

Original Article

Adult serum 25(OH)D3 in Gansu province, northwest China: a cross-sectional study

Jing Liu MD¹, Wenjuan Ma MSc¹, Lianhua Wei MD², Yan Yang MSc³, Ruifei Yang MSc¹, Feifei Shao MSc¹, Yu Wang MSc¹, Limin Tian MD¹

¹Department of Endocrinology, Gansu Provincial Hospital, Lanzhou, People's Republic of China

²Department of Laboratory, Gansu Provincial Hospital, Lanzhou, People's Republic of China

³Department of Medical Record, Gansu Provincial Hospital, Lanzhou, People's Republic of China

Background and Objectives: This analytical cross-sectional study investigated the prevalence of vitamin D deficiency and its association with metabolic risk factors in the adult population of Gansu Province, China. **Methods and Study Design:** In total, 11,157 healthy participants (4,740 men and 6,417 women) were enrolled. A questionnaire was used to assess general characteristics and personal habits. We detected 25-hydroxyvitamin D and associated metabolic parameters through electrochemiluminescence immunoassays. **Results:** The prevalence of severe deficiency (<10 ng/mL), deficiency (10–20 ng/mL), insufficiency (20–30 ng/mL), and sufficiency (≥30 ng/mL) among the participants was 17.3%, 64.6%, 11.8%, and 6.3%, respectively. Vitamin D deficiency was more prevalent in women than in men (82.5% vs 81.1%, $p < 0.001$). The significant predictors of vitamin D deficiency included younger age and female sex ($p < 0.05$), whereas sun exposure, physical activity, and calcium (Ca) supplementation were associated with less vitamin D deficiency ($p < 0.05$). Serum 25(OH)D3 was inversely associated with parathyroid hormone ($r = -0.279$, $p < 0.001$) and positively associated with serum Ca ($r = 0.239$, $p < 0.001$), serum P ($r = 0.090$, $p = 0.018$), LDL cholesterol ($r = 0.100$, $p = 0.008$), and BMI ($r = 0.093$, $p = 0.014$). No significant association was observed between serum 25(OH)D3 and metabolic disorders. **Conclusions:** Vitamin D deficiency is highly prevalent among the adult population of Gansu Province, northwest China, especially young physically inactive and overweight women with limited sunlight exposure, whose biomarkers put them at greater risk of osteoporosis and cardiovascular disease.

Key Words: vitamin D deficiency, gender, sun exposure, physical activity, Gansu, China

INTRODUCTION

Vitamin D is a vital endogenous secosteroid hormone, and its major source is cutaneous synthesis from 7-dehydrocholesterol following solar ultraviolet-B radiation exposure. Traditionally, the active form of vitamin D, 1,25(OH)₂D, regulates mineral and bone metabolism by balancing calcium (Ca) and phosphorus (P) levels. Recent studies have implicated low serum 25(OH)D3 in the causation of nonskeletal chronic diseases such as diabetes, cardiovascular diseases, autoimmune diseases, and metabolic syndrome.^{1,2} It is perhaps surprising, given its perceived essential role to public health, to find that hypovitaminosis D is highly prevalent worldwide (30%–50%). Approximately one billion people were estimated to have vitamin D deficiency.^{3–6}

More than 90% of vitamin D is derived from the cutaneous production, and other factors believed to be related to the lack of sunlight exposure, such as the season, latitude, skin pigmentation, and clothing, can also affect the vitamin D status.^{5,7} However, some studies have reported a considerable increase in vitamin D deficiency, even in some countries with plentiful sunshine, such as Saudi Arabia,⁸ India,⁹ and Iran,¹⁰ and countries located in northern latitudes, such as the United Kingdom¹¹ and Norway.¹² China, with the highest population in the world

and various living habits, is encountering a growing vitamin D deficiency pandemic. Cross-sectional studies have reported that the prevalence of vitamin D deficiency is 69.2% in Shanghai and Beijing¹³ and 75.2% in Lanzhou.¹⁴ However, few studies have examined the current vitamin D status in the Gansu Province, northwest China.

Gansu is a developing province with a population of 3 million and is located at a latitude of 32°31'–42°57' N, longitude of 92°13'–108°46' E, and altitude of 1000–1500 m in the northwest of the People's Republic of China. This mid-latitude area has a continental monsoon climate, with an average annual temperature of 0–16 °C. Determination of the vitamin D status in Gansu Province is necessary and has profound implications for public health. Therefore, this study investigated the vitamin D status and the potential determinants of low serum

Corresponding Author: Dr Limin Tian, Department of Endocrinology, Gansu Provincial Hospital, 204 Dong Gang West Road, Lanzhou, 730000, People's Republic of China.

Tel: +86-15293184257; Fax: 0931-8281582

Email: tlm6666@sina.com

Manuscript received 19 November 2016. Initial review completed 15 February 2017. Revision accepted 25 April 2017.

doi: 10.6133/apjn.092017.06

25(OH)D₃ and their relationship with metabolic risk factors in the adult population of Gansu Province, China.

METHODS

Participants

This study used data from a cross-sectional study that examined the vitamin D status of residents of Gansu Province. From June 2014 to December 2015, 11,300 adults voluntarily participated in the survey. Participants were arbitrarily chosen from seven representative geographical cities in Gansu Province through stratified, multistage probability population sampling. The smallest investigation unit was a natural village in rural areas and a city community in urban areas. Only people who had been living in their current residence for at least 5 years were eligible to participate.

In this study, free-living residents of Gansu Province who were aged ≥ 18 years and had not received sex hormones, steroid hormones, parathyroid hormones (PTHs), calcitonins, and bisphosphonates in the last 6 months were enrolled. Pregnant or lactating women; patients with chronic illnesses; those who had undergone enterectomy, gastrointestinal fistulation, subtotal gastrectomy, and liver and kidney transplantation; those with abnormal liver and renal function; and those using medicines known for affecting bone metabolism were excluded.

Questionnaire

Information regarding demographic factors, namely name, region, age, sex, and education (primary school, junior high school, senior high school, or college), and the menopausal status of women (a woman who reported that her menses had ceased for 1 year or more was considered postmenopausal) was included in the questionnaire.

Information regarding participants' history of diseases including cancer; autoimmune disease; cardiovascular disease; hypertension; dyslipidemia; diabetes mellitus; and bone, renal, and gastrointestinal disorders was obtained.

Information regarding the following behavioral factors was collected: smoking behavior (never or current), alcohol consumption (never or current), amount of physical activity performed recently (physical activity was defined as moderate strenuous effort for at least half an hour, e.g., walking, cycling, or gardening, and dichotomized into 2 or less days per week vs 3 or more days per week), supplemental Ca (yes or no), and exposure to sunlight (≤ 30 min/d or >30 min/d). Participants' duration of sun exposure sufficient to induce cutaneous vitamin D synthesis was evaluated. In addition, the duration of sun exposure or outdoor activity between 10:00 AM and 3:00 PM was examined. Participants' use of a sun protection factor (SPF) product or a veil while being outside was also evaluated, and the time spent outdoors when using SPF products or a veil was accounted for (i.e., excluded) while calculating the total duration of sun exposure. All self-reported information in the questionnaire was documented by the same staff group, who were trained in the methods used.

Anthropometric and biochemical assessments

To calculate the BMI, height was recorded without shoes,

and weight was measured wearing light clothing (weight in kilograms divided by height in meter squared). The waist and hip circumferences were measured to calculate the waist-to-hip ratio (WHR). Systolic and diastolic blood pressure were measured by trained nurses using a mercury sphygmomanometer on the right arm of participants after 5-min rest in a comfortable sitting position.

Blood samples were drawn from all participants after overnight fasting for measuring the serum 25(OH)D₃ as well as other biochemical parameters including bone turnover markers (serum Ca, P, PTH, osteocalcin, and β -CTx) and other metabolic parameters related to metabolic diseases (total cholesterol, triglyceride, HDL cholesterol, LDL cholesterol, and glucose). The total serum 25(OH)D₃ was assayed through a chemiluminescence particle immunoassay (Abbott Laboratories, Barcelona, Spain). All these measurements were enzymatically measured using an AU5400 automatic analyzer (Olympus, Beckman Coulter, USA).

The areal bone mineral density (BMD; g/cm²) was measured at the forearms through dual-energy X-ray absorptiometry (Osteometer MediTech, Hawthorne, CA, USA).

Serum 25(OH)D₃ thresholds

The serum 25(OH)D₃ was categorized into four ordinal categories according to the commonly accepted cutoff: severe 25(OH)D₃ deficiency (<10 ng/mL), deficiency (10–20 ng/mL), insufficiency (20–30 ng/mL), and sufficiency (30–150 ng/mL). A serum 25(OH)D₃ level of >150 ng/mL was considered vitamin D intoxication.^{3,15}

Statistical analyses

The statistical software SPSS, version 19.0 (IBM Corp, Armonk, New York), was used for statistical analyses. Continuous variables are expressed as the mean (standard deviation [SD]), whereas skewed variables are presented as the median (interquartile range) and categorical variables as frequencies. For continuous variables, the rank sum test and t test were used for comparing independent samples, and one-way ANOVA was used for comparing different group characteristics. Comparative analyses of categorical variables were performed using the chi-square test. To assess the determinants of vitamin D deficiency, variables derived from the questionnaire were separately included in a logistic regression model. Pearson's correlations were used to assess the association between variables. $p < 0.05$ was considered statistically significant.

Ethical approval and informed consent

Ethical approval was obtained from the Gansu Provincial Hospital Ethics Committee (ethical approval number: 2014-050) and all participants signed the informed consent.

RESULTS

Descriptive characteristics of the study population

In total, 11,157 adults (4,740 men and 6,471 women) were recruited in this study. The characteristics of the study participants are listed in Table 1. The average age of the participants was 53.6 (10.7) years (range, 18–79 years). The overall mean serum 25(OH)D₃ was 13.8

Table 1. Demographic characteristics of the study population

Characteristics	No. of participants		25(OH)D3 (ng/mL)		<i>p</i>
	n	%	Median	Q25-Q75	
All	11157	100	13.8	11.0-17.8	
Gender					<0.001
Men	4740	42.5	15.0	12.1-18.5	
Women	6417	57.5	13.1	10.4-17.2	
Premenopause	3690	57.5	13.7	10.9-18.3	<0.001
Postmenopause	2727	42.5	12.3	9.9-15.9	
Age groups (year)					<0.001
18~	111	1.0	12.8	9.5-16.6	
30~	1020	9.1	13.7	10.9-17.2	
40~	2833	25.4	13.0	10.2-16.9	
50~	3333	29.9	14.4	11.3-18.3	
60~	2803	25.1	14.2	11.4-18.5	
70~	1057	9.5	13.5	10.7-17.7	
Region					<0.001
Urban area	3916	35.1	11.8	9.3-15.1	
Rural area	7241	64.9	15.0	12.0-19.9	
Educational level (years)					<0.001
Primary school	2311	20.7	11.7	9.5-15.1	
Junior high school	2261	20.3	13.5	10.7-17.2	
Senior high school	3888	34.8	14.7	11.9-18.6	
College	2697	24.2	14.9	11.8-18.9	
Personal habits					
Current smoker					0.073
yes	2019	18.1	14.8	11.7-18.1	
no	9138	81.9	13.6	10.8-17.7	
Alcohol use					0.055
yes	2678	24.0	15.2	12.2-18.5	
no	8479	76.0	13.5	10.7-17.5	
Sunlight exposure (min/day)					0.027
≤30	9316	83.5	13.8	11.0-17.7	
>30	1841	16.5	14.3	11.5-18.9	
Physical activity (days/week)					<0.001
0-2	5322	47.7	13.5	10.6-17.1	
≥3	5835	52.3	14.3	11.5-18.9	
Use of calcium supplement					<0.001
yes	3448	30.9	15.0	11.8-19.9	
no	7709	69.1	13.4	10.6-17.1	
BMI (kg/m ²)					0.244
<18.5	290	2.6	13.3	9.6-16.8	
18.5-24.9	6538	58.6	13.6	10.8-17.3	
25.0-29.9	3749	33.6	14.3	11.2-18.3	
≥30	580	5.2	13.8	11.1-18.0	

(11.0–17.8) ng/mL (range, 1.1–121.9 ng/mL).

Vitamin D status of study participants

The prevalence of vitamin D deficiency, stratified by vitamin D status, is shown in Table 2, together with the median (Q25–Q75) serum 25(OH)D3 of subgroups listed in Table 1. In total, 1,927 (17.3%), 7,210 (64.6%), 1,312 (11.8%), and 708 (6.3%) participants had a serum 25(OH)D3 level of <10, 10–19.9, 20–29.9, and ≥30 ng/mL, respectively.

Women had a significantly lower serum 25(OH)D3 than did men [13.1 (10.4–17.2) vs 15.0 (12.1–18.5) ng/mL; $p<0.001$]. In addition, the prevalence of vitamin D deficiency was higher in women (82.5%) than in men (81.1%; $p<0.001$), especially in postmenopausal women [13.7 (10.9–18.3) vs 12.3 (9.9–15.9) ng/mL and 78.5% vs 87.8%].

The results indicated a strong age dependence with vitamin D status; younger adults (18–30 years) generally had a higher prevalence of vitamin D deficiency (87.9%)

than did older adults (60–80 years; 80.3%; $p<0.001$). The total serum 25(OH)D3 was higher in participants who had a higher educational level, a higher sunlight exposure duration, and a higher physical activity frequency; used Ca supplements; and resided in rural areas ($p<0.05$). The vitamin D status was not affected by smoking and drinking ($p>0.05$).

Association of vitamin D deficiency with metabolic parameters

Biochemical parameters and their comparisons of the subgroup of the hypovitaminosis status are listed in Table 3. Compared with the control participants (serum 25(OH)D3 ≥20 ng/mL), participants with serum 25(OH)D3 <20 ng/mL had significantly lower Ca, serum β-CTx, and PTH levels and BMD ($p<0.05$). However, no significant differences were observed in the metabolism-associated variables. In all participants, serum 25(OH)D3 was positively associated with serum Ca ($r=0.239$, $p<0.001$), serum P ($r=0.090$, $p=0.018$), LDL ($r=0.100$, p

Table 2. Prevalence of vitamin D statuses

Characteristics	25(OH)D3 (ng/mL)								<i>p</i>
	<10		10-20		20-30		≥30		
	n	%	n	%	n	%	n	%	
All	1927	17.3	7210	64.6	1312	11.8	708	6.3	
Gender									<0.001
Men	476	10.0	3368	71.1	692	14.6	204	4.3	
Women	1451	22.6	3842	59.9	620	9.7	504	7.8	
Premenopause	668	18.1	2229	60.4	435	11.8	358	9.7	
Postmenopause	783	28.7	1613	59.1	185	6.8	146	5.4	
Age groups(year)									<0.001
18~	34	30.3	64	57.6	10	9.1	3	3.0	
30~	181	17.7	708	69.4	101	9.9	30	3.0	
40~	644	22.7	1729	61.1	332	11.7	128	4.5	
50~	507	15.2	2172	65.2	399	12.0	255	7.6	
60~	383	13.7	1866	66.6	342	12.2	212	7.5	
70~	178	16.8	671	63.5	128	12.1	80	7.6	
Region									<0.001
Urban area	1225	31.3	2482	63.4	182	4.6	27	0.7	
Rural area	702	9.7	4728	65.3	1130	15.6	681	9.4	
Educational level (year)									<0.001
Primary school	714	30.9	1353	58.6	159	6.8	85	3.7	
Junior high school	443	19.6	1439	63.6	257	11.4	122	5.4	
Senior high school	477	12.3	2578	66.3	531	13.7	302	7.7	
College	293	10.9	1840	68.2	365	13.6	199	7.3	
BMI (kg/m ²)									0.828
<18.5	51	17.6	169	58.3	45	16.6	22	7.5	
18.50–24.99	1190	18.2	4178	63.9	745	11.4	425	6.5	
25.00–29.99	570	15.2	2478	66.1	484	12.9	217	5.8	
≥30	116	20.0	385	66.4	35	6.0	44	7.6	

Table 3. Metabolic parameters according to the serum 25(OH)D3 level

Characteristics	Total		25(OH)D3 (ng/mL)				<i>p</i>
	Mean	SD	<20		≥20		
			Mean	SD	Mean	SD	
Age (years)	53.6	10.7	53.4	10.7	56.6	10.6	0.035
CA (mmol/L)	2.4	0.2	2.4	0.2	2.6	0.2	<0.001
P (mmol/L)	1.1	0.3	1.1	0.3	1.2	0.2	0.034
PTH (pg/mL)	78.1	32.2	79.4	32.6	61.5	21.0	<0.001
OSTEOC (ng/mL)	19.1	7.9	19.0	7.9	20.3	8.1	0.277
β-CTx (ng/mL)	0.4	0.6	0.4	0.6	0.6	1.3	0.029
SBP (mmHg)	131.7	22.4	131.8	22.5	129.8	21.9	0.520
DBP (mmHg)	83.4	13.5	83.4	13.5	83.6	13.2	0.902
CHOL (mmol/L)	4.9	2.0	4.9	2.1	5.1	1.2	0.594
TG (mmol/L)	1.8	1.2	1.8	1.2	1.9	1.2	0.730
LDL (mmol/L)	3.2	0.9	3.2	0.9	3.3	1.1	0.468
HDL (mmol/L)	1.5	0.4	1.5	0.4	1.5	0.5	0.307
FBG (mmol/L)	5.7	1.9	5.7	1.9	5.4	1.1	0.379
WHR	0.9	0.1	0.9	0.1	0.9	0.1	0.482
BMI (kg/m ²)	24.2	3.5	24.2	3.4	24.7	3.6	0.238
BMD	0.5	0.2	0.5	0.1	0.5	0.2	0.016

CA: calcium; P: phosphorus; PTH: parathyroid hormone; OSTEOC: osteocalcin; β-CTx: beta-isomerised C-terminal telopeptide of collagen type I; SBP: systolic blood pressure; DBP: diastolic blood pressure; CHOL: cholesterol; TG: triglyceride; LDL: low-density lipoprotein cholesterol; HDL: high-density lipoprotein cholesterol; FBG: fasting blood glucose; WHR: waist-to-hip ratio; BMI: body mass index; BMD: bone mineral density.

=0.008), and BMI ($r=0.093$, $p=0.014$) and inversely associated with PTH ($r=-0.279$, $p<0.001$) (Table 4).

Significant predictors of vitamin D deficiency

Table 5 lists the demographic, social, and behavioral factors associated with the risk of vitamin D deficiency in the study participants. Multiple logistic regression analysis indicated that younger age ($OR=0.971$; $p=0.035$) and female sex ($OR=2.017$; $p=0.014$) were independent risk

factors for vitamin D deficiency. Notably, sun exposure ($OR=0.604$; $p=0.034$), physical activity ($OR=0.864$; $p=0.026$), and Ca supplementation ($OR=0.489$; $p=0.019$) prevented vitamin D deficiency.

DISCUSSION

The results of this study revealed that vitamin D deficiency is highly prevalent among the adult population of Gansu Province, northwest China. To the best of our

Table 4. Correlations of serum 25(OH)D3 with descriptive and metabolic variables

Variable	r	p
Age (years)	0.063	0.099
CA (mmol/L)	0.239	<0.001
P (mmol/L)	0.090	0.018
PTH (pg/mL)	-0.279	<0.001
OSTEOC (ng/mL)	0.030	0.981
β-CTX (ng/mL)	0.050	0.189
SBP (mmHg)	0.012	0.751
DBP (mmHg)	0.034	0.373
CHOL (mmol/L)	0.032	0.393
TG (mmol/L)	0.063	0.098
LDL (mmol/L)	0.100	0.008
HDL (mmol/L)	0.005	0.892
FBG (mmol/L)	-0.057	0.135
WHR	-0.020	0.596
BMI (kg/m ²)	0.093	0.014
BMD	0.022	0.355

Abbreviation cross-referenced to Table 3.

Table 5. Independent predictors of vitamin D deficiency (total 25(OH)D3 <20 ng/mL)

Variable/group	OR	95 % CI	p
Age (years)	0.97	0.95, 0.99	0.035
Gender			
Men	1.00	Ref.	
Women	2.02	1.15, 3.52	0.014
Premenopause	Ref.		
Postmenopause	2.32	0.90, 5.98	0.080
Region			
Urban area	1.00	Ref.	
Rural area	0.83	0.29, 2.38	0.730
Educational level (years)	1.76	0.61, 5.01	0.289
Personal habits			
Current smoker			
no	1.00	Ref.	
yes	0.45	0.24, 0.83	0.100
Alcohol use			
no	1.00	Ref.	
yes	0.44	0.24, 0.81	0.069
Sunlight exposure (min/day)			
≤30	1.00	Ref.	
>30	0.60	0.21, 1.72	0.034
Physical activity (days/week)			
0–2	1.00	Ref.	
≥3	0.86	0.64, 2.09	0.026
Use of calcium supplement			
no	1.00	Ref.	
yes	0.49	0.27, 0.89	0.019

Ref.: reference category. Abbreviation: cross-referenced to Table 3.

knowledge, this is the first large-scale cross-sectional investigation of the vitamin D status and the independent predictors of vitamin D deficiency in adults living in Gansu Province. The results indicated that vitamin D deficiency is a severe health problem in Gansu Province, particularly in women and younger people.

Approximately 81.9% of study participants were diagnosed as having vitamin D deficiency (<20 ng/mL). Compared with the prevalence rate of vitamin D deficiency reported in Caucasian Americans in the United States,¹⁶ Norwegians,¹⁷ and Africans,¹⁸ the prevalence rate was extremely higher in the residents of Gansu Province. Additionally, the prevalence rate in our study was higher than that reported in several cities in China, such

as Beijing,¹⁹ Shanghai, and Lanzhou,¹⁴ the provincial capital of Gansu. This high prevalence may be due to the location of these areas; compared with Gansu Province, Shanghai and Beijing are located at a lower latitude (31°N and 40°N, respectively). In addition, the personal habits of the residents of these cities differ.

In general, the cutaneous production of vitamin D declines with age,^{20,21} and elderly people are usually confined indoors for prolonged periods of time, which compounds the problem. However, in contrast to the general finding, we found that the serum 25(OH)D3 increased with age. This finding is consistent with that of a previous study performed in five cities in China, which reported that younger adults (18–39 years) generally had a lower

25(OH)D3 level than did those above 49 years.²² This may be because in our study, relatively young adults had a median age of 54 years and older people received Ca supplements. Similarly, vitamin D deficiency is higher in women because of the use of sunscreen and parasols or a higher amount of time spent indoors,²³⁻²⁵ and our result is consistent with those of previous studies reporting that vitamin D deficiency or insufficiency was more severe in women,²⁶ especially in postmenopausal women.²⁷ In addition, vitamin D deficiency was equally prevalent among urban and rural participants²⁸ in some studies, whereas urban participants were found to have higher deficiency^{29,30} in some other studies. In South India (13°N), vitamin D levels were significantly lower in urban participants than in rural participants.³¹ Consistent with these studies, our finding also indicated this phenomenon may be due to urbanization^{29,30,32} and air pollution.³³

The aforementioned factors, together with personal habits, such as sun exposure,^{34,35} physical activity,³⁶ and use of Ca supplementation,³⁷ are independent risk factors for vitamin D deficiency. The cumulative effects of such factors play an influential role in maintaining vitamin D levels. This phenomenon was also observed in our study.

We observed that serum 25(OH)D3 was positively associated with serum Ca and P levels because the intestinal absorption of Ca and P is positively affected by vitamin D sufficiency.^{3,38} An inverse association between PTH and serum 25(OH)D3, which has been reported in several studies,^{15,39,40} was also observed in our study. Furthermore, vitamin D deficiency, especially severe vitamin D deficiency (25(OH)D3 <10 ng/mL), was significantly associated with metabolic syndrome.⁴¹ However, we did not find a relationship between hypertension, diabetes, or dyslipidemia and vitamin D deficiency in all participants. In contrast to some previous cross-sectional studies that have proposed that vitamin D plays a protective role in cardiovascular disease,^{42,43} we observed that serum 25(OH)D3 was positively associated with serum LDL in adults. Studies have reported inconsistent results^{42,44,45} regarding the correlation of serum 25(OH)D3 with LDL. Several possible explanations that can explain our findings were previously reported in a study of a cohort of British Bangladeshis, which also observed a positive correlation between serum 25(OH)D3 and serum LDL.⁴⁶ Zitterman et al postulated that vitamin D can increase fat absorption from the gut by inducing the formation of Ca fatty soaps.⁴⁴ By contrast, the lower content of Ca in the gut may also reduce the compound of Ca and bile acids, subsequently reducing cholesterol excretion.⁴⁴ Therefore, a diet rich in Ca may help offset the increase in serum LDL. Another reason may be that the clearance of serum LDL from circulation is potentially attenuated by the compound of 1,25(OH)₂D and LDL.⁴⁷ Because the effect of serum 25(OH)D3 on lipid levels is currently unclear, additional studies evaluating the mechanistic link between lipid metabolism and vitamin D are required. In addition, in our study, serum 25(OH)D3 was positively associated with BMI, a finding inconsistent with earlier studies that have reported that BMI/WHR is inversely associated with serum 25(OH)D3,^{48,49} nevertheless, our finding is consistent with that of a study conducted in China.²²

Our study has some major strengths. We included a large, broadly representative sample frame of adults from Gansu Province. In addition, we conducted a comprehensive analysis of various potential risk factors for vitamin D deficiency, facilitated by the availability of background data including demographic characteristics, personal habits, and anthropometric and metabolic parameters. However, our study has some limitations. First, blood samples were not collected round the year; this failed to help us analyze the effect of seasonal variation on serum 25(OH)D3 which has recently been reported to follow a sinusoidal pattern together with intact PTH throughout the year at various northerly latitudes.⁵⁰ Second, the results may have selection and report biases because the self-reported data related to personal habits may not be accurate. Furthermore, some unrecognized confounding factors might be present. Finally, because of the cross-sectional nature of our study, we could not infer causality.

Conclusion

Our results suggest an alarmingly high prevalence of vitamin D deficiency (as defined by serum 25(OH)D3 <20 ng/mL) among all populations of Gansu Province, particularly functional deficiency among women, postmenopausal women, young people, and those residing in urban areas. Use of Ca supplements, sunlight exposure, and physical activity were highly protective against vitamin D deficiency. Moreover, the results indicated that serum 25(OH)D3 was positively associated with serum LDL and BMI, whereas serum 25(OH)D3 and metabolic syndrome were not. To maintain the health of residents of Gansu Province, further research on epidemiological and targeted future prevention measures is imperative.

ACKNOWLEDGEMENTS

The study is a collaboration between the Gansu Provincial Hospital and the local health services of seven regions. We thank the local general practitioners and their staff who participated in the study. We thank the management, research, and clerical team for their outstanding work. We especially thank the study participants.

AUTHOR DISCLOSURES

No authors receive financial support or relationships with industry that might pose a conflict of interest.

REFERENCES

1. Pittas AG, Joseph L, Hu FB, Bess DH. 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. doi: 10.1210/jc.2007-0298.
2. Kim KT, Kang KC, Shin DE, Lee SH, Lee JH, Kwon TY. Prevalence of vitamin D deficiency and its association with metabolic disease in Korean orthopedic patients. *Orthopedics.* 2015;38:e898-903. doi: 10.3928/01477447-20151002-57.
3. Holick MF. Vitamin D deficiency. *N Engl J Med.* 2007;357:266-81. doi: 10.1056/NEJMra070553.
4. Lips P. Worldwide status of vitamin D nutrition. *J Steroid Biochem Mol Biol.* 2010;121:297-300. doi: 10.1016/j.jsbmb.2010.02.021.
5. Mithal A, Wahl DA, Bonjour JP, Burckhardt P, Dawson-Hughes B, Eisman JA et al. Global vitamin D status and

- determinants of hypovitaminosis D. *Osteoporos Int.* 2009;20:1807-20. doi: 10.1007/s00198-009-0954-6.
6. Holick MF. The vitamin D deficiency pandemic and consequences for nonskeletal health: mechanisms of action. *Mol Aspects Med.* 2008;29:361-8. doi: 10.1016/j.mam.2008.08.008.
 7. Holick MF. McCollum Award Lecture, 1994: vitamin D--new horizons for the 21st century. *Am J Clin Nutr.* 1994;60:619-30.
 8. Aly YF, El Koumi MA, Abd El Rahman RN. Impact of maternal vitamin D status during pregnancy on the prevalence of neonatal vitamin D deficiency. *Pediatr Rep.* 2013;5:e6. doi: 10.4081/pr.2013.e6.
 9. Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. *Am J Clin Nutr.* 2005;81:1060-4.
 10. Salek M, Hashemipour M, Aminorroaya A, Gheiratmand A, Kelishadi R, Ardestani PM et al. Vitamin D deficiency among pregnant women and their newborns in Isfahan, Iran. *Exp Clin Endocrinol Diabetes.* 2008;116:352-6.
 11. Gale CR, Robinson SM, Harvey NC, Javaid MK, Jiang B, Martyn CN et al. Maternal vitamin D status during pregnancy and child outcomes. *Eur J Clin Nutr.* 2008;62:68-77.
 12. Madar AA, Stene LC, Meyer HE. Vitamin D status among immigrant mothers from Pakistan, Turkey and Somalia and their infants attending child health clinics in Norway. *Br J Nutr.* 2009;101:1052-8. doi: 10.1017/S0007114508055712.
 13. 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. doi: 10.2337/dc09-0209.
 14. Zhen D, Liu L, Guan C, Zhao N, Tang X. High prevalence of vitamin D deficiency among middle-aged and elderly individuals in northwestern China: Its relationship to osteoporosis and lifestyle factors. *Bone.* 2015;71:1-6. doi: 10.1016/j.bone.2014.09.024.
 15. 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. doi: 10.1210/jc.2011-0385.
 16. Looker AC, Pfeiffer CM, Lacher DA, Schleicher RL, Picciano MF, Yetley EA. Serum 25-hydroxyvitamin D status of the US population: 1988-1994 compared with 2000-2004. *Am J Clin Nutr.* 2008;88:1519-27. doi: 10.3945/ajcn.2008.26182.
 17. Larose TL, Chen Y, Camargo CA, Jr., Langhammer A, Romundstad P et al. Factors associated with vitamin D deficiency in a Norwegian population: the HUNT Study. *J Epidemiol Community Health.* 2014;68:165-70. doi: 10.1136/jech-2013-202587.
 18. Pettifor JM. Nutritional rickets: deficiency of vitamin D, calcium, or both? *Am J Clin Nutr.* 2005;80:1725-9.
 19. Lu L, Yu ZJ, Pan A, Hu FB, Franco OH, Li HX et al. Plasma 25-hydroxyvitamin D concentration and metabolic syndrome among middle-aged and elderly Chinese individuals. *Diabetes Care.* 2009;32:1278-83. doi: 10.2337/dc09-0209.
 20. Holick MF, Matsuoka LY, Wortsman J. Age, vitamin D, and solar ultraviolet. *Lancet.* 1989;2:1104-5.
 21. Maclaughlin J, Holick MF. Aging decreases the capacity of human skin to produce vitamin D3. *J Clin Invest.* 1985;76:1536-8.
 22. Yu S, Fang H, Han J, Cheng X, Xia L, Li S et al. The high prevalence of hypovitaminosis D in China: a multicenter vitamin D status survey. *Medicine (Baltimore).* 2015;94:e585. doi: 10.1097/MD.0000000000000585.
 23. van der Wielen RP, Löwik MR, van den Berg H, de Groot LC, Haller J, Moreiras O, van Staveren WA. Serum vitamin D concentrations among elderly people in Europe. *Lancet.* 1995;346:207-10.
 24. Snijder MB, van Dam RM, Visser M, Deeg DJ, Dekker JM, Bouter LM, Seidell JC, Lips P. Adiposity in relation to vitamin D status and parathyroid hormone levels: a population-based study in older men and women. *J Clin Endocrinol Metab.* 2005;90:4119-23.
 25. Smith BM, Schwartzman K, Bartlett G, Menzies D. Potentially modifiable determinants of vitamin D status in an older population in the Netherlands: the Hoorn Study. *Am J Clin Nutr.* 2007;85:755-61.
 26. Lips P. Worldwide status of vitamin D nutrition. *J Steroid Biochem Mol Biol.* 2010;121:297-300. doi: 10.1016/j.jsbmb.2010.02.021.
 27. Lim S, Kung A, S, Soontrapa S, Tsai K. Vitamin D inadequacy in postmenopausal women in Eastern Asia. *Curr Med Res Opin.* 2008;24:99-106.
 28. Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. *Am J Clin Nutr.* 2005;81:1060-4.
 29. Puri S, Marwaha RK, Agarwal N, Tandon N, Agarwal R, Grewal K et al. Vitamin D status of apparently healthy schoolgirls from two different socioeconomic strata in Delhi: relation to nutrition and lifestyle. *Br J Nutr.* 2008;99:876-82.
 30. Harinarayan CV, Ramalakshmi T, Prasad UV, Sudhakar D, Srinivasarao PV, Sarma KV et al. High prevalence of low dietary calcium, high phytate consumption, and vitamin D deficiency in healthy south Indians. *Am J Clin Nutr.* 2007;85:1062-7.
 31. Harinarayan CV, Ramalakshmi T, Prasad UV, Sudhakar D. Vitamin D status in Andhra Pradesh: a population based study. *Indian J Med Res.* 2008;127:211-8.
 32. Gannage-Yared MH, Chemali R, Yaacoub N, Halaby G. Hypovitaminosis D in a sunny country: relation to lifestyle and bone markers. *J Bone Miner Res.* 2000;15:1856-62. doi: 10.1359/jbmr.2000.15.9.1856.
 33. Agarwal KS, Mughal MZ, Upadhyay P, Berry JL, Mawer EB, Puliyl JM. The impact of atmospheric pollution on vitamin D status of infants and toddlers in Delhi, India. *Arch Dis Child.* 2002;87:111-3.
 34. Rosen CJ. Clinical practice. Vitamin D insufficiency. *N Engl J Med.* 2011;364:248-54. doi: 10.1056/NEJMc1009570.
 35. Junaid K, Rehman A, Jolliffe DA, Wood K, Martineau AR. High prevalence of vitamin D deficiency among women of child-bearing age in Lahore Pakistan, associating with lack of sun exposure and illiteracy. *BMC Womens Health.* 2014;15:1-8. doi: 10.1186/s12905-015-0242-x.
 36. Man PW, Lin W, van der Meer IM, Heijboer AC, Wolterbeek R, Numans ME et al. Vitamin D status in the Chinese population in the Netherlands: The DRAGON study. *J Steroid Biochem Mol Biol.* 2015. doi: 10.1016/j.jsbmb.2015.12.004.
 37. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. *Endocr Rev.* 2001;22:477-501.
 38. Heaney RP. Functional indices of vitamin D status and ramifications of vitamin D deficiency. *Am J Clin Nutr.* 2004;80:1706S-9S.

39. Ross AC, Taylor CL, Yaktine AL, Valle HBD. Dietary Reference Intakes for Calcium and Vitamin D. Washington, DC: National Academies Press; 2011.
40. Lips P, Duong T, Oleksik A, Black D, Cummings S, Cox D et al. A global study of vitamin D status and parathyroid function in postmenopausal women with osteoporosis: baseline data from the multiple outcomes of raloxifene evaluation clinical trial. *J Clin Endocrinol Metab.* 2001;86:1212-21.
41. Strange RC, Shipman KE, Ramachandran S. Metabolic syndrome: a review of the role of vitamin D in mediating susceptibility and outcome. *World J Diabetes.* 2015;6:896-911. doi: 10.4239/wjd.v6.i7.896.
42. Major GC, Alarie F, Doré J, Phouuttama S, Tremblay A. Supplementation with calcium + vitamin D enhances the beneficial effect of weight loss on plasma lipid and lipoprotein concentrations. *Am J Clin Nutr.* 2007;85:54-9.
43. Chiu KC, Chu A, Go VLW, Saad MF. Hypovitaminosis D is associated with insulin resistance and β cell dysfunction. *Am J Clin Nutr.* 2004;79:820-5.
44. Zittermann A, Frisch S, Berthold HK, Götting C, Kuhn J, Kleesiek K et al. Vitamin D supplementation enhances the beneficial effects of weight loss on cardiovascular disease risk markers. *Am J Clin Nutr.* 2009;89:1321-7. doi: 10.3945/ajcn.2008.27004.
45. John WG, Noonan K, Mannan N, Boucher BJ. Hypovitaminosis D is associated with reductions in serum apolipoprotein A-I but not with fasting lipids in British Bangladeshis. *Am J Clin Nutr.* 2005;82:517-22.
46. Ashraf AP, Alvarez JA, Gower BA, Saenz KH, McCormick KL. Associations of serum 25-hydroxyvitamin D and components of the metabolic syndrome in obese adolescent females. *Obesity (Silver Spring).* 2011;19:2214-21. doi: 10.1038/oby.2011.110.
47. Teramoto T, Endo K, Ikeda K, Kubodera N, Kinoshita M, Yamanaka M et al. Binding of vitamin D to low-density lipoprotein (LDL) and LDL receptor-mediated pathway into cells. *Biochem Biophys Res Commun.* 1995;215:199-204.
48. Foo LH, Zhang Q, Zhu K, Ma G, Trube A, Greenfield H et al. Relationship between vitamin D status, body composition and physical exercise of adolescent girls in Beijing. *Osteoporos Int.* 2009;20:417-25. doi: 10.1007/s00198-008-0667-2.
49. Reis JP, Mühlen DV, Miller ER, Michos ED, Appel LJ. Vitamin D status and cardiometabolic risk factors in the United States adolescent population. *Pediatrics.* 2009;124:e371-9. doi: 10.1542/peds.2009-0213.
50. Kroll MH, Bi C, Garber CC, Kaufman HW, Liu D, Caston-Balderrama A et al. Temporal relationship between vitamin D status and parathyroid hormone in the United States. *PLoS One.* 2015;10:e0118108. doi: 10.1371/journal.pone.0118108.