulation is not known. Nevertheless, several studies suggest that circulating 1,25-$(OH)_2$ D is elevated in AA compared with that in whites.[34–38]

Raised PTH levels, as a consequence of low 25-OH D and/or decreased calcium intake, stimulate a rise in intracellular calcium level in adipocytes via activation of phospholipase C-β.[39] Likewise, increased circulating levels of 1,25-$(OH)_2$ D, as a consequence of PTH-induced renal 1α-hydroxylation of 25-OH D, raise intracellular calcium levels in adipocytes via a nongenomic action by activating the putative 1,25 D_3-membrane-associated rapid response to steroid, a membrane vitamin D receptor (VDR).[39–44] The increased intracellular calcium is an important second messenger that triggers various pathways that promote the accumulation of adipose tissue, including activation of lipogenesis by augmenting fatty acid synthase activity,[42,43] suppression of catecholamine-induced lipolysis by activating phosphodiesterase-3B[42,45] and augmentation of reactive oxygen species (ROS), promoting adipocyte proliferation by activating oxidative enzymes [such as nicotinamide adenine dinucleotide phosphate (NADPH) oxidase and myeloperoxidase] and protein kinase C that stabilizes NADPH oxidase complex to generate more ROS.[46] In addition, increased ROS levels further augment intracellular calcium levels. Furthermore, 1,25-$(OH)_2$ D also binds to nuclear VDR (nVDR) down-regulating uncoupling protein 2 expression and activity; this genomic effect inhibits adipocyte apoptosis and activates adipocyte proliferation.[47,48] 1,25-$(OH)_2$ D also suppresses the activity of caspases 1 and 3, leading to suppression of adipocyte apoptosis by enhancing Bcl2/Bax.[47,48] A recent study by Sun and Zemel (2008) showed that 1,25-$(OH)_2$ D increases glucocorticoid production by binding to nVDR. Increased glucocorticoid increases nVDR, thereby creating a positive feedback that promotes further synthesis of glucocorticoid.[49] Moreover, 1,25-$(OH)_2$ D augments adipocyte lipid accumulation through increased fatty acid uptake via activation of lipoprotein lipases.[50] Therefore, it is physiologically plausible, though unproven, that low levels of circulating 25-OH D and reactive rise in PTH levels contribute to accumulation of adipose tissue.

Limitations

The current study is cross-sectional and therefore the cause and effect between low 25-OH D, raised PTH and obesity cannot be established. We enrolled a relatively modest sample size and therefore may have inadequate power to detect definitively important associations. The majority, though not all, of our participants were women. Thus, we did not have enough men to report any meaningful gender-specific analyses. Furthermore, we did not determine the menopausal state of women, which may influence circulating 25-OH D levels. Moreover, we did not measure 1,25-$(OH)_2$ D, the biologically active form of vitamin D.

Conclusion

Our cross-sectional study found an association of low 25-hydroxyvitamin D and raised parathyroid hormone with greater adiposity, body mass index, and waist and hip circumferences in overweight adult African Americans. The logical next step is to design human experiments to determine if raising vitamin D levels leads to reduction in fat mass, body fat distribution and/or waist and hip circumferences.

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Conflict of interest

None of the authors have a conflict of interest.

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