Metabolically Obese Individuals of Normal Weight Have a High Risk of 25-Hydroxyvitamin D Deficiency

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ABSTRACT

Background: Vitamin D status is related to obesity-related metabolic disorders. We investigated the risk of 25-hydroxyvitamin D [25(OH)D] deficiency among different metabolic phenotypes.

Methods: This prospective cross-sectional study evaluated 1,292 individuals who were ≥40 years old. Participants were classified as metabolically healthy and normal weight (MHNW), metabolically obese but normal weight (MONW), metabolically healthy but obese (MHO) or metabolically unhealthy and obese (MUO). The demographic and clinical characteristics, as well as plasma 25(OH)D levels, were compared between the 4 groups.

Results: The prevalences of MHNW, MONW, MHO and MUO were 32.1%, 19.3%, 17.9% and 30.7%, respectively. Approximately 58.5% participants had vitamin D deficiency, and vitamin D deficiency was more common in the MONW (68.7%) and MUO (73.6%) groups (MHNW, 42.7 and MHO, 50.2%). The MONW and MUO groups had lower 25(OH)D levels (versus the MHNW and the MHO groups). Among vitamin D-deficient participants, the MONW group exhibited increased risks of abdominal obesity (odds ratio [OR]: 3.28, $P = 0.005$), hypertension (OR: 3.08, $P = 0.003$) and elevated C-reactive protein (OR: 1.97, $P = 0.03$). In addition, the MUO group exhibited increased risks of hypertriglyceridemia (OR: 2.57, $P = 0.001$), insulin resistance (OR: 2.37, $P = 0.001$) and elevated C-reactive protein level (OR: 2.09, $P = 0.003$).

Conclusions: Individuals who were MONW and MUO had increased risks of vitamin D deficiency (versus MHNW and MHO), and individuals with vitamin D deficiency had worse metabolic status. Vitamin D supplementation may improve the metabolic status of individuals who are MONW or MUO.

Key Indexing Terms: Vitamin D deficiency; Obesity; Metabolically obese but normal weight; Metabolically healthy but obese; Metabolically unhealthy and obese. **[Am J Med Sci 2016;352(4):360–367.]**

INTRODUCTION

Obesity has been recognized as one of the most important public health challenges for both developed and developing countries during recent decades. According to the World Obesity Federation, approximately 2 billion adults are overweight and at least 670 million adults are obese.[1] The latest Chinese national data indicate that the prevalence of obesity among adults has increased by 4.8% (from 7.1% to 11.9%), and the prevalence of overweight status among adults has increased by 7.3% (from 22.8% to 30.1%) between 2002 and 2012.[2]

Obesity is associated with serious health conditions that include cardiovascular diseases, type 2 diabetes, metabolic syndrome and several cancers.[3] However, obesity is not a homogeneous condition, as some individuals who are normal weight present with metabolic disabilities and insulin resistance. These individuals are classified as metabolically obese but normal weight (MONW),[4] and the prevalence of MONW was very recently reported to be 20% among the general population.[5] In contrast, a subgroup of obese individuals is protected from, or resistant to, the development of metabolic abnormalities that are associated with obesity. These individuals are classified as metabolically healthy but obese (MHO),[6] and it has been reported that 9-41% of obese individuals are MHO.[7,8] Obese individuals with metabolic syndrome are classified as metabolically unhealthy and obese (MUO) or metabolically abnormal obese.[6]

Vitamin D plays roles in maintaining calcium homeostasis and bone metabolism, and also has important effects in obesity and related metabolic disorders. Vitamin D deficiency is a common worldwide problem, although it is much more serious in urban dwellers of developing countries (e.g., China).[9] The prevalence of vitamin D deficiency varies according to geographical location, season, ethnicity and the standard laboratory values for normality or deficiency. The link between vitamin D and obesity-related metabolic disorders has gained considerable scientific attention during the last decade, and numerous studies have highlighted inverse relationships between serum D 25(OH)D status and metabolic syndrome, insulin resistance and diabetes.[10,11] However, recent data regarding 25(OH)D status among the subgroups of obese individuals are limited and controversial. An Iranian study reported that serum concentrations of 25(OH)D were lower in individuals who

were MUO, compared to individuals who were MHO.[12] In contrast, a Korean study reported no significant difference in 25(OH)D status among individuals who were MUO or MHO.[13] This discrepancy may be related to ethnicity, lifestyle or genetic factors. Furthermore, there are no studies regarding 25(OH)D status among individuals who are metabolically healthy and normal weight (MHNW), MONW, MHO or MUO. Thus, the present study evaluated 25(OH)D status and the related factors among these 4 groups.

METHODS

Study Population

This prospective cross-sectional study evaluated individuals who were ≥40 years old when they visited the First Affiliated Hospital (School of Medicine, Shihezi University) during June-August 2013 and June-August 2014 for their routine medical examinations. A total of 1,292 individuals (634 men and 658 women) with a mean age of 57.7 years (range: 40-88 years) were enrolled. All subjects provided their written informed consent, and this study's design was approved by the institutional review board of the First Affiliated Hospital. We did not consider sex as an enrollment criterion, although we excluded individuals with cancer, a history of cancer in the past 5 years, pregnancy, lactation, immunodeficiency, chronic organ disease, infectious disease and patients who were receiving immunosuppressive or hormone-containing drugs.

All participants completed a questionnaire regarding their previous diseases, medications, drinking, smoking and exercise habits. Current drinkers were defined using a frequency of ≥2 drinks/week, smoking habits were categorized as noncurrent or current and a regular exercise habit was categorized as an exercise frequency of ≥3 times/week.

Anthropometric and Biochemical Measurements

All participants underwent anthropometric and body composition measurements that were performed before breakfast. Height and weight were obtained while the participants wore light clothing without shoes. Body mass index (BMI) was calculated as kg/m^2. Waist circumference was measured at the midpoint between the costal margin and the iliac crest at the end of a normal expiration. Blood samples were withdrawn from the cubital vein, collected in evacuated sample tubes and subsequently analyzed at the First Affiliated Hospital's central laboratory.

Levels of fasting total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were analyzed using an autoanalyzer (Hitachi, Tokyo, Japan). High-sensitivity C-reactive protein (hs-CRP) and fasting plasma glucose (FPG) levels were measured via the immunoturbidimetric method and via an enzymatic colorimetric method, respectively, using an autoanalyzer (Hitachi). Fasting insulin (FINS) and plasma 25(OH)D levels were measured via electrochemiluminescence (E170, Roche, Basel, Switzerland). The intraassay and interassay coefficients of variance (CVs) for the plasma 25(OH)D assay were <5% and <10%, respectively. The homeostatic model assessment of insulin resistance (HOMA-IR) was used to evaluate insulin resistance, which was calculated as: HOMA-IR = [FINS (μU/mL) × FPG (mmol/L)]/22.5. We considered insulin resistance to be present at HOMA-IR values of ≥2.69, according to the Chinese criteria.[14] Abdominal obesity was defined as a waist-to-height ratio of >0.5,[15] and hs-CRP levels were considered elevated at values of ≥0.7mg/L.[16]

Defining the Study Groups

The participants' BMI values were used to classify them as overweight or obese (≥25kg/m^2) or nonobese (<25kg/m^2), according to the World Health Organization Western Pacific Region definitions.[17] Each weight group was further subdivided as metabolically healthy or metabolically unhealthy, according to the criteria for the Adult Treatment Panel III (ATP-III) components,[18] although the waist circumference criterion was not used because of its collinearity with BMI. Individuals who fulfilled <2 of the following criteria were considered metabolically healthy[8]: (1) triglyceride levels of ≥1.7 mmol/L or the use of lipid-lowering drugs; (2) glucose levels of ≥5.6 mmol/L or the use of diabetes medication; (3) systolic blood pressure of ≥130mm Hg, diastolic blood pressure of ≥85 mm Hg or the use of antihypertensive drugs and (4) HDL-cholesterol levels of <1.29mmol/L for women or <1.03mmol/L for men. Using these criteria, individuals were classified as MHNW, MONW, MHO or MUO. A cutoff plasma 25(OH)D value of 50 nmol/L was used to categorize participants as either vitamin D-deficient or nondeficient.[19]

Statistical Analysis

All analyses were performed using SPSS software (version 17.0; SPSS Inc., Chicago, IL), and a $P < 0.05$ was considered statistically significant. Continuous variables were reported as median (interquartile range) because of their skewed distribution. The Kruskal-Wallis test was used to compare the variables among the 4 patient subgroups, and the Mann-Whitney *U* test was used to compare variables between independent groups. Categorical variables were reported as number (%), and the chi-square test was used to evaluate the distributions of the categorical variables. Logistic regression analysis was used to calculate the odds ratios (ORs) and 95% CIs for vitamin D deficiency in each group, using the MHNW group as the reference category. We also used logistic regression analysis to calculate the ORs and 95% CIs for metabolic disorder components among individuals with vitamin D deficiency in each subgroup.

RESULTS

Among the 1,292 participants, 415 individuals (32.1%) were MHNW, 249 individuals (19.3%) were MONW, 231 individuals (17.9%) were MHO and 397 individuals (30.7%) were MUO. The prevalence of MONW was 37.5% among the normal weight participants, and the prevalence of MHO was 36.8% among the obese participants. The participants' demographic and metabolic characteristics are listed in Table 1. The MONW, MHO or MUO groups had higher blood pressure, TC, TG, LDL-C, FPG, FINS, HOMA-IR and hs-CRP values, respectively, compared with the MHNW group ($P < 0.05$). The MHNW or MONW groups had similar BMIs ($P > 0.05$), although the MONW group had a greater waist circumference ($P < 0.05$). Compared with the MHO group, the MONW group had higher blood pressure, TG, LDL-C, FPG, HOMA-IR and hs-CRP values, although the MONW group's values were lower than those in the MUO group ($P < 0.05$). Compared with the MUO group, the MHO group had lower waist circumference, blood pressure, TC, TG, LDL-C, FPG, FINS, HOMA-IR and hs-CRP values, as well as higher HDL-C levels ($P < 0.05$).

Among all participants, the median plasma 25(OH)D concentration was 45.3 nmol/L (interquartile range: 28.9-58.4 nmol/L) and the prevalence of 25(OH)D deficiency was 58.5%. The MUO group had the lowest plasma 25(OH)D levels among the 4 groups ($P < 0.05$). The 25(OH)D level in the MONW group was higher than that in the MUO group, although it was lower than those in the MHNW and MHO groups ($P < 0.05$). There was no remarked difference in the plasma 25(OH)D levels of the MHNW and MHO groups ($P > 0.05$). When we categorized the participants as 25(OH)D deficient or nondeficient, we found that the prevalences of 25(OH)D deficiency were 42.7% in the MHNW group, 68.7% in the MONW group, 50.2% in the MHO group and 73.6% in the MUO group. The prevalences of 25(OH)D deficiency in the MONW and MUO groups were significantly higher than that in the MHNW group (OR = 2.33, $P < 0.001$ and OR = 2.54, $P < 0.001$, respectively), after we adjusted for age, sex, BMI, smoking, drinking and exercise habits (Table 2). The prevalences of 25(OH)D deficiency were similar between the MHNW and MHO groups ($P > 0.05$). Similar patterns were observed in both men and women (Figure).

In the MHNW group, participants with 25(OH)D deficiency were older and had higher systolic blood pressure, compared with participants who were 25(OH)D nondeficient ($P < 0.05$). In the MONW group, participants with 25(OH)D deficiency were older and had greater BMI, waist circumference, systolic blood pressure, diastolic blood pressure, FINS and HOMA-IR values, compared with participants who were 25(OH)D

TABLE 1. Demographic and metabolic characteristics of the study population.

Demographic and metabolic characteristics	MHNW, $n = 415$	MONW, $n = 249$	MHO, $n = 231$	MUO, $n = 397$	*P* Value
Age (years)	54 (46-64)	60 (51-71)[a]	53 (46-65)[b]	59 (50-67)[a,c]	<0.001
Men (%)	202 (48.7)	109 (43.8)	137(59.3) [b]	186 (46.9)[c]	0.004
Current smokers (%)	92 (22.2)	65 (26.1)	42 (18.2)	103 (25.9)	0.10
Current drinkers (%)	98 (23.6)	57 (22.9)	49 (21.2)	106 (26.7)	0.43
Regular exercise (%)	241 (58.1)	111 (44.6)[a]	126 (54.5)	133 (33.5)[a,c]	<0.001
Body mass index (kg/m^2)	23.0 (22.1-23.9)	23.3 (22.2-24.2)	27.5 (26.1-29.1)[a,b]	27.7 (26.4-29.9)[a,b]	<0.001
Waist circumference (cm)	84 (80-86)	86 (81-90)[a]	93 (88-98)[a,b]	96 (90-102)[a,b,c]	<0.001
Systolic blood pressure (mm Hg)	120 (114-125)	125 (120-140)[a]	125 (119-127)[a,b]	135 (121-150)[a,b,c]	<0.001
Diastolic blood pressure (mm Hg)	72 (70-80)	80 (73-85)[a]	77 (70-80)[a,b]	80 (74-90)[a,c]	<0.001
Total cholesterol (mmol/L)	4.7 (4.1-5.1)	5.1 (4.5-5.9)[a]	4.9 (4.3-5.6)[a]	5.3 (4.4-6.0)[a,c]	<0.001
Triglycerides (mmol/L)	1.2 (1.0-1.5)	1.8 (1.6-2.3)[a]	1.3 (1.1-1.6)[a,b]	1.9 (1.7-2.3)[a,b,c]	<0.001
LDL cholesterol (mmol/L)	2.8 (2.3-3.2)	3.1 (2.7-3.7)[a]	2.9 (2.5-3.5)[a,b]	3.3 (2.6-3.9)[a,c]	<0.001
HDL cholesterol (mmol/L)	1.4 (1.2-1.5)	1.1 (1.0-1.2)[a]	1.3 (1.1-1.6)[b]	1.1 (0.9-1.3)[a,c]	<0.001
FPG (mmol/L)	5.0 (4.5-5.6)	5.9 (4.9-7.3)[a]	5.2 (4.7-5.5)[a,b]	6.6 (5.7-7.9)[a,b,c]	<0.001
Fasting insulin (μU/mL)	5.9 (4.9-7.4)	7.4 (6.3-8.9)[a]	7.6 (6.3-9.2)[a]	9.1 (7.1-11.9)[a,b,c]	<0.001
HOMA-IR	1.3 (1.1-1.8)	2.0 (1.7-2.4)[a]	1.7 (1.4-2.4)[a,b]	2.7 (2.1-3.4)[a,b,c]	<0.001
Hs C-reactive protein (mg/L)	0.5 (0.2-0.8)	0.7 (0.5-1.2)[a]	0.6 (0.3-0.9)[a,b]	0.9 (0.6-1.5)[a,b,c]	<0.001
25(OH)D (nmol/L)	52.6 (39.5-70.1)	39.8 (27.4-52.2)[a]	49.8 (35.8-67.6)[b]	37.2 (24.6-50.3) [a,c]	<0.001

Data are reported as median (interquartile range) or number (%).
MHNW, metabolically healthy and normal weight; MONW, metabolically obese but normal weight; MHO, metabolically healthy but obese; MUO, metabolically unhealthy and obese; LDL, low-density lipoprotein; HDL, high-density lipoprotein; FPG, fasting plasma glucose; HOMA-IR, homeostatic model assessment of insulin resistance; Hs, high sensitivity; 25(OH)D, 25-hydroxyvitamin D.
[a] Compared to MHNW; $P < 0.05$.
[b] Compared to MONW; $P < 0.05$.
[c] Compared to MHO; $P < 0.05$.

TABLE 2. Risk of vitamin D deficiency according to metabolic status.

Variable	*n*	Vitamin D deficiency *n* (%)	OR (95% CI)	
			Unadjusted	Adjusted
MHNW	415	177 (42.7)	1 (reference)	1 (reference)
MONW	249	171 (68.7)	2.94 (2.12-4.10), $P < 0.001$	2.33 (1.65-3.29), $P < 0.001$
MHO	231	116 (50.2)	1.36 (0.98-1.87), $P = 0.06$	1.23 (0.78-1.94), $P = 0.33$
MUO	397	292 (73.6)	3.74 (2.78-5.03), $P < 0.001$	2.54 (1.64-3.94), $P < 0.001$

Adjusted for age, sex, body mass index, smoking, drinking and regular exercise.
MHNW, metabolically healthy and normal weight; MONW, metabolically obese but normal weight; MHO, metabolically healthy but obese; MUO, metabolically unhealthy and obese.

nondeficient ($P < 0.05$). In the MHO group, participants with 25(OH)D deficiency were older and had higher systolic blood pressure and lower HDL-C levels, compared with participants who were 25(OH)D nondeficient ($P < 0.05$). In the MUO group, participants with 25(OH)D deficiency had greater waist circumference, systolic blood pressure, diastolic blood pressure, TC, TG, FPG, FINS, HOMA-IR and hs-CRP values, compared with participants who were 25(OH)D nondeficient ($P < 0.05$) (Table 3).

Among the metabolic disorder components, individuals who were MONW and had vitamin D deficiency had increased risks of abdominal obesity (OR = 3.28, $P = 0.005$), hypertension (OR = 3.08, $P = 0.003$) and elevated hs-CRP (OR = 1.97, $P = 0.030$). Furthermore, individuals who were MUO and had 25(OH)D deficiency had increased risks of hypertriglyceridemia (OR = 2.57, $P = 0.001$), insulin resistance (OR = 2.37, $P = 0.001$) and elevated hs-CRP (OR = 2.09, $P = 0.003$) (Table 4). There were no other significant differences in the metabolic disorder components when we compared individuals with and without 25(OH)D deficiency for the various groups ($P > 0.05$).

DISCUSSION

The present study evaluated vitamin D status according to various metabolic phenotypes (MHNW, MONW, MHO and MUO). Although the data were limited to adults who were 40-88 years old, we observed a high prevalence of vitamin D deficiency (58.5%), which was defined as plasma 25(OH)D levels of <50nmol/L. Furthermore, the plasma 25(OH)D levels were markedly lower in the metabolically unhealthy groups (MONW and MUO) compared to those in the metabolically healthy groups (MHNW and MHO). Moreover, the MUO group exhibited the lowest 25(OH)D levels, and vitamin D deficiency was most common in the MONW and MUO groups (for both men and women). To the best of our knowledge, this is the first data regarding vitamin D status and its relationship with obesity and metabolic disorders among adults who are ≥40 years old in Xinjiang province (northwest China).

After using the ATP-III criteria to categorize the participants, we found that the prevalences of MONW, MHO and MUO were 19.3%, 17.9% and 30.7%, respectively. The MONW group represents a nonnegligible proportion of individuals with a BMI < 25kg/m^2 and an increased risk of obesity-related complications.[20] In the present study, the MONW group exhibited higher blood pressure, glucose, inflammation marker (hs-CRP) and insulin resistance (HOMA-IR) values, and a worse lipid profile, compared with the MHNW group. Despite the similar BMI values, the MONW group had more visceral fat (i.e., a larger waist circumference), compared to the MHNW group. Interestingly, a previous study has demonstrated that abnormal visceral adiposity was strongly related to MONW,[21] and visceral adiposity is a major risk factor for the development of insulin resistance and a common pathophysiological link for metabolic disorders.[22] In contrast, individuals who are MHO have excessive body fat, although they also have a favorable metabolic profile that is characterized by high insulin sensitivity and no hypertension, as well as favorable lipid, inflammation and immune profiles.[6] Unfortunately, there is currently no standardized method for identifying MHO individuals in research protocols or clinical practice, although we used the widely accepted ATP-III criteria. The prevalences of MHO were 17.9% among all participants, and 36.8% among the obese participants. Compared with the MONW and MUO groups, the MHO group had lower blood pressure, glucose, TG, LDL-C, hs-CRP and insulin resistance values, as well as higher HDL-C levels. However, these metabolic indexes were less optimal than those in the reference group (MHNW). Therefore, MHO may reflect a transitional stage before metabolic dysfunction, and additional prospective studies are needed to clarify the final outcomes of MHO.

During recent decades, considerable research has helped identify the pleiotropic functions of vitamin D in a wide range of physiological processes. In this context, vitamin D mediates calcium and bone metabolism, and is also involved in regulating homeostasis at the cellular, organ and organism levels. Furthermore, vitamin D may play roles in the development of obesity and its related disorders.[10,23,24] In this study, the plasma 25(OH)D levels were lower in the metabolically abnormal groups (MONW and MUO), compared to those in the

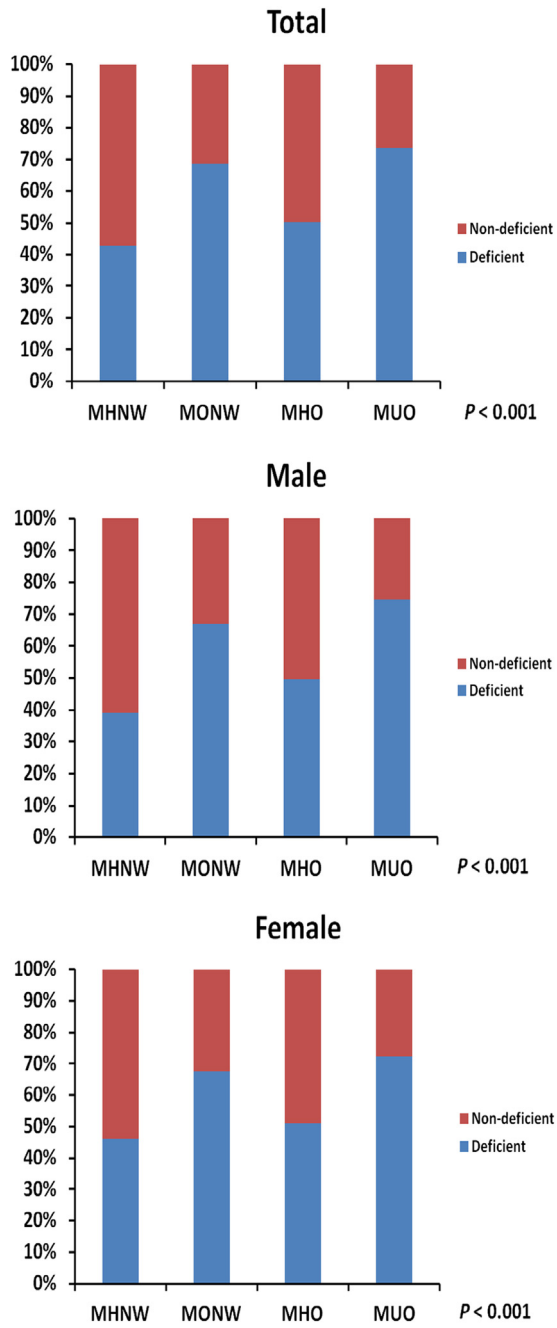

FIGURE. The prevalence of 25(OH)D deficiency according to metabolic status. The prevalances of 25(OH)D deficiency were higher among individuals who were metabolically obese but normal weight (MONW) or metabolically unhealthy and obese (MUO), compared with those among individuals who were metabolically healthy and normal weight (MHNW) or metabolically healthy but obese (MHO). Similar patterns were seen among men and women.

metabolically normal groups (MHNW and MHO). In addition, vitamin D deficiency was more frequent in the MONW and MUO groups, compared to in the MHNO and MHO groups. Although previous studies have reported decreased 25(OH)D levels in obese individuals,[25,26] those studies did not evaluate the participants' metabolic status. Therefore, ours is the first study to evaluate vitamin D status according to metabolic phenotype among individuals who are obese and normal weight. Our findings indicate that individuals who were metabolically abnormal and had a normal weight were more severely vitamin D deficient, whereas obese individuals with a healthy metabolic profile had better vitamin D status. These results indicate that metabolic status is a crucial mediator of 25(OH)D levels.

It is difficult to determine whether vitamin D deficiency leads to obesity-related disorders, or vice versa. For example, an inverse relationship between low levels of 25(OH)D and adiposity has been reported.[26] Obesity may contribute to low plasma 25(OH)D levels via the sequestration of vitamin D to adipose tissue.[27] In contrast, vitamin D may regulate adipose tissue mass, differentiation and metabolism, which might contribute to obesity and its related metabolic disorders.[27] Furthermore, obese individuals have a sedentary lifestyle and spend less time outdoors, which may reduce their skin production of vitamin D.[28] In the present study, the MUO group exhibited the most pronounced vitamin D deficiency, which is consistent with the findings of previous reports.[12] In addition, the MONW group exhibited abdominal obesity and had a similar vitamin D status compared to the MUO group. This may be because individuals who are MONW have lower levels of physical activity, energy expenditure and resting metabolism, compared with controls.[29] Thus, individuals who are MONW may be vulnerable to vitamin D deficiency. In contrast, individuals who are MHO may be protected from vitamin D deficiency, as their plasma 25 (OH)D levels were comparable to those in the MHNW group. This may be because individuals who are MHO have less visceral fat,[30] or due to the potential roles of genetic background, vitamin D receptor and vitamin D-binding protein gene polymorphisms.

Among the metabolic disorder components, individuals who were MONW and vitamin D deficient had higher risks of abdominal obesity, hypertension and elevated hs-CRP levels. In addition, individuals who were MUO and vitamin D deficient had higher risks of hypertriglyceridemia, insulin resistance and elevated hs-CRP levels. Given the elevated levels of hs-CRP (a marker for chronic inflammation), it appears that a chronic and systemic inflammation response may be a central mechanism in the pathophysiology of metabolic syndrome and insulin resistance.[22] Furthermore, the systemic inflammatory response is a risk factor for low 25(OH)D levels.[31] Moreover, Liefaard et al[32] have recently reported an inverse correlation between the levels of 25(OH)D and C-reactive protein in their prospective cross-sectional study of 9,649 adults who were $\geq$55 years old. Other studies have indicated that vitamin D may directly mediate adipose tissue and immune cell–derived inflammation.[33] Therefore, the decreased bioavailability of vitamin D may contribute to the

TABLE 3. Demographic and metabolic marker levels according to vitamin D status.

Demographic and metabolic characteristics	Deficient				Nondeficient			
	MHNW, *n* = 177	MONW, *n* = 171	MHO, *n* = 116	MUO, *n* = 292	MHNW, *n* = 238	MONW, *n* = 78	MHO, *n* = 115	MUO, *n* = 105
Age (years)	60 (48-71) [a]	64 (53-72) [b]	59 (48-68) [c]	60 (50-67)	50 (46-59)	55 (47-66)	49 (45-63)	59 (52-66)
Body mass index (kg/m^2)	23.0 (22.1-23.7)	23.5 (22.2-24.3) [b]	27.4 (26.0-29.2)	27.7 (26.4-30.1)	23.1 (22.1-23.9)	22.9 (22.1-23.9)	27.6 (26.2-29.1)	27.7 (26.3-29.3)
Waist circumference (cm)	84 (80-86)	87 (81-90) [b]	94 (88-99)	96 (91-103) [d]	83 (80-86)	85 (81-87)	93 (89-98)	94 (89-99)
Systolic blood pressure (mm Hg)	124 (115-126)[a]	130 (120-145)[b]	125 (120-128)[c]	140 (124-150)[d]	120 (110-125)	123 (120-128)	122 (115-126)	130 (120-140)
Diastolic blood pressure (mm Hg)	75 (70-80)	80 (70-90) [b]	77 (71-80)	80 (77-90) [d]	70 (68-80)	78 (74-81)	76 (70-80)	76 (70-86)
Total cholesterol (mmol/L)	4.7 (4.1-5.3)	5.1 (4.4-5.8)	5.0 (4.5-5.7)	5.4 (4.5-6.1) [d]	4.6 (4.1-5.1)	5.1 (4.6-5.9)	4.8 (4.2-5.5)	5.1 (4.2-5.8)
Triglycerides (mmol/L)	1.2 (1.0-1.5)	1.9 (1.6-2.3)	1.4 (1.1-1.6)	2.1 (1.8-2.5) [d]	1.1 (1.0-1.5)	1.8 (1.6-2.2)	1.3 (1.1-1.6)	2.0 (1.5-2.4)
LDL cholesterol (mmol/L)	2.8 (2.3-3.2)	3.2 (2.7-3.8)	3.0 (2.5-3.5)	3.3 (2.6-3.9)	2.7 (2.3-3.2)	3.1 (2.7-3.6)	2.9 (2.5-3.4)	3.1 (2.4-3.8)
HDL cholesterol (mmol/L)	1.3 (1.2-1.5)	1.0 (0.9-1.2)	1.3 (1.1-1.5)[c]	1.1 (0.9-1.3) [d]	1.4 (1.3-1.6)	1.1 (1.0-1.2)	1.4 (1.2-1.6)	1.1 (1.0-1.3)
FPG (mmol/L)	4.9 (4.4-5.5)	5.8 (5.0-7.3)	5.1 (4.7-5.5)	6.7 (5.7-8.1) [d]	5.0 (4.5-5.8)	5.9 (4.8-7.0)	5.3 (4.9-5.5)	6.5 (5.7-7.3)
Fasting insulin (μU/mL)	5.9 (4.9-7.5)	7.5 (6.5-9.0) [b]	7.6 (6.3-10.0)	9.1 (7.3-12.2)[d]	5.8 (4.9-7.2)	6.9 (5.6-8.4)	7.6 (6.2-9.0)	8.4 (6.5-11.3)
HOMA-IR	1.4 (1.11.9)	2.2 (1.8-2.5) [b]	1.8 (1.4-2.4)	2.9 (2.4-3.4) [d]	1.3 (1.1-1.8)	1.9 (1.5-2.2)	1.7 (1.4-2.4)	2.3 (1.9-3.4)
Hs C-reactive protein (mg/L)	0.4 (0.2-0.7)	0.8 (0.5-1.3)	0.6 (0.3-1.2)	1.1 (0.5-1.7) [d]	0.5 (0.2-0.9)	0.7 (0.5-0.9)	0.5 (0.3-0.7)	0.7 (0.6-1.0)

Data are reported as median (interquartile range) or number (%).
MHNW, metabolically healthy and normal weight; MONW, metabolically obese but normal weight; MHO, metabolically healthy but obese; MUO, metabolically unhealthy and obese; LDL, low-density lipoprotein; HDL, high-density lipoprotein; FPG, fasting plasma glucose; HOMA-IR, Homeostasis Model Assessment of insulin resistance; Hs, high sensitivity.
[a] 25(OH)D-deficient vs. nondeficient MHNO; $P < 0.05$.
[b] 25(OH)D-deficient vs. nondeficient MONW; $P < 0.05$.
[c] 25(OH)D-deficient vs. nondeficient MHO; $P < 0.05$.
[d] 25(OH)D-deficient vs. nondeficient MUO; $P < 0.05$.

TABLE 4. Risk of metabolic disorder components according to metabolic status among individuals who were vitamin D deficient.

Variable	MHNW OR (95% CI)	MONW OR (95% CI)	MHO OR (95% CI)	MUO OR (95% CI)
Abdominal obesity	1.64 (0.78-3.44), $P = 0.19$	3.28 (1.43-7.51), $P = 0.005$	1.13 (0.56-2.27), $P = 0.73$	1.72 (0.88-3.37), $P = 0.11$
Hyperglycemia	0.66 (0.38-1.18), $P = 0.13$	1.08 (0.50-2.32), $P = 0.84$	1.05 (0.50-2.19), $P = 0.90$	1.08 (0.61-1.89), $P = 0.80$
Hypertension	0.93 (0.49-1.78), $P = 0.83$	3.08 (1.45-6.52), $P = 0.003$	0.81 (0.38-1.72), $P = 0.58$	1.55 (0.92-2.61), $P = 0.10$
Hypertriglyceridemia	0.87 (0.29-2.55), $P = 0.79$	1.58 (0.71-3.50), $P = 0.26$	0.71 (0.27-1.90), $P = 0.50$	2.57 (1.46-4.51), $P = 0.001$
Low HDL-C	1.02 (0.51-2.06), $P = 0.95$	1.22 (0.54-2.77), $P = 0.64$	1.28 (0.49-3.32), $P = 0.62$	1.17 (0.69-1.99), $P = 0.57$
Insulin resistance	1.59 (0.70-3.60), $P = 0.26$	1.90 (0.54-6.64), $P = 0.32$	0.86 (0.42-1.75), $P = 0.67$	2.37 (1.45-3.86), $P = 0.001$
Elevated hs-CRP ($\geq$0.7 mg/L)	0.82 (0.50-1.33), $P = 0.41$	1.97 (1.07-3.63), $P = 0.03$	1.43 (0.78-2.63), $P = 0.25$	2.09 (1.28-3.42), $P = 0.003$

Odds ratios were adjusted for age, sex, body mass index, smoking, drinking and regular exercise.
MHNW, metabolically healthy and normal weight; MONW, metabolically obese but normal weight; MHO, metabolically healthy but obese; MUO, metabolically unhealthy and obese; OR, odds ratio; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein.

pathogenesis of obesity-related metabolic disorders, although there is currently no evidence regarding the causality of that relationship. Thus, we hypothesize that vitamin D supplementation may alleviate the metabolic abnormalities among individuals who are MONW or MUO. However, future studies are needed to identify and evaluate the underlying mechanism(s) by which vitamin D status may affect obesity-related metabolic disorders.

In the present study, individuals who are MONW and MUO had less regular exercise and thus were outdoors less often. Because 25(OH)D is largely derived from solar UVB exposure, that is an assignable cause for their lower blood level of 25(OH)D. It was reported that solar UVA can lower blood pressure through liberation of cutaneous nitric oxide.[34] Individuals in MONW and MUO groups presented with higher blood pressure, which may relate to their less sun exposure.

Several limitations should be considered when interpreting the results of this study. First, the cross-sectional design cannot confirm the direction or causality of the relationship between vitamin D deficiency and metabolic disorders. Second, we did not have access to information regarding sun exposure and food-based vitamin D intake, which are important confounding factors. Finally, this study had a relatively small population, which made it difficult to compare vitamin D status among the different age groups.

CONCLUSIONS

In conclusion, individuals who were MONW and MUO had increased risks of vitamin D deficiency. We suggest vitamin D supplementation for treatment of low vitamin D status in individuals with MONW and MUO. Just as important, increased sun exposure, which could also increase physical activity, should be recommended.

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