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Original article

Prevalence of vitamin D deficiency and association of serum vitamin D level with anthropometric and metabolic factors in metabolic syndrome patients

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Background: Accumulating evidence suggests that vitamin D deficiency may contribute to an increased risk of glucose intolerance, diabetes, insulin resistance, and metabolic syndrome. Vitamin D levels vary between different populations and their association with metabolic syndrome in non-western populations remains equivocal.
Objective: We examined the prevalence of vitamin D deficiency and association of vitamin D levels with anthropometric and metabolic factors in metabolic syndrome patients.
Methods: A cross-sectional study was conducted in 300 patients with metabolic syndrome. Patients were prospectively recruited, physically examined, and assessed for vitamin D levels and other laboratory data.
Results: The prevalence of vitamin D deficiency [25(OH)D ≤20 ng/mL] was 40.7% [95% CI = 35% to 46%]. In multivariate analysis, after adjustment for all variables, we found that increased waist circumference (WC) (adjusted odds ratio [AOR] = 1.058; 95% CI = 1.016–1.103), decreased hand skin color darkness (AOR = 0.757; 95% CI = 0.597–0.959), increased total cholesterol (AOR = 1.019; 95% CI = 1.005–1.032), and increased systolic blood pressure (SBP) (AOR = 1.029; 95% CI = 1.003–1.055) were significantly associated with an increased risk of vitamin D deficiency.
Conclusion: High prevalence of vitamin D deficiency has been observed in metabolic syndrome patients. After multivariate adjustment for all variables, high WC, light skin color, high total cholesterol levels, and high SBP were significantly associated with an increased risk of vitamin D deficiency.

Keywords: Anthropometric, association, metabolic syndrome, prevalence, vitamin D deficiency

Metabolic syndrome has become a global epidemic. It refers to the clusters of several cardio-metabolic risk factors including abdominal obesity, hyperglycemia, dyslipidemia, and elevated blood pressure that are likely to be linked to insulin resistance [1]. The clinical relevance of metabolic syndrome is that it identifies people who are at increased long-term risk of cardiovascular disease and type 2 diabetes mellitus. Large epidemiological surveys show that metabolic syndrome is common and age related. Its prevalence in the United States is 34.6% by National Cholesterol Education Program (NCEP) and 39.1% by International Diabetes Federation (IDF) reports [2].

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Vitamin D is known for the maintenance of mineral homeostasis and normal skeletal architecture. The precursor provitamin D, 7-dehydrocholesterol, absorbs ultraviolet radiation in the skin and is transformed into previtamin D_3, which is rapidly converted to vitamin D_3. The latter is metabolized in the liver to 25-hydroxyvitamin D_3, and then in the kidney to its biologically active form 1,25-dihydroxyvitamin D_3 [3]. Vitamin D also comes from diet in the form of vitamin D_2 (ergocalciferol), mostly from fortified foods, but also in small quantities from plant sources and irradiated yeast, and in the form of vitamin D_3 (cholecalciferol) from animal sources.

Vitamin D deficiency, as determined by decreased serum levels of 25-hydroxyvitamin D [4, 5], not only causes metabolic bone disease, but may also increase the risk of other chronic disorders [6]. During the past few years, vitamin D deficiency has been linked to

type 2 diabetes mellitus [6, 7] and cardiovascular risk [5, 8]. Furthermore, a possible role of vitamin D deficiency in the pathogenesis of metabolic syndrome has recently been suggested [9-11]. In cross-sectional studies, an inverse association between serum 25-hydroxyvitamin D [25(OH)D] levels and anthropometric and metabolic factors have been reported in several cohorts [12-19], but the association is not consistent. Previous reports [14] indicated that there was no association of 25(OH)D level with metabolic syndrome among community-dwelling older adults. However, Lu et al. [16] found a significant association of low 25(OH)D level with an increased risk of having metabolic syndrome and its individual components (i.e. fasting plasma glucose, HbA_{1c}, triglycerides, waist circumference and diastolic blood pressure). Similarly, Gannage-Yared et al. [18] observed relationships between 25(OH)D level, and several metabolic risk factors (i.e. body mass index, systolic blood pressure, fasting plasma glucose, waist circumference, and insulin levels).

Additionally, vitamin D levels vary among different populations [19]. Soontrapa et al. [20] explored the prevalence of vitamin D deficiency in the elderly Thai women in municipality of Khon Kaen Province, Thailand. Percentages of vitamin D deficiency [25(OH)D <35 ng/mL] was 66.3. A recent study [21] determined the prevalence and correlation with severity of hypovitaminosis D [25(OH)D <30 ng/mL] in 80 heart failure patients. The prevalence of hypovitaminosis D was 82.4%. To our knowledge, no previous study has explored the prevalence of vitamin D deficiency and association of vitamin D levels with anthropometric and metabolic factors in metabolic syndrome patients. Therefore, the purpose of our study was to investigate the prevalence of vitamin D deficiency and its association with metabolic syndrome.

Materials and methods

Study population

A cross-sectional study of outpatients at the Family Medicine and Cardiology Department of Phramongkutklao Hospital, Thailand, was conducted between September 2010 and May 2011. The study protocol was approved by the Human Subjects Research Committee of Phramongkutklao Hospital. The consent forms were sent and signed by the patients. We prospectively recruited 300 patients, aged more than 20 years, who met the criteria of diagnosis with metabolic syndrome according to NCEP ATP III guidelines [22]. All patients signed informed consent forms. We excluded patients who were pregnant, patients who received drugs or dietary supplements containing any vitamin D component, and patients who required drugs that affect the level of vitamin D, such as corticosteroids. Patients with malabsorption diseases were also excluded.

Data collection

Each subject completed a detailed demographic and medical data assessment, which included items on present medical problem, current medications, and allergy. Physical examination was performed by physicians, except for body weight, height, waist circumference (WC), hip circumference, and skin color test, which were measured by the investigators. Blood pressure was measured by well-trained paramedical staffs using a standard protocol. Automatic blood pressure measurement machines (Omron IA2, Omron, Japan) were used in this study. All subjects rested at least 5 minutes in a sitting position before measurement. Blood pressure was measured at least two to three times using a cuff suitable for the subject's arm circumference and the mean value was recorded. All skin color tests were measured using a skin color scale designed by Garnier L'Oreal, Thailand [23]. The scale is a 16-point shade of skin color tones, ranging from one to 16, with one representing the lightest skin color, and 16 representing the darkest possible skin color. Blood samples of participants were drawn and centrifuged within one day in the research unit at Phramongkutklao Hospital. Fasting blood samples were collected for glucose, HbA_{1c}, lipid profiles, alanine aminotransferase (ALT), calcium, phosphorus, serum creatinine, high sensitivity C-reactive protein (hs-CRP), and plasma 25-hydroxyvitamin D level (25(OH)D). Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Metabolic syndrome was defined according to NCEP ATP III guidelines [22]. However, waist circumference criteria for Asian populations (i.e., 80 cm for female and 90 cm for male) were used for diagnosing metabolic syndrome. Serum 25(OH)D were measured using a chemiluminescent immunoassay (Diasorin, Stillwater, MN, USA) [24]. This immunoassay defined normal vitamin D level as serum 25(OH)D levels 30–100 ng/mL, which was similar to the normal range defined by mass spectroscopy. Vitamin D insufficiency and deficiency

were defined as serum 25(OH)D levels in the range from 21 to 29 ng/mL and ≤20 ng/mL, respectively [25].

Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) software, version 17.0 (Chicago, IL, USA). Data are presented as mean ± SD for normally distributed continuous variables or median (25% and 75% interquartile values) for the continuous variables that were not normally distributed. Categorical variables were presented as number and percent. Comparisons between patients' characteristics in each vitamin D group were performed using a one-way analysis of variance (ANOVA) or a Kruskal–Wallis test, as appropriate. Statistical comparisons for categorical variables were performed using Chi-square or Fisher's exact tests. Pearson's correlation coefficient was used to calculate the linear relationship between two variables. Univariate and multivariate logistic regression analysis was used to test the significant determinants of vitamin D deficiency and normal vitamin D status. Stepwise backward selection was used as the method of variable selection with a criterion for inclusion and exclusion of a variable at $p < 0.05$ and 0.25, respectively. A 2-sided probability value ≤0.05 was considered statistically significant.

Results

The characteristics of the 300 patients are shown in **Table 1**. The majority of the patients were elderly with an average age of 63.77±11.00 years. One hundred fifty nine patients were males (53%) and 141 were females (47%). The mean weight and height were 68.04±12.79 kg and 160.03±8.92 cm. The median BMI was 26 kg/m^2. The mean waist circumference was 91.95±9.83 cm considered to be at a higher level than standard values according to NCEP ATP III guidelines [22]. Among subjects who had underlying diseases, 252 patients (84.0%) were diagnosed as having hypertension. The mean serum 25(OH)D level in our population was 22.46±7.93 ng/mL. The overall prevalence of hypovitaminosis D [25(OH)D <30 ng/mL] was 84% [95% confidence interval (CI) = 80% to 88%]. Among these, vitamin D insufficiency [25(OH)D = 21–29 ng/mL] was 43.3% [95% confidence interval (CI) = 38% to 49%]. The prevalence of vitamin D deficiency [25(OH)D ≤20 ng/mL] was 40.7% [95% confidence interval (CI) = 35% to 46%] as shown in **Figure 1**. Waist circumference was not correlated with vitamin D levels ($r = –0.083$, $p = 0.156$), whereas hip circumference was weakly inversely related with vitamin D level. In addition, we found a significant positive correlation between vitamin D levels and hand skin color ($r = 0.193$, $p = 0.001$). Serum 25(OH)D level was negatively correlated with total cholesterol ($r = –0.123$; $p = 0.033$) and triglycerides ($r = –0.163$; $p = 0.005$).

Univariate logistic regression analysis showed that patients who had vitamin D deficiency were significantly associated with a higher BMI (OR = 1.129; 95% CI = 1.034–1.234), increased WC (OR = 1.041; 95% CI = 1.004–1.080), increased hip circumference (OR = 1.061; 95% CI = 1.017–1.107), increased SBP (OR = 1.029; 95% CI = 1.005–1.054), increased total cholesterol (OR = 1.020; 95% CI = 1.008–1.032), increased triglyceride (OR = 1.011; 95% CI = 1.003–1.019), increased low-density lipoprotein cholesterol (LDL-C) (OR = 1.018; 95% CI = 1.003–1.032), and being female (OR = 0.476; 95% CI = 0.240-0.945) compared with those who had normal vitamin D levels. However, the vitamin D deficiency group were significantly associated with a lower point shade of skin color tone (i.e., decreased skin darkness) compared with patients who had normal vitamin D levels (OR = 0.775; 95% CI = 0.618–0.971). When patients with vitamin D insufficiency were compared with those who have normal vitamin D levels using univariate logistic regression analysis, patients who had vitamin D insufficiency were significantly associated with higher BMI (OR = 1.134; 95% CI = 1.038–1.238), increased WC (OR = 1.043; 95% CI = 1.006–1.081), increased hip circumference (OR = 1.051; 95% CI = 1.008–1.096), increased SBP (OR = 1.026; 95% CI = 1.002–1.051), increased total cholesterol (OR = 1.015; 95% CI = 1.003–1.027), increased triglyceride (OR = 1.008; 95% CI = 1.000–1.016), and increased LDL-C (OR = 1.016; 95% CI = 1.002–1.031) compared with those who had normal vitamin D levels.

In multivariate logistic regression analysis, after adjustment for all variables (**Table 1**), antihypertensive agents, and lipid lowering agents, variables that were significantly associated with an increased risk of vitamin D deficiency included high WC, light skin color, high total-cholesterol, and high SBP ($p \leq 0.05$) (**Table 2**). While variables that were significantly associated with an increased risk of vitamin D insufficiency included only high WC and high total-cholesterol ($p = 0.009$ and 0.034, respectively).

Table 1. Baseline demographic data of the metabolic syndrome patients (n = 300)

Characteristics	Total (n = 300)	25(OH)D ≤20 ng/mL (n = 122)	25(OH)D 21–29 ng/mL (n = 130)	25(OH)D 30–100 ng/mL (n = 48)	*p*†
Age (yrs)	63.77±11.00	64.23±12.07	62.92±10.75	65.35±8.53	0.376
30 to 59	114 (38.0%)	45 (36.9%)	53 (40.8%)	16 (33.3%)	
≥60	186 (62.0%)	77 (63.1%)	77 (59.2%)	32 (66.7%)	
Sex					0.036*
Male	159 (53%)	54 (44.3%)	75 (57.7%)	30 (62.5%)	
Female	141 (47%)	68 (55.7%)	55 (42.3%)	18 (37.5%)	
Weight (kg)	68.04±12.79	68.21±12.19	69.03±13.15	64.85±13.28	0.155
Height (cm)	160.03±8.92	159.17±8.07	160.38±9.60	161.01±9.04	0.387
BMI (kg/m^2)	26 (24, 29)	27 (24,30)	26 (24, 29)	25 (23, 27)	0.165
Waist circumference (cm)	91.95±9.83	92.46±9.48	92.61±10.34	88.83±9.03	0.057
Hip circumference (cm)	98.78±8.73	99.76±8.24	99.05±9.27	95.63±8.11	0.019*
Hand skin color (point shade)	15 (13, 16)	14 (13, 15)[a]	15 (13, 16)	15 (14, 16)[a]	0.002*
SBP (mmHg)	134 (126, 145)	135 (128,148)	135 (126,144)	129 (120,141)	0.079
DBP (mmHg)	78 (70, 86)	78 (70, 86)	77 (70, 88)	78 (73, 82)	0.785
ALT (U/L)	21 (15, 29)	22 (16, 29)	21 (15, 30)	19 (15, 27)	0.448
Serum calcium (mg/dL)	9.5 (9.2, 9.8)	9.5 (9.2, 9.8)	9.6 (9.2, 9.7)	9.6 (9.3, 9.9)	0.385
Serum creatinine (mg/dL)	1.0 (0.8, 1.2)	0.9 (0.7, 1.2)	0.9 (0.8, 1.1)	1.0 (0.9, 1.3)	0.799
Total Cholesterol (mg/dL)	170±33	175±32[b]	170±32	156±36[b]	0.004*
Triglyceride (mg/dL)	114 (83, 147)	119 (92, 156)	114 (79, 149)	96 (78, 126)	0.109
HDL Cholesterol (mg/dL)	52 (45, 60)	53 (46, 61)	53 (45, 59)	50 (45, 58)	0.466
LDL Cholesterol (mg/dL)	97 (81, 113)	101 (85, 116)[c]	98 (84, 115)[d]	91 (72, 107)[c,d]	0.035*
FPG (mg/dL)	106 (96, 124)	106 (94, 131)	105 (98, 121)	109 (96, 129)	0.660
HbA_{1c} (%)	6.2 (5.9, 6.8)	6.3 (5.9, 6.9)	6.2 (5.8, 6.7)	6.3 (6.0, 7.0)	0.700
hs-CRP (mg/L)	1.4 (0.7, 3.1)	1.7 (0.9, 3.3)	1.3 (0.6, 2.7)	1.2 (0.7, 2.5)	0.122
Phosphorus (mg/dL)	3.40±0.51	3.40±0.50	3.42±0.54	3.35±0.43	0.675

BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, ALT = alanine aminotransferase, FPG = fasting plasma glucose, HbA_{1c} = hemoglobin A_{1c}, hs-CRP = high sensitivity C-reactive protein, *Significance at $p \leq 0.05$, Data are mean±SD for normally distributed continuous variables or median (25% and 75% interquartile values) for nonnormally distributed continuous variables, or n (%) for categorical variables. †Comparisons between patients' characteristics in each vitamin D group were performed using a one-way analysis of variance (ANOVA) or Kruskal–Wallis test, as appropriate. Statistical comparisons for categorical variables were performed using chi-square tests. [a]Pair-wise comparison after a Kruskal–Wallis test showed significance between 25(OH)D ≤20 ng/mL and 25(OH)D 30–100 ng/mL ($p = 0.003$). [b]Pair-wise comparison after an ANOVA showed significance between 25(OH)D ≤20 ng/mL and 25(OH)D 30–100 ng/mL ($p = 0.003$). [c]Pair-wise comparison after a Kruskal–Wallis test showed significance between 25(OH)D ≤20 ng/mL and 25(OH)D 30–100 ng/mL ($p = 0.009$). [d]Pair comparison after a Kruskal–Wallis test showed significance between 25(OH)D 21–29 ng/mL and 25(OH)D 30–100 ng/mL ($p = 0.011$)

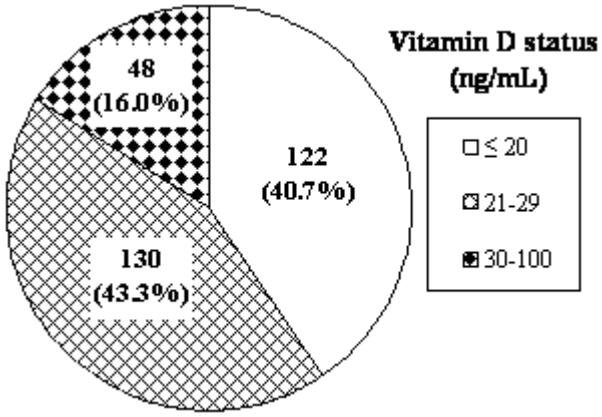

Figure 1. Prevalence of the distribution of vitamin D (n = 300)

Table 2. Multivariate logistic regression analysis showing odds of vitamin D deficiency (≤20 ng/mL) and insufficiency (21 to 29 ng/mL) compared with normal vitamin D status (30 to 100 ng/mL)

Variables	Unadjusted OR		Adjusted OR		95% CI of Adjusted OR		*p*	
	Deficiency	Insufficiency	Deficiency	Insufficiency	Deficiency	Insufficiency	Deficiency	Insufficiency
Waist circumference□ (cm)	1.041	1.043	1.058	1.056	1.016–1.103	1.014–1.099	0.007*	0.009*
Hand skin color□ (point shade)	0.775	0.899	0.757	0.882	0.597–0.959	0.695–1.119	0.021*	0.301
Total cholesterol□ (mg/dL)	1.020	1.015	1.019	1.014	1.005–1.032	1.001–1.027	0.006*	0.034*
Systolic blood pressure□ (mmHg)	1.029	1.026	1.029	1.024	1.003–1.055	0.999–1.050	0.029*	0.062

□Adjusted for all variables in table 1, antihypertensive agents, and lipid lowering agents, *Significance at $p \leq 0.05$

Discussion

In this study, the prevalence of vitamin D deficiency among metabolic syndrome patients is 40.7%. The main new finding of the present study is the positive relationship between 25(OH)D level and skin color. Our data suggests that vitamin D deficiency is commonly found in the elderly with metabolic syndrome (i.e., 40.7% patients with 25(OH)D levels ≤20 ng/mL). Similarly, Botella-Carretero et al. [26] found that vitamin D deficiency was present in 50.7% [37 of 73 morbidly obese patients (BMI ≥40 kg/m^2)]. While Pinelli et al. [27] found that vitamin D deficiency was present in 75% of Arab Americans with insulin resistance (46%), metabolic syndrome (33%), and glucose intolerance (42%). However, latitude relative to the equator is one of the most important factors affecting vitamin D status and examined plasma vitamin D concentration among adults with metabolic syndrome in Northern California (sunny climate) [28]. 25(OH)D levels were significantly decreased in metabolic syndrome compared to controls. Eight percent of controls and 30% of patients with metabolic syndrome in North American adult subjects were deficient in 25(OH)D (≤20 ng/mL; $p = 0.0236$).

The high prevalence of vitamin D deficiency in metabolic syndrome patients has been hypothesized to result from the sequestering effect of high quantity of subcutaneous fat on circulating vitamin D [29]. Furthermore, metabolic syndrome patients, because of their lower physical activity, might have less exposure to solar ultraviolet radiation, which is responsible for more than 90% of the vitamin D requirement for most people [30]. Bell et al. [31] proposed that the vitamin D endocrine system is altered in obese subjects, with increased production of $1,25(OH)_2D$ exerting negative feedback control on the hepatic synthesis of 25(OH)D. In addition, animal studies have shown that $1,25(OH)_2D$ increases lipogenesis and decreases lipolysis [32], and, therefore, may contribute to obesity; however, $1,25(OH)_2D$ level is not consistently higher in obese subjects [33, 34].

We have shown that 25(OH)D level is associated with hand skin color. Human skin color is primarily the result of the presence of melanin in the skin. Varying amounts of melanin (skin pigment) is determined by genes and the body's response to sun exposure [35]. Although the variation in natural skin color is mainly the result of genetics, this study conducted in a Thai population, in which approximately 10% of variance in skin color occurs within the same group of East Asian populations [36]. Therefore, we believe that our population has a homogeneous baseline skin color and increase in skin color should come mainly from sun exposure. The major cause of vitamin D deficiency is inadequate exposure to natural sunlight. It is plausible that sunlight exposure takes into account that vitamin D intake is different in individual patients. Therefore, more sunlight exposure might be responsible for dark skin color and high serum 25-hydroxyvitamin D levels. Decreased sun exposure and the use of sunscreens reduce the risk of skin cancer, but also sharply limit the production of vitamin D in the skin.

Additionally, we found that, independent of hip circumference, total cholesterol and triglyceride are inversely correlated with vitamin D levels. The relationship between 25(OH)D levels and lipid profile has also been the subject of several reports. Many [37-39], but not all, studies have shown inverse relationships between 25(OH)D level and triglyceride. Martins et al. [38] showed that in US adults, triglyceride was lower in those in the top quartile of 25(OH)D (≥92.5 nmol/L) than in those in the bottom quartile (<52.5 nmol/L). However, there was no association between 25(OH)D levels and total

cholesterol. In a smaller sample of 126 glucose-tolerant healthy adults [40] an inverse association between 25(OH)D levels and total cholesterol, and LDL-C (adjusting for sex, age, ethnicity, season, SBP and DBP, BMI, and waist-to-hip ratio) was observed. However, no association between 25(OH)D levels and high-density lipoprotein cholesterol (HDL-C) or triglyceride was apparent in this study. Results of all of these studies are consistent with what we have found in our study population. It is plausible that ultraviolet-irradiation has a beneficial effect on lipids through the photo conversion of 7-dehydrocholesterol to lumisterol [41]. It is also possible that an influx of cholesterol from plasma lipoproteins could increase 7-dehydrocholesterol levels, which in turn increase vitamin D synthesis.

From multivariate logistic regression analysis, after adjusted for all variables, antihypertensive agents, and lipid lowering agents, increased WC and high total cholesterol levels were both associated with an increased risk of vitamin D deficiency and vitamin D insufficiency. We found that a higher point shade of skin color tone (i.e., increased skin darkness) and lower SBP could reduce the risk of vitamin D deficiency. Consistently, data from the study on 243 ambulant adults (BMI 28–50 kg/m^2) enrolled in a weight-loss study, 25(OH)D level was inversely associated with weight ($p = 0.0009$), BMI ($p = 0.005$) and WC ($p = 0.03$) [42]. This study also estimated a decrease of 0.74 nmol/L in 25(OH)D per 1 kg/m^2 increase in BMI. Another study [43] found that the relationship between 25(OH)D levels and HDL-C remained significant ($p < 0.001$) after adjustment for established determinants of the HDL-C. Serum triglycerides ($p = 0.008$), WC ($p < 0.001$), and body mass index ($p < 0.001$) showed significantly graded, inverse relationships with 25(OH)D levels.

Several epidemiological studies have shown that there may be an association between hypertension and_vitamin D status. A recent article [44] reported the relationship between serum 25(OH)D level and blood pressure._When patients were divided into 25(OH)D quintiles, mean SBP was 3.0 mmHg lower ($p = 0.0004$) and DBP was 1.6 mmHg lower ($p = 0.011$) for patients in the highest quintile (25(OH)D level ≥85.7 nmol/L) compared with those in the lowest (25(OH)D level ≤40.4 nmol/L), adjusting for age, sex, ethnicity, and physical activity. The inverse association between 25(OH)D level and SBP was stronger in patients aged ≥50 years than in younger patients ($p = 0.021$). Judd et al. [45] also showed a statistically significant inverse association between circulating 25(OH)D concentrations and SBP. However, this association was not statistically significant when age was included in the multiple regression model, nor was it significant in the black subpopulation. The regulation of the renin angiotensin system (RAS) has been proposed as a potential mechanism for the relationship between vitamin D deficiency and hypertension [46]. The RAS is a regulatory cascade that plays a critical role in the regulation of blood pressure, electrolyte, and plasma volume homeostasis [46]. Inappropriate stimulation of the RAS has been associated with hypertension. Li et al. [47] demonstrated that vitamin D is a potent endocrine suppressor of renin biosynthesis to regulate the RAS. Mice lacking a vitamin D receptor (VDR) have elevated production of renin and angiotensin II, leading to hypertension, cardiac hypertrophy, and increased water intake. Another relationship to be explained is that between parathyroid hormone (PTH) and hypertension in patients with primary and secondary hyperparathyroidism (HPT). High prevalence of vitamin D deficiency was found in patients with primary HPT [48]. Primary HPT with an inappropriately elevated PTH level has been shown to be associated with hypertension, but the mechanism for developing hypertension has remained controversial. Low vitamin D status is also associated with secondary elevation of PTH and an increased arterial resistance leading to hypertension [49]. Jorde et al. [50] found that serum PTH was a significant predictor of rising in SBP over a period of seven years in men ($p < 0.01$), but not in women.

There is a growing body of evidence that links vitamin D deficiency to factors associated with metabolic syndrome. The number of individuals with risk factors for metabolic syndrome continues to increase [51]. It is important to increase vitamin D intake. Considering that vitamin D deficiency is very common in all age groups and that few foods contain vitamin D, the endocrine society [25] provides guidelines to clinicians for the evaluation, treatment, and prevention of vitamin D deficiency. The guideline suggests that adults aged 19 to 50 years require at least 600 IU per day of vitamin D to maximize bone health and muscle function. However, to raise the blood level of 25(OH)D consistently above 30 ng/mL may require at least 1500 to 2000 IU per day of vitamin D [25]. Treatment with either vitamin D_2 or vitamin D_3 has been recommended for deficient patients.

There is currently not sufficient evidence to recommend vitamin D to attain a noncalcemic benefit for cardiovascular protection.

There are potential limitations in our study. First, factors influencing skin synthesis of vitamin D such as ultraviolet exposure, sunscreen utilization, and dietary consumption of vitamin D were not assessed. Second, the cross-sectional design of our study limited our ability to examine the causal relationships between 25(OH)D levels and metabolic syndrome.

Conclusion

This study shows the prevalence of vitamin D deficiency and the association of serum vitamin D level with anthropometric and metabolic factors in patients with metabolic syndrome. We have found a relationship between 25(OH)D levels and skin color. In addition, we described the inverse relationships between hip circumferences, total-cholesterol, triglyceride and 25(OH)D levels, suggesting a robust inverse association between serum 25(OH)D level with anthropometric and metabolic indicators of adiposity. Increased WC, light skin color, increased total cholesterol levels, and increased SBP were significantly associated with an increased risk of vitamin D deficiency. This finding should be further investigated in other populations, either by cross-sectional or interventional studies.

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References

1. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet. 2005; 365:1415-28.
2. Ford ES. Prevalence of the metabolic syndrome defined by the International Diabetes Federation among adults in the US. Diabetes Care. 2005; 28: 2745-9.
3. Holick MF. Vitamin D: A millennium perspective. J Cell Biochem. 2003; 88:296-307.
4. Holick MF. McCollum Award Lecture: Vitamin D-new horizons for the 21st century. Am J Clin Nutr. 1994; 60: 619-30.
5. Holick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. Am J Clin Nutr. 2004; 80: 1678s-88s.
6. Mathieu C, Gysemans C, Giulietti A, Bouillon R. Vitamin D and diabetes. Diabetologia. 2005; 48: 1247-57.
7. Pittas AG, Dawson-Hughes B, Li T, Van Dam RM, Willett WC, Manson JE, et al. Vitamin D and calcium intake in relation to type 2 diabetes in women. Diabetes care. 2006; 29:650-6.
8. Grandi NC, Breitling LP, Brenner H. Vitamin D and cardiovascular disease: systematic review and meta-analysis of prospective studies. Prev Med. 2010; 51: 228-33.
9. Muldowney S, Kiely M. Vitamin D and cardiometabolic health: a review of the evidence. Nutr Res Rev. 2011; 24:1-20.
10. 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.
11. Liu S, Song Y, Ford ES, Manson JE, Buring JE, Ridder PM. Dietary calcium, vitamin D, and the prevalence of metabolic syndrome in middle-aged and older US women. Diabetes Care. 2005; 28:2926-32.
12. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. J Clin Endocrinol Metab. 2007; 92: 2017-29.
13. Kayaniyil S, Vieth R, Harris SB, Retnakaran R, Knight JA, Geratein HC, et al. Association of 25(OH)D and PTH with metabolic syndrome and its traditional and nontraditional components. J Clin Endocrinol Metab. 2011; 96:1-8.
14. 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.
15. Reis JP, von Muhlen D, Miller ER. Relation of 25-hydroxyvitamin D and parathyroid hormone levels with metabolic syndrome among US adults. Eur J Endocrinol. 2008; 159:41-8.
16. 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.
17. Lee DM, Rutter MK, O'Neil TW, Boonen S, Vanderschueren D, Bouillon R, et al. Vitamin D, parathyroid hormone and the metabolic syndrome in

middle-aged and older European men. Eur J Endocrinol. 2009; 161:947-54.
18. 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. Eur J Endocrinol. 2009; 160: 965-71.
19. Kim MK, Kang MI, Oh KW, Kwon HS, Lee JH, Lee WC, et al. The association of serum vitamin D level with presence of metabolic syndrome and hypertension in middle-aged Korean subjects. Clin Endocrinol. 2010; 73: 330-8.
20. Soontrapa S, Soontrapa S, Chailurkit L. The prevalence and the calcidiol levels of vitamin D deficiency in the elderly Thai women in municipality of Khon Kaen province, Thailand. Srinagarind Med J. 2002; 17:231-8.
21. Athisakul S, Songmuang SB, Buddhari W. Prevalence of hypovitaminosis D in heart failure patients at King Chulalongkorn Memorial hospital. Thai Heart Journal. 2010; 23:154-63.
22. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 2005; 112: 2735-52.
23. Garnier L'Oreal Thailand Company Limited. The skin color scale. [online] [cited 2011 Dec 12]; Available from: URL: http://www.garnierthailand.com//index.html.
24. DiaSorin Inc. 1951 Northwestern Ave - Stillwater, MN 55082 - USA. Manual of LIAISON 25 OH Vitamin D total assay (310600).
25. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2011; 96:1911-30.
26. Botella-Carretero JI, Alvarez-Blasco F, Villafruela JJ, Balsa JA, Vazquez C, Escobar-Morreale HF. Vitamin D deficiency is associated with the metabolic syndrome in morbid obesity. Clin Nutr. 2007; 26:573-80.
27. Pinelli NR, Jaber LA, Brown MB, Herman WH. Serum 25-Hydroxyvitamin D and insulin resistance, metabolic syndrome, and glucose intolerance among Arab Americans. Diabetes Care. 2010; 33:1373-5.
28. Devaraj S, Jialal G, Cook T, Siegel D, Jialal I. Low vitamin D levels in northern American adults with the metabolic syndrome. Horm Metab Res. 2011; 43: 72-4.
29. Wortsman J, Matsuoka LY, Chen TC, Luz, Holick MF. Decreased bioavailability of vitamin D in obesity. Am J Clin Nutr. 2000; 72:690-3.
30. Arunabh S, Pollack S, Yeh J, Aloia JF. Body fat content and 25-hydroxyvitamin D levels in healthy women. J Clin Endocrinol Metab. 2003; 88:157-61.
31. Bell NH, Epstein S, Greene A, Shary J, Oexmann MJ, Shaw S. Evidence for alteration of the vitamin D-endocrine system in obese subjects. J Clin Invest. 1985; 76:370-3.
32. Shi H, Norman AW, Okamura WH, Sen A, Zemel MB. 1,25-dihydroxyvitamin D_3 modulates human adipocyte metabolism via nongenomic action. FASEB J. 2001; 15:2751-3.
33. Parikh SJ, Edelman M, Uwaifo GI, Freedman RJ, Semega-Janneh M, Reynolds J, et al. The relationship between obesity and serum 1,25-dihydroxyvitamin D concentrations in healthy adults. J Clin Endocrinol. 2004; 89:1196-9.
34. Konradsen S, Ag H, Lindberg F, Hexeberg S, Jorde R.. Serum 1,25-dihydroxyvitamin D is inversely associated with body mass index.. Eur J Nutr. 2008; 47:87-91.
35. Human skin color [Internet] 2011. Available from: URL:http//en.wikipedia.org/w/index.php?oldid=449873303, 2011.
36. Jablonski Nina G, Jablonski G, Chaplin. The evolution of human skin coloration. J Hum Evol. 2000; 39: 57-106.
37. Liu E, Meigs JB, Pittas AG, Mc Keown NM, Economos CD, Booth SL, et al. Plasma 25-hydroxyvitamin D is associated with markers of the insulin resistant phenotype in nondiabetic adults. J Nutr. 2009; 139: 329-34.
38. Martins D, Wolf M, Pan D, Zadshir A, Tareen N, Thadhani R, et al. Prevalence of cardiovascular risk factors and the serum levels of 25-hydroxyvitamin D in the United States: data from the Third National Health and Nutrition Examination Survey. Arch Intern Med. 2007; 167:1159-65.
39. Cigolini M, Iagulli MP, Miconi V, Galiotto M, Lombardi S, Targher G. Serum 25-hydroxyvitamin D_3 concentrations and prevalence of cardiovascular disease among type 2 diabetic patients. Diabetes Care. 2006; 29:722-4.
40. Chiu KC, Chu A, Go VL, Saad MF. Hypovitaminosis D is associated with insulin resistance and beta cell dysfunction. Am J Clin Nutr. 2004; 79:820-5.
41. Slominski A, Zjawiony J, Wortsman J, Semak I, Stewart J, Pisarchik A, et al. A novel pathway for sequential transformation of 7-dehydrocholesterol

and expression of the P450 system in mammalian skin. Eur J Biochem. 2004; 271:4178-88.
42. McGill AT, Stewart JM, Lithander FE, Strik CM, Poppitt SD. Relationships of low serum vitamin D_3 with anthropometry and markers of the metabolic syndrome and diabetes in overweight and obesity. Nutr J. 2008; 7: 1-5.
43. Maki KC, Rubin MR, Wong LG, McManus JF, Jensen CD, Marshall JW, et al. Serum 25-hydroxyvitamin D is independently associated with high-density lipoprotein cholesterol and the metabolic syndrome in men and women. J Clin Lipidol. 2009; 3:289-96.
44. Scagg R, Sowers MF, Bell C. Serum 25-hydroxyvitamin D, ethnicity, and blood pressure in the third national health and nutrition examination survey. Am J Hypertens. 2007; 20:713-9.
45. Judd SE, Nanes MS, Ziegler TR, Wilson PF, Tangpricha V. Optimal vitamin D status attenuates the age-associated increase in systolic blood pressure in white Americans: results from the Third National Health and Nutrition Examination Survey. Am J Clin Nutr. 2008; 87:136-41.
46. Ullah MI, Uwaifo GI, Nicholas WC, Koch CA. Does vitamin D deficiency cause hypertension? current evidence from clinical studies and potential mechanisms. Int J Endocrinol. 2010: doi: 10.1155/2010.579640.
47. Li YC, Kong J, Wei M, Chen ZF, Liu SQ, Cao LP. 1,25-Dihydroxyvitamin D_3 is a negative endocrine regulator of the renin-angiotensin system. J Clin Invest. 2002; 110:229-38.
48. Silverberg S. Vitamin D deficiency and primary hyperparathyroidism. J Bone Miner Res. 2007; 22 (supplement 2):100-4.
49. Sambrook PN, Chen CS, March L. High bone turnover is an independent predictor of mortality in the frail elderly. J Bone Miner Res. 2006; 21:549-55.
50. Jorde R, Svartberg J, Sundsfjord J. Serum parathyroid hormone as a predictor of increase in systolic blood pressure in men. J Hypertens. 2005; 23:1639-44.
51. Benjamin SM, Valdez R, Geiss LS, Rolka DB, Narayan KM. Estimated number of adults with prediabetes in the US in 2000: opportunities for prevention. Diabetes Care. 2003; 26:645-9.