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Original Article

Endocrinology Section

Vitamin D and the Metabolic Syndrome in Indian Sub-population

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ABSTRACT

Introduction: Low serum 5-hydroxyvitamin D [25(OH)D] levels have been related to insulin resistance, the metabolic syndrome (MetS) and its components. The aim of our analysis was to investigate the association of 25(OH)D with IDF-defined MetS.

Design: This was a cross-sectional study of 50 participants aged 15–65 years.

Results: Mean age of the participants was 42.14 years. 25(OH)D levels were inversely associated with BMI, waist circumference, systolic and diastolic blood pressure (BP), triglycerides, and fasting blood glucose ($P<0.05$). The percentage of subjects with MetS decreased across increasing quintiles of 25(OH)D ($P<0.001$).

Conclusions: Our results demonstrate an inverse relationship between 25(OH)D levels and MetS in the Indian sub-population studied. Further investigations are required to clarify the clinical significance of these findings.

Key Words: Metabolic syndrome, Vitamin D, Body Mass Index, Blood Glucose, Lipids, LDL, Triglycerides, Waist circumference, Blood pressure

INTRODUCTION

Recent population-based cross-sectional studies suggest that 5-Hydroxyvitamin D (25(OH)D) plays an important role in metabolism in addition to functioning as a physiological regulator of extra-cellular calcium homoeostasis. [1-5] Many studies have described a marked inverse relationship between 25(OH)D levels and the metabolic syndrome (MetS) and essentially with almost all components of the MetS. Moreover, vitamin D deficiency may be a risk factor for the MetS, a condition that is highly prevalent in the Indian population. We undertook this study to investigate the cross-sectional trends and associations between 25(OH)D levels and MetS and its components in a small Indian subpopulation.

METHODS

Subjects

Men and pre-menopausal women aged between 15 and 65 years who attended the OPD or wards of the institution and provided written informed consent for participation according to the ICH-Good Clinical Practices Guidelines were recruited for the study. Ethical approval was obtained from the Institution's ERB. Subjects with chronic renal, hepatic, cardiac, gastro-intestinal, skeletal, or endocrine diseases (except diabetes), acute critical illness, and pregnancy were excluded from the study. Subjects on calcium or vitamin D supplementation were also excluded from the study.

Assessments

Blood pressure was measured after a 5-min rest period to the nearest 1 mmHg while participants were seated using a sphygmomanometer (*Infi Mercurial, India*). Height was measured barefoot to the nearest 1 mm using an anthropometric tape. Weight was measured to the nearest 0.1 kg using an electronic scale (*Atlas Weighing Equipments, India*) with subjects wearing light clothing. Waist circumference was measured mid-way between the iliac crest and lowest rib, to the nearest 1 mm using anthropometric tape, with the subject standing.

Biochemistry

Phlebotomy was performed prior to 1100 h to obtain a fasting blood sample from all subjects. Processed serum was stored and protected from light at –80°C prior to analysis. Serum 25(OH)D levels were determined using RIA (*DiaSorin, Stillwater, MN, USA*). Intra- and inter-assay coefficients of variation (CV) for 25(OH)D were 11% and 8% respectively. The detection limit of the RIA kit was 5.0 nmol/l 25(OH)D.

Analyses for cholesterol, high-density lipoprotein (HDL) cholesterol and triglycerides were performed using commercially available enzymatic methods (*Biosystems, Barcelona, Spain*).

Metabolic Syndrome and Control

To assess the prevalence of MetS among the study subjects, we used the current IDF guidelines [6]. The IDF definition of MetS was met if subjects had central obesity (BMI>30 kg/m^2) and any two of the following: a triglyceride level >150 mg/dl, an HDL cholesterol level <40 mg/dl in men or <50 mg/dl in women, systolic blood pressure >130 mmHg and/or diastolic blood pressure >85 mmHg, and fasting glucose >100 mg/dl.

Analysis

25(OH)D levels were treated as continuous variables or classified into quintiles. Individual components of the MetS were examined as continuous variables in linear regression models. The association of 25(OH)D levels with MetS components was investigated using linear regression, and results were expressed as beta-coefficients and 95% confidence intervals (CI). 25(OH)D values were then classified into quintiles and the frequency of MetS subjects falling in each quintile was calculated and expressed as percentages. These percentages were examined by Pearson's Chi-square test.

RESULTS

Subjects

The clinical characteristics of the 50 men and women included in the analysis are shown in [Table/Fig-1]. Overall, females comprised 52% of the subjects (n=26) and males comprised 48% of the study population (n=24). Baseline differences in subjects with MetS and in subjects without MetS are given in [Table/Fig-2].

Metabolic Syndrome

MetS was present in half of the subjects [Table/Fig-1].The prevalence of individual MetS components according to the current IDF guidelines ranged from 20% of subjects with high fasting plasma glucose to 44% of subjects with systolic blood pressure >130 mmHg.

Associations between 25(OH)D and components of the MetS are presented in [Table/Fig-3]. Increasing 25(OH)D levels were associated with lower values for waist circumference, systolic blood pressure, diastolic blood pressure, triglycerides and glucose, and higher values for HDL cholesterol.

The associations of quintiles of 25(OH)D with MetS are summarised in [Table/Fig-4]. The percentage of MetS subjects decreased with increasing quintiles of 25(OH)D (*P*<0.001). All subjects with 25(OH)D <9 ng/ml had MetS. None of the subjects with 25(OH)D≥39.1 ng/ml had MetS.

Variable	Mean (SD)
Age (years)	42.1 (12)
Waist Circumference (cm)	88 (12.7)
Mean Blood Pressure (mm Hg)	99.4 (11.2)
HDL Cholesterol (mg/dl)	50.5 (7.5)
Triglycerides (mg/dL)	130 (33.9)
Fasting Plasma Glucose (mg/dl)	98.7 (18.6)
Body Mass Index (kg/m^2)	27.2 (6.1)
25(OH)D (ng/ml)	22.7 (10.7)
	%
IDF Metabolic Syndrome	50
BMI>30 kg/m^2	50
Systolic Blood Pressure>130 mmHg	44
Diastolic Blood Pressure>85 mmHg	32
HDL Cholesterol<40 mg/dl in males or <50 mg/dl in females	24
Triglycerides>150 mg/dl	36
Fasting Plasma Glucose> 100 mg/dl	20

[Table/Fig–1]: Baseline Characteristics (n=50)

Variable	Control (n=25) Mean (SD)	Cases (n=25) Mean (SD)
Age (years)	41.6 (8.7)	42.7 (14.8)
Waist Circumference (cm)	76.9 (5.5)	99.1 (6.3)*
Systolic Blood Pressure (mm Hg)	115.6 (5.1)	147.2 (16.4)*
Diastolic Blood Pressure (mm Hg)	78.4 (3.7)	88.8 (7.5)*
HDL Cholesterol (mg/dl)	53.4 (5.7)	47.6 (8)**
Triglycerides (mg/dl)	101.4 (14.3)	158.6 (20.9)*
Fasting Plasma Glucose (mg/dl)	90.7 (6)	106.8 (23)**
Body Mass Index (kg/m^2)	21.4 (1.5)	33 (2)*
25(OH)D (ng/ml)	27.3 (10.5)	18.1 (9)**

[Table/Fig–2]: Baseline Characteristics of Controls and Cases
**P<0.001*
***P<0.01*

Dependent Variable	Independent Variable 25(OH)D-(per ng/ml) β–Coefficients (95% CI)
Body Mass Index (kg/m^2)	–0.57 (–0.34, –0.73)*
Systolic Blood Pressure (mm Hg)	–0.36 (–0.09. –0.66)*
Diastolic Blood Pressure (mm Hg)	–0.44 (–0.19, –0.76)*
HDL Cholesterol (mg/dl)	+0.22 (0, 0.47)
Triglycerides (mg/dl)	–0.38 (–0.12, –0.4)**
Fasting Plasma Glucose (mg/dl)	–0.39 (–0.12, –0.6)**
Waist Circumference (cm)	–0.55 (–0.32, –0.72)*

[Table/Fig-3]: Associations between 25–hydroxyvitamin D (25(OH)D) and components of the metabolic syndrome: linear regressions
**P<0.01*
***P<0.05*

	Quintiles of 25(OH)D (range ng/ml)					
	n=4	n=16	n=13	n=12	n=5	
	I (<9)	II (9.1–19.0)	III (19.1–29.0)	IV (29.1–39.0)	V (≥39.1)	P
Normal	0	6	6	8	5	
MetS	4	10	7	4	0	
% MetS	100	62.5	53.9	33.3	0	<0.001*

[Table/Fig-4]: Percentage of MetS subjects with increasing quintiles of 25–hydroxyvitamin D [25(OH)D]
**by Pearson Chi-square test*

DISCUSSION

In this sub-population study of Indian men and women, 25(OH)D levels were significantly associated with all components of MetS, except for HDL-cholesterol. The most significant relationship of 25(OH)D levels was with BMI and waist circumference. This is in agreement with the study by Ford *et al* [1] who observed that the only age-adjusted trend in the NHANES population that matched the magnitude of the rate of decrease in the serum 25(OH)D level over time was the rate of increase in the BMI in that period (National Center for Health Statistics, 2009: In the NHANES III dataset, a significant stepwise quartile drop in the serum 25(OH)D levels is observed with the reverse quartile trend upward in BMI in that population).

Recently it was shown that the serum 25(OH)D levels rise significantly in extremely obese patients who undergo intestinal bypass surgery that induces a rapid reduction in fat mass in the host. [7] Low 25(OH)D levels observed in association with obesity may be explained in part by the increased volume of distribution to fat of lipid soluble vitamin D as it leaves the general circulation after being synthesized in the skin or obtained through the diet and preferential retention of vitamin D in these fat stores.

In our study, the percentage of MetS subjects decreased with increasing quintiles of 25(OH)D. This is in resonance with the study by Ford *et al* [1] as well as with a separate study in NHANES subjects, in which Reis and co-workers [5] reported a strong inverse relationship between 25(OH)D levels and prevalent MetS that is independent of important confounders. These studies and our findings suggest that a threshold may exist at and below which vitamin D deficiency may influence the incidence of MetS, whereas higher levels may not.

The mechanism(s) by which low vitamin D could be associated with MetS remain to be elucidated. Research in humans suggests that low 25(OH)D levels are associated with glucose intolerance and insulin resistance. [8-10] Further studies are required to delineate the exact mechanism.

Limitations

We have studied a small, population-based sample of Indian men and women. Our study has a number of limitations. The cross-sectional design limits conclusions about causal relationships. We enrolled institutionalised men and women which limits the generalisability to other groups. We have not adjusted for age, physical-activity, parathyroid hormone or calcium status and drug usage. We also have not determined glycated haemoglobin levels (HbA1c), a marker of the average blood glucose levels for the preceding few months that would have served as a better indicator of the plasma glucose levels.

CONCLUSION

We have shown that in a sub-population-based study of Indian men and women that low 25(OH)D levels were linked to prevalent MetS. Further large, population-based prospective studies are needed to ascertain the relationship between vitamin D and MetS.

REFERENCES

[1] Ford ES, Ajani UA, McGuire LC & Liu S. Concentrations of serum vitamin D and the metabolic syndrome among US adults. *Diabetes Care* 2005;28:1228–30.
[2] Gannage-Yared MH, Chedid R, Khalife S, Azzi E, Zoghbi F & Halaby G. Vitamin D in relation to metabolic risk factors, insulin sensitivity and adiponectin in a young Middle-Eastern population. *European Journal of Endocrinology* 2009;160:965–71.
[3] Lu L, Yu Z, Pan A, Hu FB, Franco OH, Li H, et al. Plasma 25-hydroxyvitamin D concentration and metabolic syndrome among middle-aged and elderly Chinese individuals. *Diabetes Care* 2009;32:1278–83.
[4] Reis JP, von Muhlen D, Kritz-Silverstein D, Wingard DL & Barrett Connor E. Vitamin D, parathyroid hormone levels, and the prevalence of metabolic syndrome in community-dwelling older adults. *Diabetes Care* 2007;30:1549–55.
[5] Reis JP, von Muhlen D & Miller ER III. Relation of 25-hydroxyvitamin D and parathyroid hormone levels with metabolic syndrome among US adults. *European Journal of Endocrinology* 2008;159:41–48.
[6] The IDF Consensus worldwide definition of the Metabolic Syndrome. International Diabetes Federation. IDF 2006:10-11. Available at: http://www.idf.org/webdata/docs/IDF_Meta_def_final.pdf.
[7] de Luis DA, Pacheco D, Izaola O, Terroba MC, Cuellar L, Martin T 2008 Clinical results and nutritional consequences of biliopancreatic diversion: three years of follow-up. *Ann Nutr Metab* 53:234–39.
[8] Chiu KC, Chu A, Go VL & Saad MF. Hypovitaminosis D is associated with insulin resistance and beta cell dysfunction. *American Journal of Clinical Nutrition* 2004;79:820–25.
[9] Liu E, Meigs JB, Pittas AG, McKeown NM, Economos CD, Booth SL, et al. Plasma 25-hydroxyvitamin D is associated with markers of the insulin resistant phenotype in non-iabetic adults. *Journal of Nutrition* 2009;139:329–34.
[10] Forouhi NG, Luan J, Cooper A, Boucher BJ & Wareham NJ. Baseline serum25-hydroxy vitamin D is predictive of future glycaemic status and insulin resistance: the Medical Research Council Ely Prospective Study 1990–2000. *Diabetes* 2008;57:2619–25.

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