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SHORT COMMUNICATION

Vitamin D status and metabolic syndrome in Asian Indians

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In this study, we aimed to estimate serum 25-hydroxy vitamin D (25-OH-D) in Asian Indians and test for association between 25-OH-D levels, insulin resistance (IR) and metabolic syndrome (MS). Serum 25-OH-D was measured in a cross-sectional sample of 441 Indians, aged 39.7 ± 12.8 years (237 men and 204 women) with 27.9% prevalence of MS. Vitamin D insufficiency (12.5 to $<50\,nmol\,l^{-1}$) and hypovitaminosis D (50 to $<100\,nmol\,l^{-1}$) were present in 65.6 and 31.1% of participants, respectively. The 25-OH-D levels did not differ significantly between sexes ($P=0.057$). Multivariate regression analysis indicated a positive relationship between 25-OH-D and β-cell function (homeostasis model assessment (HOMA)-B; $\beta=0.245$, $P=0.006$), whereas regression coefficients for fasting glucose ($\beta=0.262$, $P=0.794$), insulin ($\beta=-0.140$, $P=0.889$) and HOMA-IR ($\beta=-0.119$, $P=0.172$) were insignificant. Sex-stratified analysis showed no linear trend for increasing quintiles of 25-OH-D with prevalence of MS or its components ($P>0.05$). Although highly prevalent, vitamin D insufficient status was not associated with MS or IR in Asian Indians of either sex.
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Keywords: vitamin D; Asian Indians; metabolic syndrome; HOMA-B, HOMA-IR

Introduction

Vitamin D deficiency and metabolic syndrome (MS) are two major global health concerns. Though inconsistent, inverse relationships have been demonstrated between circulating levels of 25-hydroxy vitamin D (25-OH-D), the main metabolite of vitamin D, and MS or the metabolic abnormalities associated with it, namely, elevated fasting glucose and insulin resistance (IR)/diabetes.[1–6] Ford *et al.*[1] have reported that the odds of MS were 54% lower among US adults in the highest quintile of 25-OH-D compared with those in the lowest quintile, with a significant trend of decreasing odds ratios across increasing quintiles ($P_{trend}<0.001$). Recently, Pinelli *et al.*[2] have also found an association between low vitamin D levels and IR, MS and glucose intolerance in Arab American men. Hypovitaminosis D has been proposed to influence insulin sensitivity/secretion through its effects on intracellular calcium or through direct modulation of gene expression via vitamin D receptors.[3] Despite high prevalence of IR and vitamin D deficiency in India,[7,8] there is paucity of data on the relationship between vitamin D status and MS in the Indian population. Hence, our aim was to measure and report the levels of vitamin D and to test for association between serum vitamin D levels, IR and MS among Asian Indians living in south India.

Methods

This study was approved by the ethics committee of our Institute and written informed consent was obtained from all the participants. We investigated 441 randomly selected subjects 18–75 years of age. Demographic and anthropometric analyses included the following variables: age, sex, smoking status, height, weight and waist circumference. The body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Clinical laboratory measurements included serum levels of 25-OH-D, insulin, high-density lipoprotein-cholesterol (HDL-C), triglycerides and glucose. Serum glucose, triglycerides and HDL-C concentrations were determined enzymatically using commercially available kits and auto analyzer (Olympus AU640, Munich, Germany). Serum insulin was measured using enzyme immunoassay kits (Calbiotech Inc., Spring Valley, CA, USA). The intra- and inter-assay coefficients of variation were 5.5 and 7.8%, respectively.

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Homeostasis model assessment estimates of IR (HOMA-IR) and β-cell function (HOMA-B) were calculated using fasting glucose and insulin measurements.[9]

Serum 25-OH-D was measured using enzyme immunoassay kits (Immunodiagnostic Systems Ltd, Boldon, Tyne & Wear, UK) with quality control materials provided by the manufacturer. The intra- and inter-assay coefficients of variation were 4.6 and 5.0%, respectively. Serum 25-OH-D status was classified as: deficiency: $<12.5\,nmol\,l^{-1}$ ($<5\,ng\,ml^{-1}$); insufficiency: 12.5 to $<50\,nmol\,l^{-1}$ (5 to $<20\,ng\,ml^{-1}$); hypovitaminosis D: 50 to $<100\,nmol\,l^{-1}$ (20 to $<40\,ng\,ml^{-1}$); sufficiency: 100 to $<250\,nmol\,l^{-1}$ (40 to $<100\,ng\,ml^{-1}$); and toxicity: $\geqslant 250\,nmol\,l^{-1}$ ($\geqslant 100\,ng\,ml^{-1}$).[2,10] Subjects were classified as having MS according to the National Cholesterol Education Program/Adult Treatment Panel III definition (blood pressure of $\geqslant$130/85 mm Hg; triglycerides $\geqslant 1.7\,mmol\,l^{-1}$ ($\geqslant$150 mg per 100 ml); HDL cholesterol $<1.0\,mmol\,l^{-1}$ ($<$40 mg per 100 ml) and $<1.3\,mmol\,l^{-1}$ ($<$50 mg per 100 ml) in men and women, respectively; and fasting blood glucose $\geqslant 6.1\,mmol\,l^{-1}$ ($\geqslant$110 mg per 100 ml) with modified waist circumference cut off values (males $>$90 cm, females $>$80 cm) appropriate for Indians.[11,12] Presence of three or more parameters was considered for defining MS-positive subjects. Obesity was defined as BMI $\geqslant 25\,kg\,m^{-2}$.[13]

Multiple linear regression coefficients for BMI, blood pressure, fasting glucose, insulin, HOMA-IR and HOMA-B function as outcome variables were calculated against serum 25-OH-D as the independent variable, adjusting for age and sex. Surrogates of IR (fasting insulin, HOMA-IR) were additionally adjusted for BMI. Quantitative characteristics were summarized by arithmetic mean and standard deviation. The differences in the anthropometric and biochemical parameters were compared using *t*-test or Mann–Whitney test. χ^2-tests for trend were performed by entering the categorical 25-OH-D variables as an ordinal term using the SPSS and are reported with *P*-values. Sex-specific logistic regression models were fitted to estimate the odds of MS and its components across quintiles of 25-OH-D after adjusting for age (years), smoking and BMI ($kg\,m^{-2}$). Models of MS components were additionally adjusted for other components.

Results

A total of 441 subjects with a mean age of 39.7 ± 12.8 years were included in the study. Among them, 14.1% were smokers and 53.7% were men. MS was present in 27.9% of the total participants. In all, 44.7% of subjects were obese, whereas abdominal obesity was present in 27.1%. Although men (39.8 ± 13.0 years) and women (39.7 ± 12.7 years) were of similar age, prevalence of MS differed significantly between men and women, $P=0.034$; 32.8% of women had MS compared with only 23.6% of men. Sex-specific differences were also found in the prevalence of the components of MS. Abdominal obesity (52.1 versus 7.2%, $P<0.0001$) and low HDL-C (76.1 versus 57.5%, $P=0.0001$) were found to be more prevalent in women compared with men. Men had higher triglycerides compared with women (52.1 versus 35.9%, $P=0.002$). Except for HDL-C levels ($P=0.339$) in women, all the other metabolic parameters (waist circumference, fasting glucose, triglycerides, systolic and diastolic blood pressure) were found to be differentially distributed between subjects with and without MS in both the sexes ($P<0.0001$; Table 1).

Concentrations of 25-OH-D ranged from 5.5 to 181.2 $nmol\,l^{-1}$. Vitamin D insufficient status was found to be present in 65.6% and hypovitaminosis in 31.1% of subjects. Only two participants had optimal 25-OH-D status (100 to $<250\,nmol\,l^{-1}$).[2,10] Women had lower vitamin D concentrations than men though the difference was not statistically significant (40.2 ± 18.0 versus 43.7 ± 19.0 $nmol\,l^{-1}$, $P=0.057$). Mean 25-OH-D levels were not found to be influenced by the presence of MS in either sexes; $P=0.574$ and 0.734, in men and women, respectively (Table 1).

Multiple linear regression analysis showed an association between 25-OH-D and HOMA-B ($\beta=0.245$, $P=0.006$) and BMI ($\beta=-0.183$, $P=0.013$), while coefficients for 25-OH-D and fasting glucose ($\beta=0.262$, $P=0.794$), insulin ($\beta=-0.140$, $P=0.889$), HOMA-IR ($\beta=-0.119$, $P=0.172$), systolic blood pressure ($\beta=0.063$, $P=0.422$) and diastolic blood pressure ($\beta=-0.107$, $P=0.161$) were not significant.

The prevalence of MS did not show a linear trend across the quartiles of Vitamin D in either sex (Table 2). Amongst

Table 1 Distribution of MS components and 25-OH-D levels in men and women with and without MS

	Men			*Women*		
	MS negative (n = *181*)	*MS positive* (n = *56*)	P-*value*	*MS negative* (n = *137*)	*MS positive* (n = *67*)	P-*value*
Age (years)	35.3 ± 12.4	48.3 ± 7.9	<0.0001	37.7 ± 13.3	45.6 ± 9.0	<0.0001
25-OH-D ($nmol\,l^{-1}$)	44.5 ± 19.7	41.7 ± 16.4	0.574	39.0 ± 17.1	42.5 ± 19.7	0.734
MS components						
Waist circumference, cm	87.1 ± 7.7	95.0 ± 9.1	<0.0001	84.8 ± 7.9	95.4 ± 8.1	<0.0001
SBP, mm Hg	122.7 ± 10.0	131.7 ± 14.5	<0.0001	118.4 ± 12.1	127.6 ± 11.6	<0.0001
DBP, mm Hg	79.8 ± 7.5	89.4 ± 13.4	<0.0001	78.0 ± 6.2	85.4 ± 10.3	<0.0001
Fasting glucose ($mmol\,l^{-1}$)	4.7 ± 1.2	6.2 ± 3.2	<0.0001	4.6 ± 0.9	5.9 ± 2.8	<0.0001
Triglycerides ($mmol\,l^{-1}$)	1.7 ± 0.8	2.9 ± 1.4	<0.0001	1.2 ± 0.6	2.1 ± 0.9	<0.0001
HDL-C ($mmol\,l^{-1}$)	1.0 ± 0.2	0.9 ± 0.2	0.001	1.1 ± 0.3	1.0 ± 0.2	0.339

Abbreviations: 25-OH-D, 25-hydroxy vitamin D; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein-cholesterol; MS, metabolic syndrome; SBP, systolic blood pressure.

Table 2 Prevalence of metabolic syndrome and its components across quintiles of 25-OH-D

Quintiles of 25-OH-D (nmol l^{-1})	*Metabolic syndrome*		*Abdominal obesity*		*Hyperglycemia*		*High triglycerides*		*High BP*		*Low HDL*	
	Prevalence (%)	*OR*[a]	*Prevalence (%)*	*OR*[b]	*Prevalence (%)*	*OR*[b]	*Prevalence (%)*	*OR*[b]	*Prevalence (%)*	*OR*[b]	*Prevalence (%)*	*OR*[b]
Men (n = 237)												
I (< 28.2)	31.8	1.0 (ref)	6.7	1.0 (ref)	23.8	1.0 (ref)	64.4	1.0 (ref)	46.3	1.0 (ref)	62.9	1.0 (ref)
II (28.2–38.0)	15.2	0.3 (0.1–0.9)	6.5	0.9 (0.2–5.1)	13.3	0.4 (0.1–1.4)	59.1	1.2 (0.5–3.0)	55.8	1.4 (0.5–3.3)	47.5	0.5 (2–1.3)
III (38.1–47.0)	26.1	0.8 (0.3–2.0)	6.5	1.1 (0.2–6.0)	10.9	0.4 (0.1–1.3)	55.8	1.1 (0.5–2.7)	51.1	1.1 (0.5–2.8)	56.1	0.7 (0.3–1.8)
IV (47.1–57.8)	28.3	0.9 (0.3–2.3)	9.1	1.8 (0.4–9.1)	6.8	0.2 (0.6–1.0)	60.1	0.3 (0.1–0.8)	41.9	0.9 (0.3–2.1)	58.1	0.8 (0.3–2.1)
V (> 57.8)	22.2	0.6 (0.2–1.7)	8.9	1.7 (0.3–8.5)	11.1	0.3 (0.1–1.2)	53.8	1.7 (0.7–4.0)	30.9	0.5 (0.2–1.3)	67.4	1.2 (0.5–3.1)
P_{trend}	0.785		0.574		0.053		0.062		0.064		0.364	
Women (n = 204)												
I (< 25.2)	28.9	1.0 (ref)	54.1	1.0 (ref)	8.1	1.0 (ref)	50.0	1.0 (ref)	23.3	1.0 (ref)	74.2	1.0 (ref)
II (25.2–34.2)	34.2	1.1 (0.4–3.4)	52.6	0.9 (0.3–2.3)	10.8	1.1 (0.2–5.6)	33.3	1.4 (0.5–4.0)	40.6	2.3 (0.7–7.2)	71.4	0.9 (0.3–2.6)
III (34.3–42.9)	38.5	1.1 (0.4–3.4)	54.1	0.8 (0.3–2.1)	5.3	0.4 (0.1–2.8)	32.4	0.9 (0.3–2.5)	44.1	2.0 (0.6–6.3)	64.9	0.6 (0.2–1.8)
IV (43.0–53.5)	26.3	1.5 (0.5–4.9)	48.6	1.2 (0.4–3.4)	8.6	1.4 (0.2–8.0)	27.3	0.7 (0.2–2.1)	25.0	1.5 (0.4–5.1)	87.5	2.3 (0.6–8.8)
V (> 53.5)	38.5	1.2 (0.4–3.6)	47.4	0.6 (0.2–1.6)	10.5	1.1 (0.2–5.4)	30.5	2.0 (0.7–5.4)	43.7	2.2 (0.7–7.1)	86.1	2.1 (0.6–7.4)
P_{trend}	0.640		0.502		0.854		0.075		0.372		0.079	

Abbreviations: 25-OH-D; 25-hydroxy vitamin D; BP, blood pressure; HDL, high-density lipoprotein; OR, odds ratio; ref, reference. [a]Model adjusted for age, body mass index and smoking habits. [b]Adjusted additionally to other components of metabolic syndrome. For prevalence, P_{trend} value is for a test for linear trend. Cutoffs used to define metabolic syndrome components, abdominal obesity: waist circumference (males > 90 cm, females > 80 cm), hyperglycaemia: fasting blood glucose $\geqslant$ 6.1 mmol l^{-1}, high triglycerides: triglycerides $\geqslant$ 1.7 mmol l^{-1}, high BP: $\geqslant$ 130/85 mm Hg, low HDL: HDL cholesterol < 1.0 mmol l^{-1} and < 1.3 mmol l^{-1} in men and women.

MS components, hyperglycemia, high blood pressure and high triglycerides in men showed trends toward inverse relationship across the increasing vitamin D quintiles in men ($P_{trend} = 0.053$, 0.064 and 0.062, respectively); and high triglycerides ($P_{trend} = 0.075$) and low HDL-C ($P_{trend} = 0.079$) in women.

Discussion

Our study provides estimates of vitamin D status among Asian Indians and shows lack of association between serum 25-OH-D and MS or IR, but significant relationships could be established between 25-OH-D, β-cell function and BMI. Concordant with previous studies, we found a high prevalence of poor vitamin D status in Indians.[7,14,15] We observed an inverse relationship of serum 25-OH-D with BMI in this study that has been previously accounted by the solubility and storage of the compound in enlarged fat mass.[16] Interestingly, Asian Indians have been included in the category of 'metabolically obese normal weight' group, as they tend to have more disproportionately higher total body fat at any given BMI compared with those of the other ethnicities[7,17] that might also lead to a false characterization of individuals as vitamin D deficient, based on their serum estimates.

We found a lack of association between serum 25-OH-D concentrations and MS. Our observations are in line with those of Reis *et al.*,[18] who demonstrated lack of association between serum vitamin D levels and MS in adult Caucasian population from the southern California community of Rancho Bernardo. In the Longitudinal Aging Study conducted in old subjects in Amsterdam, Snijder *et al.*[19] failed to find any association between diabetes and 25-OH vitamin D. Similarly, Scragg *et al.*[6] observed no association between vitamin D status and type 2 diabetes in non-Hispanic blacks despite their poor vitamin D status and independent associations between 25-OH-D and risk of diabetes in other ethnicities (non-Hispanic whites and Mexican–Americans). They speculated that it could be due to an altered vitamin D endocrine system and low sensitivity to vitamin D in blacks.

The lack of association between vitamin D status and MS in this study can be attributed to the proposed nugatory metabolic effects of vitamin D in some populations and different optimum serum vitamin D concentrations in different ethnicities.[4] It can also be because of the fact that a major portion (65.6%) of our study sample was comprised of subjects from vitamin D insufficient range (12.5 to < 50 nmol l^{-1}). Owing to this reduced variability in the 25-OH-D levels, the protective effects of higher vitamin D levels could have been compromised and hence, no association could be established between the studied parameters.

There is substantial evidence that suggests an essential role of vitamin D in insulin secretion and β-cell function.[4,5] The beneficial effect of vitamin D in glucose metabolism,

particularly insulin secretion/synthesis cannot be ignored in Indians, as we have found an association of serum 25-OH-D levels with β-cell function, estimated by HOMA-B. However, owing to the lack of association of Vitamin D with fasting glucose, and insulin parameters, it can merely be a type I error. This study is limited by the small sample size, cross-sectional design and by the possibility that unmeasured confounding factors may explain our findings. Moreover, our observations are not based on dynamic techniques, such as hyperglycemic clamp. Hence, studies on a larger scale of Indian population involving direct measures of assessment of insulin sensitivity/β-cell function are warranted.

Conflict of interest

The authors declare no conflict of interest.

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Author contribution

Vijaya Majumdar researched the data and wrote the manuscript. Dindagur Nagaraja reviewed and edited the manuscript. Rita Christopher researched the data and reviewed and edited the manuscript.

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