Sex-Specific Association between Serum Vitamin D Status and Lipid Profiles: A Cross-Sectional Study of a Middle-Aged and Elderly Chinese Population

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Summary Studies have shown that vitamin D status might be associated with dyslipidaemia, but results are conflicting and there might exist sex differences. The aim of our study was to explore the sex-specific association between vitamin D status and serum lipids and atherogenic index of plasma (AIP, a predictor for atherosclerosis) among Chinese middle-aged and elderly adults. A total of 4,021 middle-aged and elderly participants from a health management centre were included in this cross-sectional study. The individuals were classified into tertiles according to serum 25(OH)D. Linear and logistic regression models were used to estimate the association between vitamin D levels and serum lipids among the tertiles. The mean serum 25(OH)D level was 21.60 (16.60–27.20) ng/mL in all participants. After adjusting for potential confounders, a 10 ng/mL increase in 25(OH)D was associated with decreases of 1.156 mmol/L in triglycerides (TGs) and 0.068 in the AIP and an increase of 0.051 mmol/L in high-density lipoprotein cholesterol (HDL-C) in all subjects. In addition, 25(OH)D deficiency was associated with an increased prevalence of hypertriglyceridaemia (odds ratio (OR), 1.880; 95% confidence interval (CI), 1.351–2.615), hypoalphalipoproteinaemia/HDL (OR, 1.505; 95% CI, 1.146–1.977) and abnormal AIP (OR, 1.933; 95% CI, 1.474–2.534) in males, and 25(OH)D-deficient women had a 2.02-fold higher risk for hypoalphalipoproteinaemia/HDL than women with sufficient 25(OH)D levels (95% CI, 1.044–3.904; all *p* values <0.05). Vitamin D deficiency was positively associated with the prevalence of dyslipidaemia and abnormal AIP in the middle-aged and elderly Chinese population. And this association was stronger in men than in women.

Key Words vitamin D, atherogenic index of plasma, dyslipidaemia, sex difference, gerontology

Vitamin D is an essential endogenous secosteroid hormone with a multitude of functions (1). The predominant source of vitamin D is solar ultraviolet (UV) radiation, which stimulates the transformation of 7-dehydrocholesterol to previtamin D₃ in the skin. Previtamin D₃ is continuously converted to vitamin D₃ with thermal isomerization by body temperature. Vitamin D, including vitamin D₃ and vitamin D₂, can be sequentially hydroxylated into 25-hydroxyvitamin D [25(OH)D] and 1,25-dihydroxyvitamin D [1,25(OH)₂D] in the liver and the kidney (2). Currently, the vitamin D status of the body is mainly evaluated by measuring 25(OH)D (3). In addition to the traditional functions of maintaining calcium homeostasis and bone metabolism, vitamin D has been reported to be associated with a broad range of chronic conditions, such as metabolic syndrome, diabetes, and autoimmune diseases (4–6). Cardiovascular diseases (CVDs) are among the most prevalent conditions linked to vitamin D deficiency (7). Given that middle-

aged and elderly people are especially at risk of vitamin D deficiency and CVD (8), we focused on mainly this target population.

CVD is one of the main causes of death around the world, and there is accumulating evidence indicating an association between low levels of 25(OH)D and increased risk of CVD and all-cause mortality (7, 9). Disorders of lipid profiles (dyslipidaemia), including increased levels of total cholesterol (TC), triglycerides (TGs) and low-density lipoprotein cholesterol (LDL-C) and decreased levels of high-density lipoprotein cholesterol (HDL-C), have been identified as important contributing factors in atherosclerosis and CVD (10). Previous studies have reported a correlation between 25(OH)D levels and serum lipids (11, 12). However, the association between vitamin D and lipid profiles is divergent and inconclusive in the different ethnic groups that have been studied (13, 14). In addition, these inconsistencies might be caused by sex differences. Some studies have demonstrated that postmenopausal women with vitamin D deficiency had a higher risk of hypertriglyceridaemia and low HDL-C concentrations than women with sufficient vitamin D

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levels (4, 15). However, several studies of the general population have shown that vitamin D deficiency could influence men's serum lipid profiles more than those of women (16, 17). These studies have investigated only one sex or used a sample of adults rather than limiting the analyses to a middle-aged and elderly population, so data on sex differences in the association is sparse, especially from Asian populations.

Therefore, the main purpose of this study was to investigate the independent association between vitamin D and blood lipids and to show potential differences by sex in a representative sample of urban, middle-aged and elderly adults residing in central China. The atherogenic index of plasma (AIP), an index composed of TGs and HDL-C that has been reported to quantify blood lipid levels and that is used as an indicator of dyslipidaemia and CVD (18, 19), was also investigated in our study.

MATERIALS AND METHODS

Participants. The present study was a cross-sectional study that included participants aged 45–85 y from the health management centre in the Optics Valley branch of Tongji Hospital (Wuhan, China). Data were collected between January 2017 and December 2017. Initially, 4,937 individuals were identified as potential participants. Subjects were excluded for the following reasons: (1) past history of severe liver or kidney diseases, thyroid or parathyroid disorders, cardiovascular disease or diabetes ($n=408$); (2) use of vitamin D and calcium supplementation, use of medications that affect vitamin D and lipid profiles (i.e., lipid-lowering drugs) ($n=39$) and (3) missing data for any of the study variables ($n=469$). Finally, a total of 4,021 eligible participants (2,077 males and 1,944 females) were included for our analysis.

The study was approved by the Ethics Committee of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (The Institutional Review Board Approval Number: TJ-C20160115). The study conforms to the principles outlined in the Declaration of Helsinki and written informed consent was obtained from all participants.

Anthropometric and biochemical measurements. Routine anthropometric measurements were performed by trained examiners. Height and weight were measured to the nearest 0.1 cm and 0.1 kg, respectively, while the participants wore light clothing and stood barefoot. Body mass index (BMI) was calculated as weight (kg)/height (m)². After resting quietly for a minimum of 5 min, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using a standard electronic sphygmomanometer (HBP-9020; OMRON, Dalian, China). Data on sex, age, ethnicity and history of disease were obtained by using a questionnaire. Fasting (over 12 h) blood samples were collected from each participant and then sent to the clinical laboratory of Tongji Hospital for standard biochemical measurements, including TC, TGs, LDL-C, HDL-C, fasting plasma glucose (FPG), glycosylated haemoglobin (HbA1c), uric acid, creatinine, C-reactive protein (CRP), homocysteine

(Hcy), calcium and phosphate. Serum levels of 25(OH)D were determined using the LIAISON® 25-OH Vitamin D Total assay (DiaSorin, Inc., Stillwater, MN, USA) following the manufacturer's instructions.

Criteria and definitions. According to the commonly accepted cut off (20), vitamin D status was categorized as deficient (<20 ng/mL), insufficient (20–30 ng/mL), or sufficient (>30 ng/mL). On that basis, we divided the 2,077 male participants and 1,944 female participants into three tertiles. Tertile 1 (T1) had the lowest mean 25(OH)D concentration, and Tertile 3 (T3) had the highest mean 25(OH)D concentration. In our study, the cutoff values for high TC, high TGs, high LDL-C and low HDL-C were 6.22 mmol/L, 2.26 mmol/L, 4.14 mmol/L and 1.04 mmol/L, respectively (21). The AIP, calculated as the logarithmically transformed ratio of TGs to HDL-C ($\log[\text{TGs}/\text{HDL-C}]$), is thought to be a useful independent predictor of CVD. An AIP >0.15 was regarded as abnormal in this study (22).

Statistical analysis. Continuous variables are presented as the means $\pm$ standard deviations (SDs), non-normally distributed continuous variables are expressed as medians (25th–75th) and categorical variables are expressed as frequencies. Sex differences were examined using independent *t*-tests and chi-square tests. Across the 25(OH)D tertiles, comparisons of the groups were performed using one-way ANOVA for continuous variables, the Kruskal-Wallis test for non-normally distributed variables and the chi-square test for categorical variables. Multivariate linear regression models were used to examine the association between serum 25(OH)D concentrations and lipid status. Some variables were logarithmically transformed prior to being analyzed. Logistic regression models were used to determine the relationship between 25(OH)D deficiency and the prevalence of dyslipidaemia, with data presented as odds ratios (ORs) and 95% confidence intervals (CIs). In this study, we used 2 models to adjust potential confounders of dyslipidaemia. Model 1 was adjusted for age, SBP, DBP, fasting blood glucose (FBG), uric acid and creatinine. Model 2 included the variables in Model 1 and BMI. We conducted subgroup analyses to explore the association between vitamin D deficiency and dyslipidaemia according to BMI (<24 or ≥ 24 kg/m², the cutoff value of overweight for Asian individuals) and age (<53 or ≥ 53 y, the median age of the participants). We conducted tests for interactions among the subgroups using the Wald test. All statistical analyses were performed using SPSS software version 17.0 (SPSS Inc., Chicago, IL, USA). Two-tailed *p* values of <0.05 were considered statistically significant.

RESULTS

General characteristics of the participants

A total of 4,021 subjects were included in the study, and 51.7% of the subjects were male. The mean age of the study population was 55.53 y. The mean serum 25(OH)D concentration was 21.60 ng/mL. The incidence rates of vitamin D deficiency and insufficiency were 42.0% and 41.5%, respectively. Table 1 shows the

Table 1. Characteristics of subjects.

	All	Male	Female	M/F <i>p</i> value
<i>n</i>	4,021	2,077	1,944	
Age (y)	55.53±8.96	54.30±8.07	56.83±9.65	<0.001
BMI (kg/m ²)	24.18±2.99	24.82±2.90	23.50±2.94	<0.001
SBP (mmHg)	129.45±18.99	130.58±18.10	128.25±19.84	<0.001
DBP (mmHg)	77.31±12.25	80.37±11.95	74.04±11.72	<0.001
TC (mmol/L)	4.76±0.87	4.70±0.86	4.83±0.88	<0.001
TGs (mmol/L)	1.62±1.28	1.84±1.54	1.38±0.86	<0.001
LDL-C (mmol/L)	2.89±0.77	2.90±0.77	2.88±0.77	0.354
HDL-C (mmol/L)	1.31±0.32	1.19±0.27	1.44±0.32	<0.001
AIP	0.03±0.31	0.12±0.31	-0.06±0.27	<0.001
FBG (mmol/L)	5.48±1.02	5.57±1.16	5.38±0.84	<0.001
HbA1c (%)	5.69±0.63	5.70±0.69	5.68±0.54	0.672
Uric acid (μmol/L)	337.08±89.91	384.40±82.42	286.47±67.14	<0.001
Creatinine (μmol/L)	74.15±16.40	84.62±13.90	62.94±10.36	<0.001
CRP (mg/L)	2.24±7.54	2.29±6.99	2.15±8.45	0.794
Hcy (μmol/L)	13.79±7.56	16.29±8.95	11.08±4.26	<0.001
Ca (mmol/L)	2.34±0.08	2.34±0.08	2.34±0.09	0.848
P (mmol/L)	1.02±0.16	0.96±0.14	1.11±0.14	<0.001
25(OH)D (ng/mL)	21.60 (16.60–27.20)	23.10 (18.00–28.70)	20.00 (15.40–25.60)	<0.001
Dyslipidaemia, <i>n</i> (%)	1,360 (33.8)	954 (45.9)	406 (20.9)	<0.001

Data are presented as the mean±SD, median (25th–75th) or percentages.

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TGs, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; AIP, atherogenic index of plasma; FBG, fasting blood glucose; HbA1c, glycosylated haemoglobin; CRP, C-reactive protein; Hcy, homocysteine; Ca, calcium; P, phosphate.

general characteristics of the research subjects according to sex. The female participants were older; had a lower BMI; had higher levels of TC and HDL-C; had lower levels of blood pressure, TGs, AIP, FPG, Hcy, uric acid, creatinine, and 25(OH)D; and had a higher prevalence of dyslipidaemia (all *p* values <0.05).

To further investigate the characteristic differences, we divided the men and women into tertiles for comparison. The incidence of vitamin D deficiency was 34.5% and 49.9% in males and females, respectively. In males, we found significantly lower levels of TC, TGs, BMI, and AIP; a higher level of HDL-C; and a lower prevalence of dyslipidaemia in the third tertile compared with the values of the participants in the first and second tertiles (all *p* values <0.05). However, in female participants, there were significant differences in BMI, HDL-C, uric acid, creatinine, calcium and phosphate among the three tertiles (Table 2).

Association between serum 25(OH)D concentrations and serum lipids

Multiple linear regression analyses were performed to assess the relationship between 25(OH)D levels and lipid profiles. In all subjects, 25(OH)D concentrations were negatively associated with TGs and AIP and positively associated with HDL-C after adjusting for age, SBP, DBP, FBG, uric acid, and creatinine (Model 1). Further adjustment for BMI (Model 2) did not substantially alter the associations. Our results showed that each 10 ng/mL increase in 25(OH)D was associated with decreases of 1.156 mmol/L in TGs and 0.068 in AIP and an increase

of 0.051 mmol/L in HDL-C (all *p* values <0.05). However, TC and LDL-C showed no significant linear relationship with 25(OH)D (Table 3).

Moreover, we found negative associations between 25(OH)D and TC, TGs and AIP and a positive association between 25(OH)D and HDL-C in males after adjusting for the confounders in Model 1 and Model 2. A 10 ng/mL increase in 25(OH)D was associated with decreases of 1.279 mmol/L in TGs, 0.047 mmol/L in TC, and 0.119 in AIP and an increase of 0.102 mmol/L in HDL-C (all *p* values <0.05). In contrast, in female participants, there was a positive association between only 25(OH)D and HDL-C in Model 1 and Model 2 (Table 4). Each 10 ng/mL increase in 25(OH)D was associated with an increase of 0.060 mmol/L in HDL-C (*p*=0.006).

Relationship between serum 25(OH)D concentrations and the occurrence of dyslipidaemia

The ORs and 95% CIs for dyslipidaemia according to serum 25(OH)D concentrations in men and women are presented in Table 5. The OR (95% CI) for hypertriglyceridaemia, hypoalbuminoproteinaemia and abnormal AIP increased notably in vitamin D-deficient men compared to the corresponding ORs of vitamin D-sufficient men after adjustment for age, hypertension, FBG, uric acid, and creatinine. The relationship between serum 25(OH)D concentrations and the occurrences of hypertriglyceridaemia, hypoalbuminoproteinaemia and abnormal AIP remained significant after additional adjustment for BMI, with ORs and 95% CIs of 1.880 (1.351–2.615), 1.505 (1.146–1.977), and 1.933 (1.474–2.534), re-

Table 2. Characteristics of subjects according to vitamin D status in males and females.

	Male			Female		
	T1	T2	T3	T1	T2	T3
<i>n</i>	716	930	431	971	738	235
Age (y)	54.03±8.34*	53.99±7.76*	55.43±8.18	55.58±9.42**	57.63±9.43*	59.51±10.49
BMI (kg/m ²)	25.09±3.02*	24.87±2.81*	24.28±2.85	23.59±2.91*	23.55±2.95*	22.94±2.94
SBP (mmHg)	131.19±16.92	130.15±18.31	130.49±19.50	128.18±20.04	127.89±19.35	129.65±20.54
DBP (mmHg)	80.86±11.70	80.06±11.93	80.21±12.39	74.16±11.96	73.72±11.39	74.56±11.78
TC (mmol/L)	4.74±0.90*	4.71±0.86*	4.60±0.80	4.81±0.87	4.84±0.92	4.90±0.83
TGs (mmol/L)	1.56 (1.08–2.33)**	1.46 (1.01–2.10)*	1.27 (0.92–1.80)	1.41±0.95	1.35±0.79	1.33±0.68
LDL-C (mmol/L)	2.90±0.79	2.92±0.77	2.86±0.76	2.85±0.74	2.91±0.82	2.89±0.75
HDL-C (mmol/L)	1.15±0.26**	1.19±0.26*	1.24±0.28	1.42±0.32*	1.44±0.31*	1.51±0.34
AIP	0.15±0.26**	0.18±0.26*	0.04±0.29	−0.05±0.28	−0.07±0.27	−0.09±0.25
FBG (mmol/L)	5.60±1.25	5.55±1.08	5.55±1.16	5.39±0.87	5.39±0.84	5.38±0.67
HbA1c (%)	5.75±0.78	5.65±0.53	5.72±0.85	5.71±0.62	5.67±0.48	5.64±0.40
Uric acid (μmol/L)	381.81±79.89	388.09±81.32	380.76±88.55	282.28±63.27**	288.85±70.53	296.31±70.63
Creatinine (μmol/L)	84.55±14.68	84.76±13.08	84.45±14.32	61.78±9.74**	63.65±10.67*	65.54±11.17
CRP (mg/L)	2.24±6.96	2.35±7.43	2.26±5.92	2.24±10.00	1.75±5.61	2.94±7.59
Hcy (μmol/L)	17.18±10.40	15.87±8.21	15.34±6.82	11.23±4.50	11.02±4.24	10.57±3.01
Ca (mmol/L)	2.33±0.07	2.34±0.08	2.35±0.08	2.32±0.09**	2.35±0.08	2.35±0.07
P (mmol/L)	0.97±0.14	0.98±0.15	0.95±0.12	1.08±0.14**	1.13±0.13	1.15±0.14
25(OH)D (ng/mL)	16.20	24.50	35.20	15.40	24.20	34.30
Dyslipidaemia, <i>n</i> (%)	(13.80–18.10)**	(22.20–26.80)*	(32.60–39.60)	(12.90–17.70)**	(22.00–26.50)*	(31.60–37.80)
	363 (50.7)	427 (45.9)	164 (38.1)	202 (20.8)	160 (21.7)	44 (18.7)

Data are presented as the mean ± SD, median (25th–75th) or percentages.

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; AIP, atherogenic index of plasma; FBG, fasting blood glucose; HbA1c, glycosylated haemoglobin; CRP, C-reactive protein; Hcy, homocysteine; Ca, calcium; P, phosphate.

* $p < 0.05$ compared to Tertile 3; # $p < 0.05$ compared to Tertile 2.

Table 3. Adjusted regression coefficients of vitamin D status with serum lipids and AIP.

	Model 1		Model 2	
	β	<i>p</i> value	β	<i>p</i> value
TC	-0.017	0.278	-0.020	0.219
TGs	-0.077	<0.001	-0.063	<0.001
LDL-C	0.017	0.280	0.018	0.260
HDL-C	0.070	<0.001	0.051	<0.001
AIP	-0.085	<0.001	-0.068	<0.001

Model 1: adjusted for age, SBP, DBP, FBG, uric acid and creatinine.

Model 2: adjusted for the covariates in Model 1 plus BMI. SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TGs, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; AIP, atherogenic index of plasma; FBG, fasting blood glucose; BMI, body mass index.

The β coefficient is a standardized coefficient in multiple linear regression analysis.

25(OH)D and TGs were logarithmically transformed for the analysis.

spectively (all *p* values <0.05). In women, 25(OH)D deficiency was associated with an increased prevalence of hypoalphalipoproteinaemia (OR, 2.019; 95% CI, 1.044–3.904; *p*=0.037).

We further conducted subgroup analyses stratified by BMI and age in men and women (Supplemental Online Material, Tables S1–S4). There was no evidence of significant interactions between 25(OH)D deficiency, BMI and age on dyslipidaemia in men or evidence of significant interactions between 25(OH)D deficiency and BMI on dyslipidaemia in women (all *p* values for interactions >0.05). An age-specific interaction was observed in the relationship between serum 25(OH)D concentrations and the occurrence of hypercholesterolaemia in women (*p*=0.036).

DISCUSSION

In this cross-sectional study, we found that vitamin D deficiency was common in a middle-aged and elderly Chinese population and that vitamin D deficiency might be associated with a higher risk for dyslipidaemia after adjusting for potential confounders. Furthermore, hypovitaminosis D is associated with more aggressive dyslipidaemia in males but not in females. In this study population, the mean serum 25(OH)D concentration was 21.60 ng/mL, and the prevalence of vitamin D deficiency was 42.0%, which was not as notable as the figure reported by Lu et al. regarding a Chinese population (69.2% deficiency) (14). This deviation could be due to differences in sun exposure, as the participants in our study resided in areas at lower latitudes.

Mounting evidence indicates that vitamin D status may be associated with dyslipidaemia (11, 12) and, thus, cardiovascular disease (CVD) (7, 9). These studies suggest that serum 25(OH)D deficiency is associated

Table 4. Adjusted regression coefficients of vitamin D status with serum lipids and AIP in males and females.

	Model 1		Model 2	
	β	<i>p</i> value	β	<i>p</i> value
Male				
TC	-0.046	0.033	-0.047	0.032
TGs	-0.128	<0.001	-0.107	<0.001
LDL-C	0.008	0.723	0.008	0.706
HDL-C	0.126	<0.001	0.102	<0.001
AIP	-0.142	<0.001	-0.119	<0.001
Female				
TC	0.039	0.094	0.035	0.127
TGs	-0.025	0.257	-0.016	0.458
LDL-C	0.034	0.143	0.034	0.134
HDL-C	0.077	0.001	0.060	0.006
AIP	-0.047	0.027	-0.034	0.109

Model 1: adjusted for age, SBP, DBP, FBG, uric acid and creatinine.

Model 2: adjusted for the covariates in Model 1 plus BMI. SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TGs, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; AIP, atherogenic index of plasma; FBG, fasting blood glucose; BMI, body mass index.

The β coefficient is a standardized coefficient in multiple linear regression analysis.

25(OH)D and TGs were logarithmically transformed in males, and 25(OH)D was logarithmically transformed in females for the analysis.

with lower HDL-C levels and higher LDL-C and TG levels (11, 12, 23). Consistent with these studies, we also found that serum 25(OH)D concentrations had a strong negative association with TGs and a positive association with HDL-C in all subjects after adjusting for relevant confounders. But our study did not show any significant relationship of serum 25(OH)D with TC or LDL-C levels. However, the results of the relationship between vitamin D and lipid status are conflicting and inconsistent. For example, data from the study by Jorde et al. showed highly significant associations between 25(OH)D and all the lipid parameter in northern Europeans (24). But in a study conducted in American adults, no correlation between 25(OH)D and TGs or HDL-C levels was observed (25). Even in studies conducted in Chinese population, the results are inconsistent. Some studies showed relationships between 25(OH)D with TGs and HDL-C (16, 17), while another study found a relationship with LDL-C (26). The contrasting findings of these studies could be explained by the different characteristics of the study participants.

However, the mechanisms underlying how vitamin D influences the lipid profile remain unclear. One of the possible mechanisms, which was reported in an in vitro study, is the increase in intestinal calcium absorption associated with vitamin D intake. This calcium absorption could then reduce serum TGs by reducing hepatic

Table 5. Adjusted ORs and 95% CIs of dyslipidaemia and abnormal AIP according to vitamin D status in males and females.

	Male				Female			
	T3	T2	p value	T1	p value	T2	T1	p value
Hypercholesterolaemia (%)	3.5	5.3		5.7		6.4	5.8	
Model 1	1.00	1.517 (0.832–2.767)	0.174	1.638 (0.886–3.027)	0.116	1.00	1.026 (0.548–1.921)	0.936
Model 2	1.00	1.534 (0.840–2.801)	0.164	1.665 (0.899–3.083)	0.105	1.00	0.982 (0.524–1.842)	0.955
Hypertriglyceridaemia (%)	16.0	22.2		27.2		9.4	9.6	
Model 1	1.00	1.466 (1.066–2.018)	0.019	2.017 (1.465–2.793)	<0.001	1.00	1.081 (0.643–1.816)	0.770
Model 2	1.00	1.395 (1.009–1.928)	0.044	1.880 (1.351–2.615)	<0.001	1.00	1.025 (0.609–1.726)	0.925
Hypobetalipoproteinaemia/IDL (%)	4.9	6.5		6.4		6.0	6.6	
Model 1	1.00	1.354 (0.809–2.264)	0.248	1.306 (0.766–2.229)	0.327	1.00	1.265 (0.671–2.386)	0.468
Model 2	1.00	1.371 (0.819–2.294)	0.230	1.332 (0.780–2.277)	0.294	1.00	1.217 (0.644–2.299)	0.546
Hypoalphalipoproteinaemia/HDL (%)	26.2	31.4		36.5		4.7	7.6	
Model 1	1.00	1.258 (0.969–1.633)	0.085	1.606 (1.228–2.102)	0.001	1.00	1.727 (0.882–3.385)	0.111
Model 2	1.00	1.203 (0.923–1.567)	0.171	1.505 (1.146–1.977)	0.003	1.00	1.656 (0.844–3.249)	0.143
Abnormal AIP (%)	33.4	42.6		49.9		17.9	21.5	
Model 1	1.00	1.468 (1.137–1.894)	0.003	2.065 (1.584–2.693)	<0.001	1.00	1.393 (0.936–2.073)	0.103
Model 2	1.00	1.402 (1.081–1.819)	0.011	1.933 (1.474–2.534)	<0.001	1.00	1.317 (0.883–1.965)	0.176

Model 1: adjusted for age, hypertension, FBG, uric acid and creatinine.
Model 2: adjusted for the covariates in Model 1 plus BMI.
ORs, odds ratios; CIs, confidence intervals; AIP, atherogenic index of plasma; FBG, fasting blood glucose; BMI, body mass index.
Adjusted ORs and 95% CIs for the first and second tertiles were calculated using a logistic regression model using the third tertile as the reference.

TG synthesis and secretion (27). Moreover, increased levels of intestinal calcium could increase the formation of insoluble calcium-fatty complexes, thus reducing the intestinal absorption of fatty acids (28). Serum levels of TC and LDL-C would be reduced by the decreased absorption of fatty acids. Another possible explanation is that vitamin D has a suppressive effect on the serum parathyroid hormone (PTH) concentration, and a lowered level of PTH may reduce serum TGs by reducing lipolysis (29). In addition, previous studies have suggested that vitamin D deficiency may be associated with impaired β -cell function and insulin resistance, which could lead to an increase in TG levels and a decrease in HDL-C levels (25). What's more, scientists recently reported a novel mechanism that 25-hydroxyvitamin D might regulate lipid metabolism by inducing degradation of sterol regulatory element-binding protein (SREBP) and SREBP cleavage-activating protein (SCAP), a master regulator of lipogenesis and an escort protein essential for SREBP activation (30).

In the present study, we found that the associations between serum 25(OH)D levels and serum lipids were stronger in men than in women. In men, vitamin D deficiency was associated with a higher risk of hypertriglyceridaemia, hypoalphalipoproteinaemia and abnormal AIP after adjusting for potential confounders. But in women, the association only existed in hypoalphalipoproteinaemia. This finding was in agreement with some previous studies. Yin et al. found that 25(OH)D was negatively related to TGs and positively related to HDL-C in males and that 25(OH)D was negatively related to only TGs in females (17). Similarly, Wang et al. reported that 25(OH)D deficiency was correlated with increased risks of elevated TGs and AIP and reduced HDL-C in men, but the association did not exist in women (16). The mechanisms underlying the sex difference in the association between vitamin D and lipid profiles have not yet been defined. The difference in hormones and the sensitivity of hormone receptors between the sexes may affect lipid metabolism differently. Many previous studies have suggested that vitamin D concentrations are positively associated with an increase in sexual hormones, such as testosterone in men and oestrogen in women (31, 32). As men age, testosterone production decreases gradually, low testosterone has been reported to be associated with greater risks of insulin resistance (33). Therefore, we divided the population into subgroups by age to determine whether there was any difference between serum vitamin D status and lipid profiles. An age-specific interaction was observed in the relationship between serum 25(OH)D concentrations and the occurrence of hypercholesterolaemia in women ($p=0.036$). There was a positive relationship between serum 25(OH)D status and hypercholesterolaemia in women aged <53 y (mostly premenopausal participants) but not in women aged ≥ 53 y (mostly postmenopausal participants) (Supplemental Online Material, Table S4). It seems that oestrogen may be involved. An interesting finding in this study was the sex disparity. In men, vitamin D deficiency was significantly associated with a higher risk of hyper-

triglyceridaemia, hypoalphalipoproteinaemia and abnormal AIP after adjusting for potential confounders. In addition to the above reasons, we imagine that some gene clusters located on the Y chromosome may play an important role, which need to be further identified. Another possible explanation for this difference between men and women is that intestinal calcium absorption may be more vitamin D-dependent in men than in women (34). In addition, lifestyle differences such as physical activity, smoking, alcohol consumption, sun exposure and fat intake could also contribute to the dissimilar results between males and females. However, research on the sex differences in the association between vitamin D and dyslipidaemia is rare, and well-designed and prospective investigations are needed to obtain more accurate results.

AIP, the logarithmically transformed ratio of TGs to HDL-C, was first described by Dobiášová as a biomarker of plasma atherosclerosis (22). In their later study, AIP was found to be inversely correlated with the diameter of LDL-C particles and to be a surrogate for the small-dense LDL-C level, which is one of the major causative factors of arteriosclerosis and cardiovascular disease (35). In fact, a growing body of research has suggested that AIP is a strong marker for predicting the risk of CVD. In 2010, Onat et al. conducted a prospective study of 2,676 middle-aged adults and reported that AIP is a reliable biomarker for predicting CVD morbidity (18). A large-sample case-control study conducted by Cai et al. indicated that the association of AIP and coronary artery disease also existed in the Chinese population (36). In our study, serum 25(OH)D levels were inversely associated with AIP in men but were not associated with AIP in women, indicating that vitamin D concentrations might be associated with CVD as well.

Our study also has several limitations that merit consideration. First, this was a cross-sectional study, which was unable to estimate cause-effect relationships. Second, other confounding factors that may influence the relationship between vitamin D and lipid status, such as sunlight exposure, dietary vitamin D intake, waist circumference and physical activity, were not assessed. Third, the participants recruited were from a health management centre, and most were from one province. Therefore, the results might not be representative of the whole Chinese middle-aged and elderly population.

Despite these limitations, the present study has several strengths. The major strength is that we collected data from a relatively large sample of a middle-aged and elderly population residing in central China. In addition, we adjusted for many potential covariates, including age, BMI, FBG, uric acid, creatinine, CRP, Hcy, and calcium, making our results more reliable. Furthermore, we also found an association between vitamin D and AIP, which added to evidence indicating that vitamin D concentrations might be associated with CVD as well.

In summary, our findings showed that vitamin D deficiency was common in a middle-aged and elderly Chinese population and that serum 25(OH)D concentrations were associated with serum lipids. Vitamin D

deficiency might be associated with a higher risk of dyslipidaemia independent of potential confounders. The relationship between 25(OH)D and serum lipids was stronger in men than in women. Therefore, vitamin D status may serve as a biomarker for predicting dyslipidaemia or even CVD. Vitamin D status should be taken into consideration, especially in male patients. Further prospective studies with large samples are needed to provide more evidence to confirm the sex-specific relationship between vitamin D and serum lipid profiles. Further gene research may explain the sex disparity.

Author contributions

Yongman Lv and Le Wang contributed equally to this work.

Disclosure of state of COI

No conflicts of interest to be declared.

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Supporting information

Supplemental online material is available on J-STAGE.

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