

Vitamin D, parathyroid hormone levels and insulin sensitivity among obese young adult Saudis

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Abstract. – Objectives: To determine alterations of vitamin D and parathyroid hormone levels and their relationship to insulin resistance among a sample of healthy young adult obese Saudis and to identify factors that might predict these alterations.

Methods: Age and gender matched obese young (aged 18-25 years) adult Saudis (N=76) with body mass index of ≥ 30 and their lean controls (N=84) were recruited after fulfilling exclusion and inclusion criteria from attendees of health facility at King Faisal University, Saudi Arabia. Selected participants were invited to a personal interview to gather information regarding socio-demographics. Fasting blood samples were assessed for the following essays: serum calcium, 25 OH vitamin D, inorganic phosphorus, intact parathyroid hormone (iPTH), serum insulin, fasting glucose, renal and liver function tests.

Results: Vitamin D levels were significantly higher in lean controls, and showed significant decline in relation to obesity classes, hypovitaminosis D was found in 30% (38.2% obese vs. 22.7% in lean) and deficiency in 17.5% of subjects; (19% vs. obese 15.8%). iPTH was significantly higher in obese subjects. Secondary hyperparathyroidism was found in 48.1% (60.5% obese vs. 36.9% controls). Regression analysis showed that body mass index, serum calcium and creatinine levels were the main predictors for vitamin D level. Vitamin D is positively associated with fasting blood sugar ($r=-.133$, $P=0.09$) and β cell function index ($r=-.192$, $P=0.08$), negatively associated with HOMA-IR ($r=-.122$, $P=.34$) but without statistical significance after controlling of possible confounders.

Conclusion: Vitamin D level among young adult Saudi obese is negatively associated by body mass index and classes of obesity. Negative associations between vitamin D, iPTH levels and HOMA-IR exist but without statistical significance.

Key Words:

Young adults, Hypovitaminosis D, Vitamin D, Obesity, Insulin sensitivity, Saudi Arabia.

Introduction

Vitamin D and parathyroid hormone (PTH) are well known for their essential role in bone metabolism and calcium homeostasis¹. It has become increasingly clear that the vitamin D endocrine system is related to obesity in adults. Obesity has been found to be associated with lower levels of serum 25 OH Vitamin D²⁻⁴ and higher levels of serum PTH²⁻⁵. Low vitamin D intake was associated with increased body mass index (BMI)⁶. Furthermore, PTH has been postulated as an independent predictor for obesity⁷.

PTH may stimulate renal hydroxylation of 25-OH vitamin D to its active form, 1, 25-OH vitamin D, which in turn elevates calcium influx into adipocytes with consequent enhancement of intracellular lipogenesis and inhibition of lipolysis with resultant lipid storage in the fat tissue⁸⁻¹⁰, or through the direct role of PTH in suppressing lipid oxidation in the muscle¹¹. However, these hypotheses were discussed controversially since in obese adults with weight loss increased and decreased 25-OH vitamin D¹²⁻¹⁴ and PTH concentrations have been reported. The question of whether the alterations of these hormones are a consequence or cause of overweight remains open. Vitamin D also acts as a necessary cofactor for insulin secretion¹⁵⁻¹⁷. Vitamin D repletion im-

proves insulin sensitivity and insulin secretion in animal studies¹⁸.

Hypovitaminosis D has been proposed as a risk factor for reduced insulin secretion, impaired glucose tolerance, and type 2 diabetes mellitus in adults¹⁸⁻²⁰. However, studies in obese adults demonstrated no relationship between vitamin D, PTH, and insulin sensitivity^{21,22}. Data from Saudi Arabia reported a high prevalence of hypovitaminosis D among healthy adolescents and adults²³⁻²⁵ and also increasing prevalence of obesity and type 2 diabetes mellitus²⁶⁻²⁸ while those addressing the pattern of vitamin D alterations and its interrelation with obesity and development of insulin resistance are scarce. We hypothesized that vitamin D level is altered in healthy obese adults (aged 18-25 yrs) which may predispose them to the development of secondary hyperparathyroidism and alteration of insulin resistance. The objectives of this study were to determine alterations of vitamin D and parathyroid hormone levels and their relationship to insulin resistance among a sample of healthy young adult obese Saudis versus their controls and to identify factors that might predict these alterations.

Subjects and Methods

A case-control design in which both cases and controls were selected conveniently from volunteers including University's students, and attendees of the Medical Center at King Faisal University in Al-Ahsa, Saudi Arabia.

Sampling Size and Power

With inclusion of 61 subjects in each group we had more than 80.0% power to detect 8.0 standard^{26,27} deviations difference with precision of ± 2.0 between the obese and lean groups regarding vitamin D blood level at an alpha level of 0.05 (two sided). Considering a potential non-response rate of 30%, the total sample size of 160 (80 for each group) was estimated for inclusion.

Subjects' Selection

Cases

Age ranged from 18 to 25 years, Saudis, with BMI of ≥ 30 .

Controls

Age and gender matched Saudis with desirable BMI. Both groups were selected by non-probability sampling method from those attending the Medical Health center at King Faisal University through personal approach.

Ethical Considerations

Study protocol was approved from authorities at King Faisal University. Eligible subjects signed a written consent following detailed orientation regarding objectives, procedures implied and possible outcome of study. Data confidentiality was maintained all through the study according to Helsinki Declaration of Medical Bioethics. Those with abnormal biochemical results were informed and referred to KFUs' health facility for management.

Inclusion Criteria and Precautionary Measures

1. Cases and controls were screened for the possibility of diabetes through estimation of fasting blood glucose level; those with abnormal results were excluded at the outset.
2. Non smokers were included to overcome possible confounding effect of smoking.
3. Blood sampling were withdrawn during spring season to overcome possible seasonal variation of vitamin D levels (March 20th to May 3rd 2009).

Exclusion Criteria

Data were obtained through the revision of personal health records.

- Negative history of any chronic illness (especially liver and renal diseases).
- No previous use of medications known to affect calcium metabolism "e.g., antiepileptic".
- No known metabolic bone diseases and mal-absorption syndrome.
- History of immobility for more than one month and vitamin D supplement.

Data Collection

Anthropometry

Measured at the outset of the study; weight was measured using commercial scale "Seca,

Germany” with an accuracy of ± 100 g. Subjects was weighed barefooted and with minimal clothes. Standing body height was measured with the use of commercial stadiometer with the shoulder in relaxed position and arms hanging freely and without shoes to the nearest 0.5 cm. Measurements were taken by single technician to overcome inter-rater error. Scales were re-calibrated after each measurement. BMI was calculated as: “Body weight in kg/Height in meters²”.

Laboratory Measurements

After 12 hours of fasting, blood samples were collected under standardized conditions for the following biochemical assays:

- Serum calcium and phosphorus.
- 25 (OH) vitamin D and intact parathyroid hormone (iPTH).
- Lipid profile, liver function and renal function tests.
- Fasting glucose and insulin hormone level. HOMA-IR (Homeostasis Model Assessment of Insulin Resistance) was calculated according to standardized formula²⁹, for the calculation of insulin secretory capacity (HOMA-B) using the formula: (fasting insulin in $\mu\text{U/ml}$) $\times 3.33 / (\text{fasting glucose in mg/dl} - 3.5)$. All kits were supplied by Roche Diagnostics GmbH, Mannheim, Germany and estimated using Hitachi 902 Auto-Analyzer, Roche Diagnostics GmbH, Mannheim, Germany.

Fasting blood sugar: estimated automatically in serum by Gluco-quant Glucose/HK, results expressed in mg/dl.

Lipid profiles: total cholesterol and triglycerides were estimated by using CHOD-PAP, GPO-PAP, enzymatic test kits (Boehringer Mannheim GmbH, Mannheim, Germany) respectively. High density lipoprotein cholesterol was estimated without pretreatment by homogeneous enzymatic colorimetric test kit (Boehringer Mannheim GmbH, Mannheim, Germany). Low density lipoprotein cholesterol level was calculated according to Friedewald formula³⁰.

Liver function tests: activities of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were estimated in serum, results were expressed in U/serum protein. Serum albumin and total bilirubin were quantified using colorimetric albumin BCG, total bilirubin liquid and total protein kit.

Renal function tests: concentrations of blood urea (BUN) and serum creatinine were determined by kinetic UV assay and creatinine Jaffe’ kits respectively.

Serum calcium: estimated in serum using colorimetric assay kit.

25 (OH) vitamin D: determined by using HPLC (Waters 2695 Alliance HPLC System with 996 photodiode Array Detector and Column Heater, American Laboratory Trading LLC, Grotton, CT, U.S.A), using the available kit supplied by Chromsystems Diagnostic by HPLC (Instruments and Chemicals GmbH, Muenchen, Germany). Results were expressed as $\mu\text{g/L}$.

Insulin: estimated using Auto-Analyzer Elys 2010 (Roche Diagnostics, Indianapolis, IN, USA).

Data Analysis

Data analysis and processing was carried out using SPSS version 16.0 (SPSS Inc, Chicago, IL, USA). Out of 95 obese subjects approached; 19 were excluded from the final data analysis (14 refused blood sampling, 5 with insufficient samples), in the lean group out of the 112 volunteered, 28 were excluded (20 refused blood sampling and 8 subjects with insufficient samples). Data displayed non normality using Shapiro-Wilk test, were log transformed for the purpose of analysis. Categorical data were expressed using frequency and percentage. Chi-square test, Odd’s ratio with 95% confidence intervals was used as appropriate.

Statistics

Continuous data were reported as mean and standard deviation, employing t-test, Mann Whitney and Kruskal Wallis tests of significance. Effect sizes in the form of Cohen’s *d* were calculated according to Cohen³¹ who defined *d* as the difference between the means, divided by standard deviation of either group when the variances of the two groups are homogeneous, in our case we employed the pooled standard deviation to calculate the effect size (equals to the root mean square of the two standard deviations for obese and controls).

The interpretation based on the average percentile standing of the average of obese adults relative to the average of lean controls³¹.

Partial correlation coefficient was employed after controlling for possible confounders in assessing the relationship between vitamin D and parathyroid hormone levels and body mass index, insulin resistance and β cell function. Multivariate regression analyses were generated to assess the relationship between 25(OH) vitamin D and insulin sensitivity indices. *P* value of <0.05 was applied as the level of significance.

Cut-off Values:

Hypovitaminosis D: conservative definition of 25(OH) D of <37.5 nmol/L in accordance with data showing that iPTH begins to rise at this level³².

- Hyperparathyroidism (high parathormone level) was defined as serum iPTH >40 pg/ml.
- Obesity was subdivided according to BMI³³ into class I (BMI 30-34.99 kg/m²), class II (BMI 35-39.99 kg/m²), and class III (BMI \geq 40 kg/m²).

Results

Basic Characteristics

A total of 160 subjects (obese = 76, lean=84) with age ranged from 18-25 years; obese aged 22.8 \pm 1.9 years (40 males and 36 females) and their lean controls aged 22.5 \pm 1.2 years (42 males and 42 females). Table I demonstrates the baseline data including anthropometric measurements and biochemical tests results.

Lipid Profile, Liver, Renal Function Tests And Blood Sugar Serum Insulin Levels

With the exception of high density lipoproteins levels, all components of lipid profile were significantly higher in obese subjects (Table I). Total proteins, serum albumin were significantly higher in controls compared to obese subjects (*P*=0.001), while alkaline phosphatase and hepatic enzymes including (alanine aminotransferase: ALT; aspartate aminotransferase: AST) were significantly higher among obese as revealed by the effect size where the averages for these parameters were above the 33rd percentile for those of the controls. The same notion went for uric acid level and serum creatinine.

Glycemic Indices and Calcitropic Hormones

Table II demonstrates that fasting blood sugar, serum insulin, insulin resistance (HOMA-IR) and β cell function were significantly higher among obese subjects compared to controls. Fasting blood sugar showed an average among obese above the 90th percentiles of the controls, serum insulin above 79th percentiles, HOMA-IR above the 84th and β cell function above the 66th percentiles of the lean subjects.

Serum vitamin D level was significantly lower among obese compared to lean subjects, the average of vitamin D was below the 66th percentiles of the those with desirable body weight (*P*=0.004), the level of vitamin D showed significant decline in relation to obesity classes and body mass index; from 33.3 \pm 12.4 μ g/L for class I (N=67) to 33.9 \pm 9.9 for class II (N=7) and 28.0 \pm 3.3 in class III (N=2) (Kruskal Wallis, *P*=0.034). Among both groups vitamin D level was higher in males compared to females; among obese males, vitamin D level was below the 79th percentiles of the lean subjects, while among females the difference was small as obese females have an average level of vitamin D below 54th percentiles of the lean females. Figure 1 depicts the correlation between vitamin D and BMI of the included subjects.

Applying the cut-off for vitamin D deficiency and hypovitaminosis D: 48/160 (30.0%, C.I.=23.4-37.5) were classified as having hypovitaminosis, more among obese (38.2% C.I.=28.1-49.4 vs. 22.7% in lean subjects C.I.=9.3-25.6). Vitamin D deficiency was found among 28/160 (17.5%, C.I.=12.4-24.1) more in lean subjects (19.0%, C.I.=12.1-28.7 vs. 15.8%, C.I.=9.3-25.6 in obese, OR=2.1, *P*=0.023).

iPTH level was significantly higher among obese. iPTH average level among obese was above the 66th percentiles for those of the lean subjects and with proportionate increment in relation to obesity classes and BMI (Figure 2), from 45.2 \pm 19.7 pg/ml for class I, 50.3 \pm 23.8 pg/ml for class II (*P*=0.005).

Secondary hyperparathyroidism was found in 77/160 subjects (48.1%, C.I.= 40.5-55.8), more among obese 46/76 (60.5% C.I.=49.3-70.8) compared to controls 31/84 (36.9% C.I.= 27.4-47.6) (OR=2.6, C.I.=1.3-5.2, *P*=0.001), and more among obese females compared to obese males. Serum calcium levels were slightly higher among obese subjects, and it was significantly lower among obese subjects with secondary hyperparathyroidism.

Table I. Baseline anthropometric and biochemical data of the included subjects.

Variables	Obese subjects (N = 76)	Lean controls (N = 84)	Cohen's d Effect size	P value ^a
Anthropometry:				
Height (cm)	164.7 ± 7.5	163.9 ± 9.4	0.094	0.585
Weight (Kg)	87.7 ± 12.4	61.4 ± 11.2	2.230	0.001
BMI	32.5 ± 2.6	22.6 ± 2.6	3.808	0.001
Lipid profile:				
Total cholesterol (mmol/L)	4.4 ± 0.5	3.9 ± 0.6	0.843	0.001
Triglycerides (mmol/L)	1.3 ± 0.5	0.9 ± 0.4	0.922	0.001
Low density lipoproteins (mmol/L)	2.5 ± 0.6	2.1 ± 0.8	0.573	0.001
High density lipoproteins (mmol/L)	1.3 ± 0.3	1.5 ± 0.4	-0.377	0.017
Liver functions:				
Total proteins (g/L)	75.4 ± 3.8	77.8 ± 4.6	-0.582	0.001
Albumin (g/L)	44.7 ± 3.5	47.2 ± 4.2	-0.063	0.001
Total bilirubin (μ mol/L)	5.9 ± 2.3	7.9 ± 4.9	-0.488	0.002
Alkaline phosphatase (U/L)	89.9 ± 22.0	74.8 ± 25.2	-0.644	0.001
Alanine transferase (U/L)	25.2 ± 9.8	20.4 ± 10.2	0.482	0.003
Aspartate transferase (U/L)	22.9 ± 8.9	20.9 ± 4.6	0.279	0.094
Renal functions:				
Uric acid (μmol/L)	305.9 ± 37.3	285.1 ± 22.2	0.678	0.001
BUN (mmol/L)	4.9 ± 1.1	4.65 ± 1.1	0.187	0.231
Creatinine (μmol/L)	72.4 ± 11.5	66.9 ± 15.5	0.407	0.010

^at-test "Levene's test for unequal variances". ^bChi-square for independent samples. All values are presented in means ± SD unless otherwise indicated.

Table II. Glycemic indices, serum calcium, phosphorus and calcitropic hormones status in obese subjects compared to their controls.

Variables	Obese subjects (N = 76)	Lean controls (N = 84)	Cohen's d Effect size	P value ^d
Glycemic indices:				
Fasting blood sugar (mmol/L)	5.54 ± 0.95	4.46 ± 0.57	1.378	0.0001
Serum insulin level (μU/ml)	15.92 ± 9.69	8.99 ± 5.74	0.870	0.0001
HOMA-IR	3.98 ± 2.71	1.78 ± 1.12	1.061	0.001
HOMA-B%	205.0 ± 129.0	143.1 ± 97.4	0.542	0.001
Vitamin D status:				
25 (OH) vitamin D (μg/L)	35.0 (33.0 ± 12.0)	41.9 (40.4 ± 19.3)	-0.460	0.004
Gender: Males	36.2 (34.4 ± 10.3)	47.7 (46.8 ± 18.3)	-0.835	0.001
Females	33.4 (31.3 ± 13.6)	35.2 (34.0 ± 18.3)	-0.167	0.595
Hypovitaminosis Da: No. (%)	29 (38.2)	19 (22.7)		2.11 (1.01-4.46) ^{†*}
Vitamin D deficiencyb No. (%)	12 (15.8)	16 (19.0)		0.80 (0.32-1.95) [†]
Normal: No. (%)	35 (46.0)	49 (58.3)		Reference
Parathyroid hormone status:				
Intact parathormone level (pg/ml)	45.2 (49.6 ± 23.2)	34.3 (39.4 ± 20.1)	0.469	0.003
Gender: Males	43.9 (50.5 ± 24.2)	31.1 (35.6 ± 17.8)	0.701	0.001
Females	7.3 (48.6 ± 22.3)	41.6 (43.2 ± 21.8)	0.245	0.196
Hyperparathyroidismc: No. (%)	46 (60.5)	31 (36.9)		2.62 (1.32-5.23) ^{†*}
Eu status: No. (%)	30 (39.5)	53 (63.1)		Reference
Serum Calcium and phosphorus:				
Serum phosphorus (mmol/L)	1.30 (1.29 ± 0.17)	1.30 (1.28 ± 0.13)	0.066	0.830 ^d
Serum calcium (mmol/L) total:	2.50 (2.47 ± 0.22)	2.46 (2.38 ± 0.25)	0.382	0.035 ^{*d}
Hyperparathyroidism: Yes	2.19 (2.29 ± 0.23)	2.42 (2.46 ± 0.23)	-0.739	0.004 ^{*e}
No	2.40 (2.44 ± 0.24)	2.45 (2.46 ± 0.23)	-0.085	0.591 ^e

All values are given in median (means ± SD) unless otherwise stated. HOMA-IR = [serum insulin *fasting blood sugar]/22.5. HOMA-B% = [20*Fasting insulin]/[fasting glucose/3.5]. 25 (OH) D cParathormone of > 40 pg/ml. ^dt-test "Levene's". ^{*}Statistically significant. [†]Odds ratio (95% Confidence intervals).

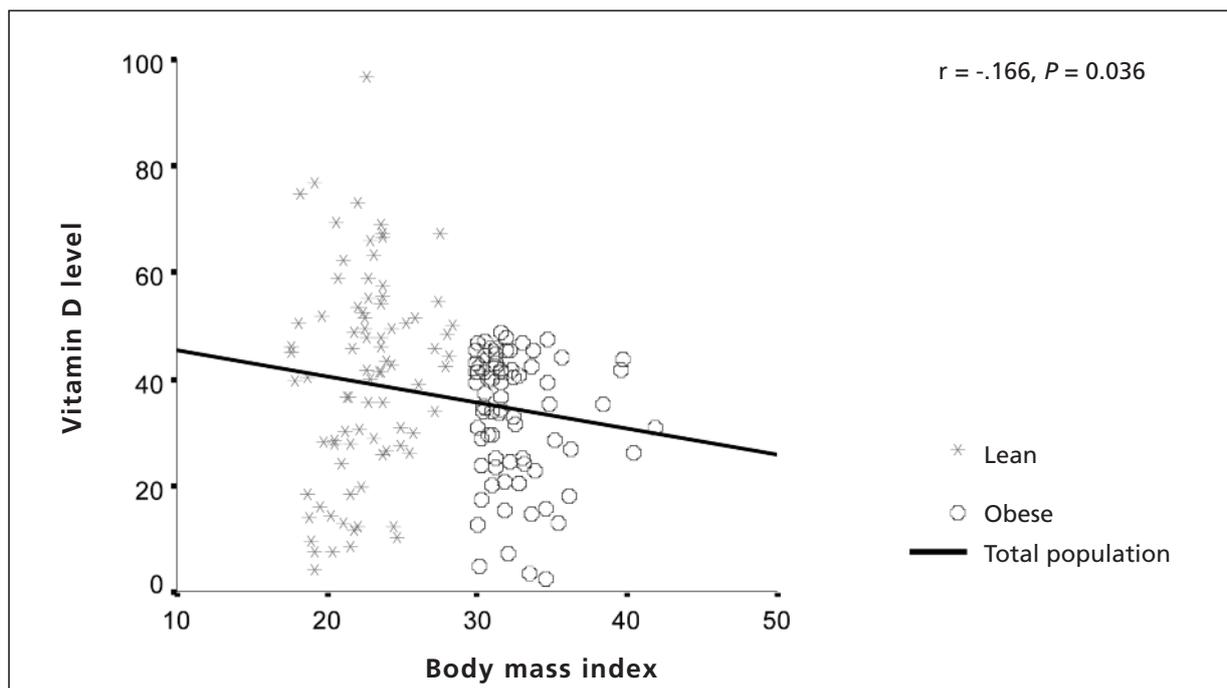


Figure 1. 25 (OH) vitamin D in relation to body mass index among obese subjects and lean controls.

Vitamin D, iPTH and Subject's Clinical and Biochemical Characteristics

Table III displays results of bivariate correlation analysis for the interaction between vitamin D, clinical and biochemical characteristics. Vita-

min D was negatively associated with BMI and gender (low among females) and positively correlated with class of obesity, serum calcium, creatinine, BUN and alanine transferase levels. Regression analysis model showed that: BMI,

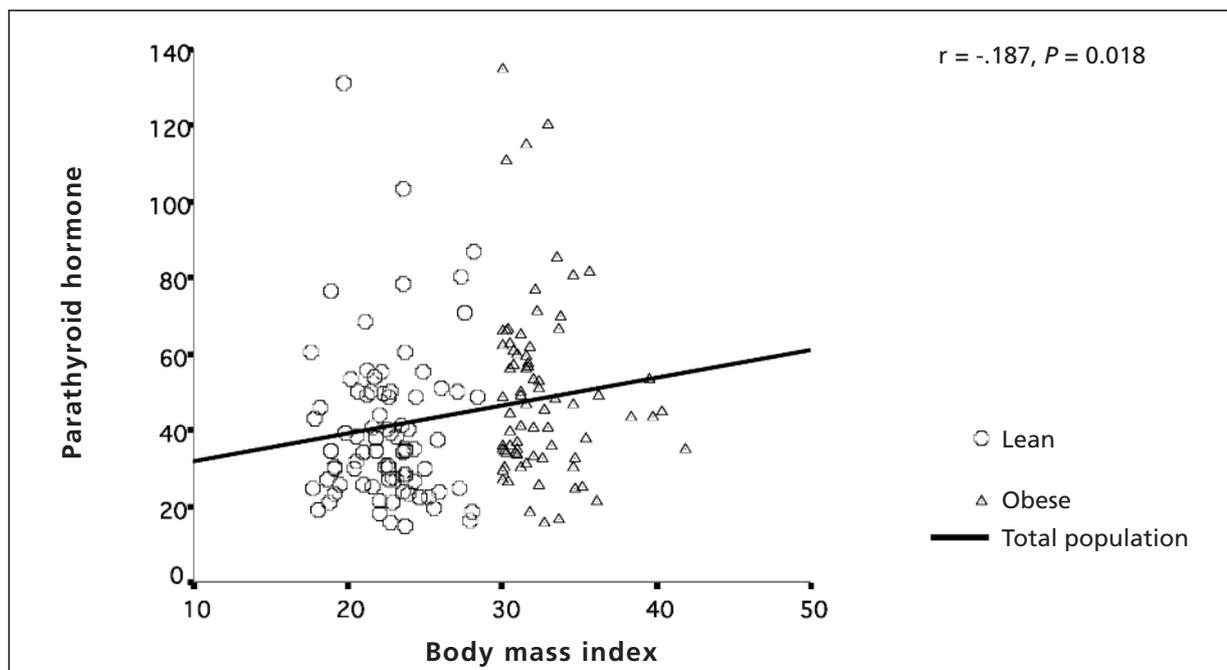


Figure 2. Parathyroid hormone level in relation to body mass index in obese subjects and lean controls.

Table III. Bivariate correlation and regression analysis of the effect of 25(OH) vitamin D on clinical and biochemical characteristics of obese subjects.

Clinical and biochemical characteristics	Bivariate correlation		Multivariate backward regression analysis			
	Coefficient	P value	β (SE)	β standardized	P value	Partial correlation
BMI	-.166	0.004*	-.882 (.218)	-.298	0.001**	-.308
Obesity class	.255	0.036*	–	–	–	–
Serum calcium	.359	0.001**	19.1 (7.51)	.237	0.012*	.200
Gender	-.242	0.002*	–	–	–	–
Serum creatinine	.344	0.001**	.261 (.128)	.220	0.043*	.161
Blood urea	.263	0.001**	–	–	–	–
Alanine transferase	.175	0.027*	–	–	–	–

Statistically significant at $P < *0.05$, ** $P < 0.001$. β (SE) = Unstandardized coefficient (Standard error). Multivariate backward stepwise regression analysis final model, constant = -3.44, $P=0.796$. $R=.472$, $R^2=.223$, $F=14.93$, percent predicted=75.9. Obesity class as ordinal: 0 (lean), obesity class I=1, class II=2, class III=3, Gender: 0=female, 1=male.

serum calcium and serum creatinine were the main predictors for vitamin D level among the included subjects. BMI was the major negative predictor for vitamin D level.

Table IV demonstrates bivariate correlation coefficient and final model of multiple regression analysis of iPTH and clinical and biochemical characteristics. BMI was the single positive predictor for iPTH level among the included subjects.

Vitamin D and iPTH in Relation to Insulin Resistance and β Cell Function Indices

Table V and Figures 3 and 4 demonstrate the relationship between vitamin D and parathyroid hormone levels in relation to insulin sensitivity as referred to HOMA-IR and β cell function

(HOMA-B%). Low vitamin D level was associated with increase in fasting blood sugar level ($r=-.133$, $P=0.093$) and HOMA-IR ($r=-.122$, $P=.341$) but without statistical significant.

Results of partial correlation coefficient (Table V) between vitamin D and insulin resistance index (HOMA-IR) after controlling for other possible confounders including clinical and biochemical variables revealed no significant relationship between vitamin D level and HOMA-IR. Also, a positive association was found between β cell function and vitamin D level but without statistical significance ($r=0.192$, $P=0.08$).

A negative association was found between iPTH level and insulin resistance (HOMA-IR) and β cell function but without statistical significance.

Table IV. Bivariate correlation and regression analysis of effect of intact parathyroid hormone on clinical and biochemical characteristics of obese subjects.

Clinical and biochemical characteristics	Bivariate correlation		Multivariate backward regression analysis		
	Coefficient	P value	β (SE)	β standardized	P value
BMI	.187	0.009**	.739 (.309)	.187	0.018*
Obesity class	.175	0.013*	–	–	–
Triglycerides	.159	0.023*	–	–	–
Serum bilirubin	-.164	0.019*	–	–	–
Alkaline phosphatase	.158	0.023*	–	–	–

Statistically significant at $*0.05$, ** $P < 0.001$. β (SE) = Unstandardized coefficient (Standard error). Multivariate stepwise regression analysis final model, constant = 24.07. $R=.187$, $R^2=.035$, $F=5.714$, percent predicted= 67.3. Obesity class as ordinal: 0 (lean), obesity class I=1, class II=2, class III=3.

Table V. Partial correlation coefficient' of the effect of 25 (HO) vitamin D on insulin sensitivity and β cell function among the obese subjects.

Variables	HOMA-IR		HOMA-B%	
	β Coefficient	P value	β Coefficient	P value
Gender	-.262	0.001	-.227	0.004
BMI	.517	0.001	.373	0.001
Serum calcium	.307	0.001	.285	0.001
Parathyroid hormone	-.031	0.704	-.014	0.863
25 (OH) vitamin D	-.066	0.408	.103	0.207
Triglycerides	.393	0.001	.217	0.001
Alkaline phosphatase	.295	0.001	.199	0.011

!Covariates considered: age, body mass index, vitamin D level, gender, HOMA-B%, total proteins, liver and renal function tests results. !!Covariates considered: age, gender, insulin sensitivity, body mass index, vitamin D level, HOMA-IR, liver and renal function tests results

Discussion

Our study is the first in Saudi Arabia that address vitamin D status in young healthy adults and its relationship to obesity and insulin resistance. Our findings revealed that hypovitaminosis D was prevalent in 30% of the included healthy adults Saudi irrespective of their BMI with secondary hyperparathyroidism in 48.1% and both parameters were altered more in obese subjects and the degree of these alterations was

proportionate to the class of obesity. Previous research had eluded that adult Saudis intake of vitamin D is about the fifth of those with similar age range in the United States but without mentioning the method used for such finding²⁵.

Our results in regard the association of hypovitaminosis D and obesity are in accordance to others who found that BMI was an independent factor predicting vitamin deficiency status^{1,2,34,35}. Furthermore, we found a significant decline of vitamin D level in relation to classes of obesity

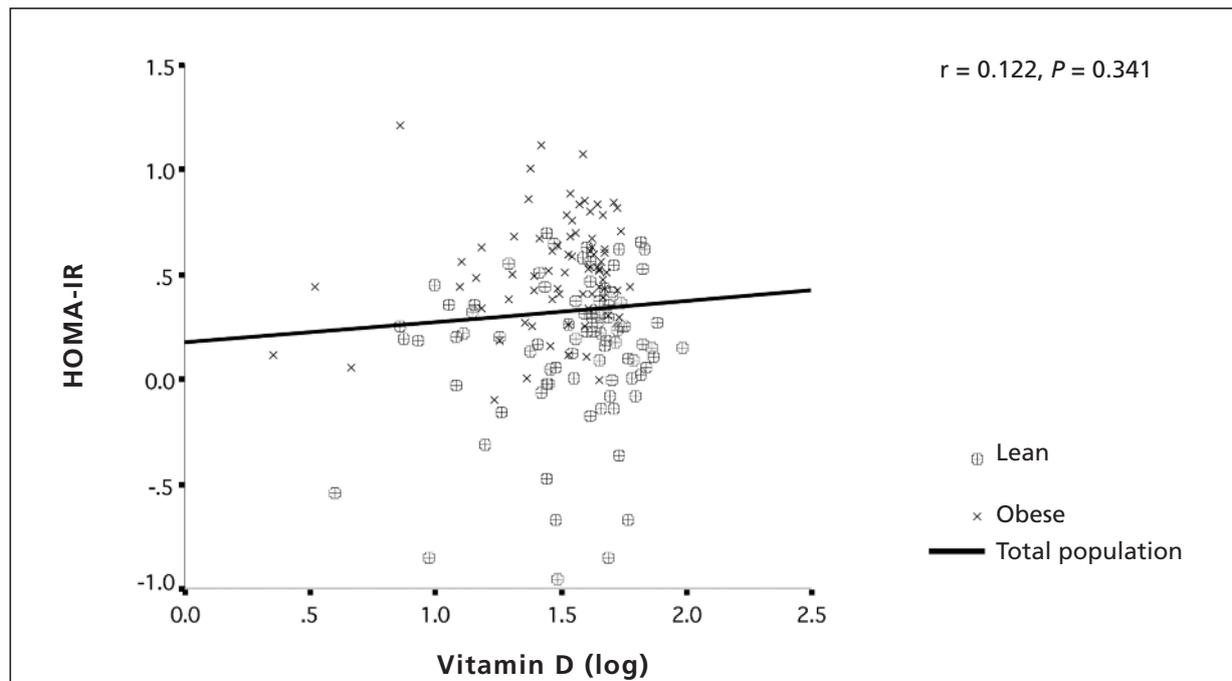


Figure 3. Insulin resistance index (HOMA-IR) in relation to 25 (HO) vitamin D level in obese and lean subjects.

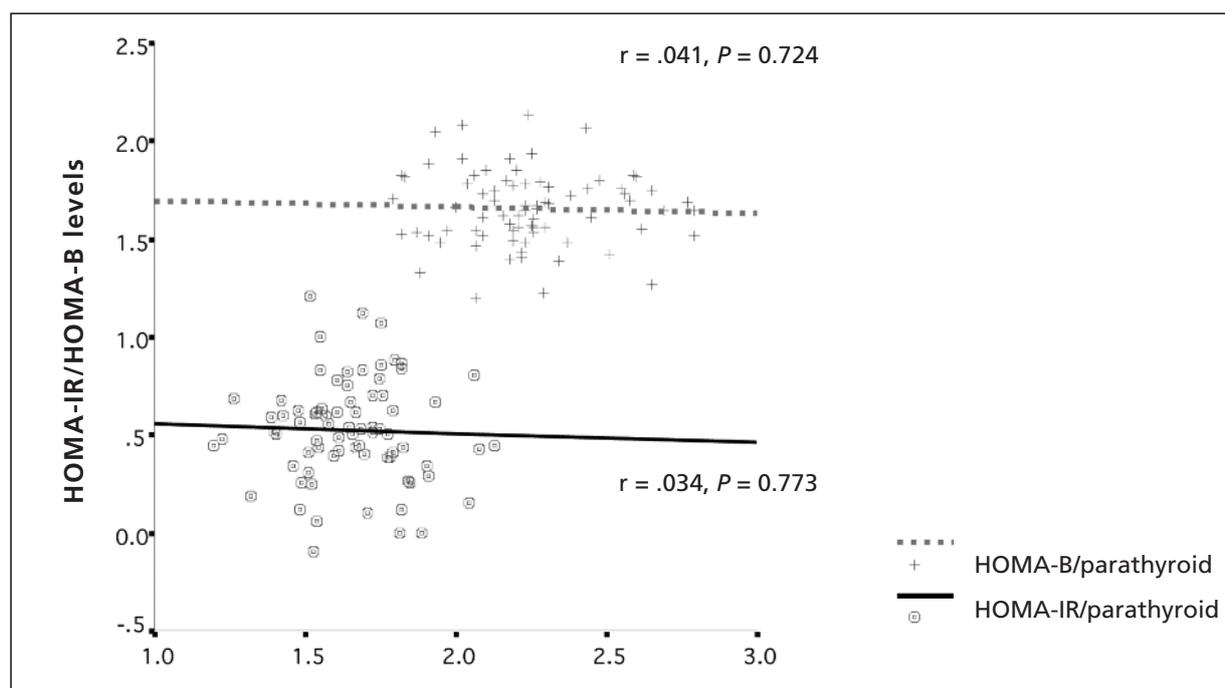


Figure 4. Relationship between parathyroid hormone, insulin resistance (HOMA-IR) and Beta cell function (HOMA-B).

which is consistent to similar finding obtained from U.S. African-American obese population²⁶. Yanoff et al²⁶ have found that the effect of adiposity on vitamin D status was independent of dietary intake, socio-economic, sex, age and season and that low vitamin D as the Odds of secondary hyperparathyroidism were significantly greater in obese subjects.

Consequences of vitamin D deficiency include a broad range of health problems. Some reports suggest the potential importance of vitamin D in prevention of certain cancers, autoimmune diseases, heart disease and hypertension^{16,36}. It has been proposed because of the association between low sun exposure and the development of many internal malignancies, the incidence and mortality from these cancer could be prevented if adequate vitamin D blood level is maintained^{37,38}. Hence, the importance of screening of those at risk especially obese adults with BMI of ≥ 35 provided that cost effective analysis is considered²⁶. The relationship between iPTH and BMI is consistent with previous studies^{4,39,40}.

In addition, our finding regarding the relationship between alkaline phosphatase level and iPTH is also consistent with other studies^{26,34,39}.

Alkaline phosphatase is marker of bone turnover, and while considering that our subjects

were free from renal damage, hepatic or significantly elevated transaminases but we can not rule out the presence of fatty liver. Our finding may point out to the possibility of metabolic bone disease among our obese adults although we did not measure the bone-specific enzymes. Lower ionized calcium level among our obese subjects may reflect their lower vitamin D level and be the proximal cause of their greater iPTH level. The mechanism underlying the lower levels of vitamin D in relation to obesity is less clear. Greater storage of vitamin D as a result of a larger fat mass has been suggested⁴², as adipose tissue has been shown to be the major storage site for vitamin D in rats⁴³ and humans⁴⁴. Compston et al³⁴ have proposed that obese individuals may spend less time outdoors and, therefore, be less exposed to ultraviolet radiation.

Our data showed that in glucose tolerant obese subjects there has been a negative correlation between vitamin D and insulin resistance and a positive correlation between vitamin D level and β cell function but without statistical significance. These findings are conflicting with previous studies^{17,45,46}, which reported that hypovitaminosis D is a risk factor for type 2 diabetes mellitus and metabolic syndrome. Several explanations could be provided for this discrep-

ancy. First, serum vitamin D concentrations and its relationship with attitude are well known. Therefore, regional differences in vitamin D are well recognized phenomenon⁴⁷. As a result, the reference range defined with the use of the regional population samples lead to different range of lower limits among various regions. In Saudi Arabia, the regional population reference range is unknown. Therefore, we employed the Western range of hypovitaminosis D which may be different and does not reflect the true population threshold for hypovitaminosis D. Second, the gold standard for the measurement of insulin sensitivity is the use the euglycemic clamp⁴⁸, instead with the used single blood sampling to estimate the fasting blood sugar and calculate insulin resistance that imposed a different results about the relationship.

Insulin sensitivity may not be influenced by circulating 25(OH) vitamin D in some populations. Manco et al¹⁵ investigated the associations of 25(OH) D with insulin sensitivity (determined with a euglycemic-hyperinsulinemic clamp) in morbidly obese Caucasian women. Serum 25(OH) D was not associated with insulin sensitivity in these subjects either before bariatric surgery or 5 and 10 years post-surgery suggesting that the found low serum 25(OH) D concentrations before and after bariatric surgery do not negatively affect insulin sensitivity.

Other anthropometric factors, such as the extreme adiposity prior to surgery and the improved metabolic and lipid profile post-surgery, likely had a greater impact than 25(OH) D on insulin sensitivity. NHANES III data did not show significant relationships between 25(OH) D and HOMA-IR in African Americans despite there are significant results in Caucasian and Mexican Americans⁴⁹. Alemzadeh et al⁵⁰ reported a significant relationship between serum 25(OH) D and Hb A1c in Caucasian but not in African Americans.

It is unclear whether diverse ethnicities have different optimal serum concentrations of 25(OH) D, and the relationships of serum 25(OH) D with glucose homeostasis should be examined in different ethnicities using direct measures of insulin sensitivity and secretion to confirm the effect of 25(OH) D with insulin sensitivity⁵¹.

Published data strongly supported the association between hypovitaminosis D and β cell dysfunction⁵². There is ample evidence in animal studies that vitamin D is essential for normal insulin secretion. Insulin secretion was im-

paired in the vitamin D-deficient pancreas, and it was improved by dietary vitamin D repletion^{53,54}.

Vitamin D repletion improved glucose clearance and insulin secretion in vivo, independent of nutritional factors and the prevailing plasma calcium and phosphorus concentrations⁵⁵. Vitamin D supplementation has been reported to improve insulin secretion in vitamin D-deficient and non-diabetic subjects⁵⁶ and in patients with type 2 diabetes mellitus^{55,56}. Our study unlike those conducted on vitamin D deprived animals or with human with profound cell dysfunction (glucose impaired intolerance or diabetics), where a profound β cell dysfunction is obvious. We found a positive association between vitamin D and β cell function. Further studies are needed to address the clinical implications of this association.

Limitations

This study has several limitations including using a proxy measures to estimate insulin sensitivity and β cell function in the form of fasting blood glucose and serum insulin to calculate the HOMA-IR and HOMA-B instead of the gold standard hyper/euglycemic clamp. The accuracy of proxy measures of insulin sensitivity may vary depending on obesity status or ethnicity. In addition, we utilized the BMI rather than a direct measure of adiposity as a covariate in analyses. The accuracy of BMI in reflecting adiposity has been questioned. Studies have used total body fat and BMI in models to predict 25(OH) D, found that only total body fat emerged as an independent predictor. Our study did not consider other confounders that may be mediating associations between 25(OH) D and insulin sensitivity, such as physical activity and calcium intake, each of which has been shown to be significantly associated with insulin sensitivity.

Conclusion

Vitamin D level among young adult Saudi obese is predicted by body mass index and classes of obesity. There are negative associations between vitamin D and parathyroid hormone and insulin sensitivity among young adult subjects but without statistical significance after controlling of the possible confounders.

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