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Gender Differences in Vitamin D Status in China

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Background: Vitamin D insufficiency is widespread in China. Various factors influence vitamin D level in the body. The present study investigated vitamin D status of residents in Jinzhong city, China, and analyzed the influence of gender on vitamin D status.

Material/Methods: In this cross-sectional study, 302 participants (176 men and 126 women) were recruited. Anthropometric data (body circumferences and height, weight) were collected, and serum vitamin D concentration was tested.

Results: Inadequate levels of vitamin D were found in 69% of men and 75% of women. Women's 25(OH)D level (38.40±12.37 nmol/l) was substantially lower than that of the men (43.49±14.78 nmol/l) ($p<0.01$). The young women group had the lowest vitamin D level, which was even significantly below that of the elderly women group. Multiple linear regression analysis showed gender was significantly associated with vitamin D status ($p<0.01$).

Conclusions: Vitamin D deficiency is common in residents of Jinzhong during the winter. Compared to men, women are more prone to have inadequate vitamin D levels.

MeSH Keywords: **Calcifediol • Female • Sexism • Vitamin D Deficiency**

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Background

Recently, vitamin D insufficiency has gained increased research attention. The major source of vitamin D in the body is skin biosynthesis from exposure to sunshine. On average, at least 80% of total vitamin D in the body is generated in the skin [1]. Diet is another source of vitamin D, but few foods contain large amounts of vitamin D, except for some fatty fish and a few animal-derived foods, like dairy, fat, and eggs [2,3]. Moreover, some sun-dried fungi contain natural vitamin D_2.

The typical biologic roles of vitamin D were thought to be regulating the metabolism of calcium and phosphorus, thereby affecting bone health [4]. However, a growing number of studies have found that many tissues and organs (not just the kidneys, as previously thought) can produce $1,25(OH)_2D$, and the vitamin D receptor was found to be expressed in most tissues, suggesting that vitamin D has non-skeletal physiological functions [5,6]. In fact, accumulating evidence suggests that $1,25(OH)_2D$, the bioactive molecule of vitamin D in the body, participates in the processes of immune regulation, apoptosis, and cellular proliferation and differentiation by directly or indirectly affecting expression of genes [5,7,8]. Thus, inadequate vitamin D could be a basic cause of many diseases, including cardiovascular disease [9], cancer [10–12], and autoimmune diseases [7]. There is a need for individuals to learn their vitamin D status through testing, and public health research is needed to better understand the factors affecting vitamin D levels.

The definition of vitamin D serum status has been controversial due to limited knowledge about physiological functions of vitamin D. At present, the cutoff values of serum vitamin D concentrations issued by the Institute of Medicine (IOM, USA) in 2011 are most widely accepted, defining vitamin D sufficiency as serum 25(OH) D >50 nmol/L, inadequacy as 30–50 nmol/L, and deficiency as <30 nmol/L [13]. It was estimated that approximately 30–50% of all people (more than 1 billion people worldwide) have vitamin D insufficiency [14,15]. The NHANES III survey (National Health and Nutrition Examination Survey III, USA) found that 25–57% of American adults in low-latitude areas in winter and 21–49% in high-latitude areas in summer had insufficient vitamin D (<62.5 nmol/L) [16]. In Europe, many people in Central and Western Europe had vitamin D concentration of 11–20 ng/mL (about 34–62 nmol/L) in winter, which was regarded as insufficient [17]. Studies from other countries, including Korea, Japan, India, Iran, Canada, Australia, and Brazil, presented similar situations, with high prevalence of serum 25(OH)D insufficiency in different groups and ethnicities [18–23]. Therefore, the worldwide population of people with vitamin D insufficiency may be huge, even in sunny areas like Singapore [24].

Vitamin D insufficiency is serious throughout the general population of China. A multicenter study carrying out in 5 large cities in China reported that the prevalence of vitamin D insufficiency (serum 25(OH)D <50 nmol/L) was 55.9% in urban populations [25]. In the elderly, vitamin D status could be worse. Two studies of residents in northern cities – Beijing and Shenyang (latitude 40° north and 42° north, respectively) – indicated that 80% of women over 60 years old had vitamin D insufficiency (<50 nmol/L) [26,27]. In Shanghai (latitude 31° north), 30% and 46% of adult men and women, respectively, had insufficient vitamin D (<20 ng/mL, equal to <60.24 nmol/L) [28]. Even in Hong Kong (latitude 22° north), 72% of young adults were reported to have vitamin D insufficiency (<30 nmol/l) [29]. Therefore, the issue of vitamin D status in Chinese people warrants more emphasis.

Many factors have been thought to affect vitamin D status. Latitude, season, age, diet, obesity, and outdoor exercise were reported to be determinants of serum vitamin D level [30,31]. The present study assessed serum vitamin D concentrations in Jinzhong city in northern China, checking their vitamin D status, and analyzing the association of gender with vitamin D levels.

Material and Methods

Participants

The study subjects were adult residents living in Jinzhong city (latitude 37.68° north). During November and December 2017, we randomly selected 500 people, stratified by age, from 10 neighborhoods. We excluded 198 of these 500 subjects due to chronic liver or kidney diseases, cancer, pregnancy, and unwillingness to participate. Finally, there were 302 (176 men and 126 women) participants taking part in the study, and they were provided free measurements of blood glucose and blood pressure. All the participants gave written consent. The study received ethics approval from the Ethics Committee of Shanxi University of Chinese Medicine (SXZYYDX0019/2016).

Data collection

Anthropometry measurements, including height, weight, waist circumference (WC), hip circumference (HC), and waist-to-hip ratio (WHR), were collected. The participants were requested to wear a single layer of clothing for anthropometry measurement (we used the automatic height-weight instrument IPR-scale 02). Body mass index (BMI) was calculated by Adolphe Quetelet's formula: BMI=weight/height^2 (kg/m^2). When taking WC and HC measurements, the participants were standing with legs and heels together and arms hanging freely. The measuring tape was placed around each side of the midpoint between the lowest rib and iliac crest for WC measurement,

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Table 1. Descriptive characteristics of the participants.

Variables	Men (n=176)	Women (n=126)	t-value or t'-value	*p*-Value
Age (y)	46.48±15.06	45.52±13.25	t=0.574	0.566
WC (cm)	87.33±6.13	76.32±5.04	t'=31.058	<0.001
HC(cm)	99.57±6.71	92.73±5.56	t'=9.662	<0.001
WHR	0.90±0.67	0.81±0.64	t=1.173	0.242
BMI (kg/m^2)	24.90±2.81	22.6±3.22	t'=6.450	<0.001
25(OH)D(nmol/L)	43.49±14.78	38.40±12.37	t'=3.248	<0.001

WC – waist circumference; HC – hip circumference; BMI – body mass index; WHR – waist circumference/hip circumference; 25(OH)D – 25-hydroxyvitamin D; t-value is for data with homogeneity of variance, and t'-value is for data with heterogeneity of variance.

and then through the pubic symphysis and double-sided highest points of the gluteus maximus for HC measurements. The data were recorded to the nearest 0.1 cm and the mean values of 3 measurements were used.

For vitamin D testing, the dried blood spots (DBS) method was used to collect blood specimens using a DBS sampling instrument (TomTec, AutoDBS-3, USA). High-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS), the standard method of vitamin D analysis at present [32], was used to test 25(OH)D concentration at the Central Laboratory of Shanxi University of Chinese Medicine. Vitamin D status was defined according to the cutoffs of IOM (USA): vitamin D sufficiency is serum 25(OH) D >50 nmol/L, inadequacy is 30–50 nmol/L, and deficiency is <30 nmol/L [13].

To improve analysis, the men and women were divided into 3 age groups: the elderly groups were older than 60 years old, the middle-aged groups were 40–60 years old, and the young groups were younger than 40 years old.

Statistical analysis

All data were analyzed using SPSS version 21 (IBM Corporation, USA) and are expressed as mean ±SD. Two groups of data with equal variance were compared by *t* test, and data with unequal variances were compared by Welch's approximate *t* test (t'-test). Multiple linear regression analysis was used for evaluating the effects of the variables on vitamin D status. A *p* value of less than 0.05 was considered to be statistically significant.

Results

The characteristics of the participants by gender are presented in Table 1. There were 176 men and 126 women. No significant differences in age and WHR were found between men and women. However, there were significant differences in BMI, WC, HC, and serum 25(OH)D concentration by gender.

Table 2 and Figure 1A show the distribution of different vitamin D status in men and women. The percentage of women with sufficient vitamin D status was lower than that of men, while the percentage of deficiency in women was far higher than that in men. The difference between men and women in the distribution of vitamin D status was statistically significant ($p<0.01$).

Table 3 and Figure 1B show that the young group of women had the lowest vitamin D level among all the age groups in both genders. The vitamin D status of the young female group was even lower than in the elderly female group, ($p<0.05$), but no difference was found between any 2 age groups in vitamin D status in men.

Multiple linear regression analysis was conducted to determine which factors (BMI, WC, HC and WHR) were more associated with vitamin D status. Table 4 shows that gender was an independent factor associated with serum 25(OH)D concentration.

Discussion

This study was carried out in winter (November and December) in Jinzhong, a northern Chinese city (latitude 37.68° north). The prevalence of 25(OH)D deficiency and inadequacy was relatively high – 69% in men and 75% in women. The results were similar to some other surveys in northern China, showing high incidence of vitamin D insufficiency [26,33,34]. The situation in Jinzhong residents might be caused by seasonal, environmental, and lifestyle factors. Firstly, along with the increase of zenith angle in winter, more ultraviolet radiation from the sun is held by earth's ozone layer and less reaches the earth's surface, which directly leads to decreased 25(OH)D_3 biosynthesis in the skin. Secondly, Jinzhong is an industrial city and

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Table 2. Distribution of different vitamin D levels in men and women.

Gender	Vitamin D status			Chi-Square	*p*-Value
	Deficiency	Inadequacy	Sufficiency		
Men (n=176)	39 (22.16%)	82 (46.59%)	55 (31.25%)	12.98	<0.01
Women (n=126)	42 (33.33%)	53 (42.06%)	31 (24.60%)		

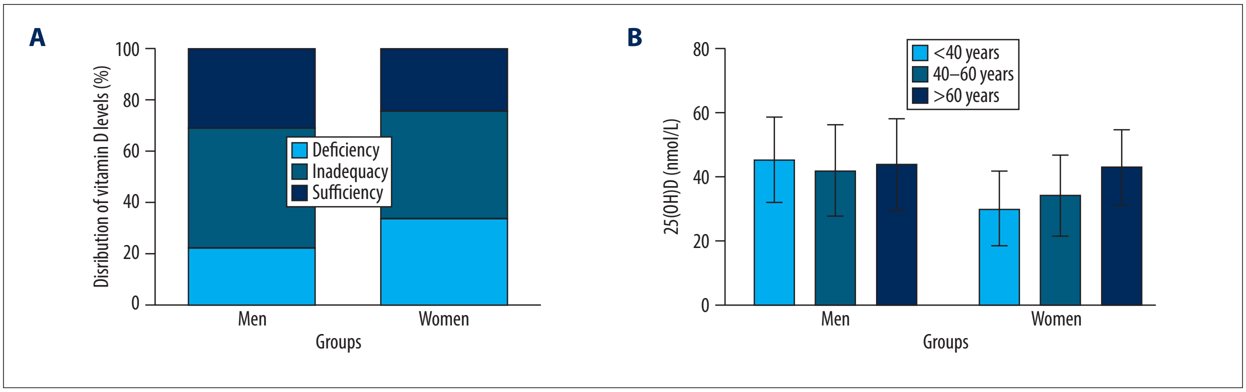

Figure 1. (**A**) Distribution comparison of vitamin D status in men and women. (**B**) Vitamin D comparisons of different age groups in men and women.

Table 3. Comparisons of 25(OH)D (nmol/L) by age rang in men and women.

Age (years)	Men (n=176)		Women (n=126)		t-Value	*p*-Value
	n	Mean ±SD	n	Mean ±SD		
<40	65	45.42±13.36	44	30.13±11.64*	6.169	<0.001
40-60	68	42.17±14.11	40	34.27±12.57*,**	2.923	0.004
>60	43	44.14±14.32	42	43.18±11.69**	0.339	0.736
F-value		0.922		13.270		
p-Value		0.400		<0.001		

Different superscripts (*, **) represent significant differences between groups in the same column at $p<0.05$; 25(OH)D – 25-hydroxyvitamin D.

Table 4. Multiple linear regression analysis for serum 25(OH)D concentration.

	B	SE	f-Value	*p*-Value
Intercept	47.35	13.12	10.2	<0.01
Gender (1=men; 2=women)	–9.48	2.97	12.6	<0.01
BMI	–2.17	0.36	5.18	0.08

BMI – body mass index.

air pollution is severe, especially in winter. Dust haze due to climate and pollution frequently occurs in the city, which also weakens the surface solar radiation intensity [35]. Last but not least, haze and air pollution also discourage people from going outside so as to avoid respiratory infections. Consequently, their sun exposure time is greatly shortened and vitamin D synthesis was decreased.

In addition, the consumption of vitamin D from diet of the residents is limited. Jingzhong is located far inland on the Loess

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Plateau, and daily foods with high vitamin D content such as sea food are not commonly consumed. Also, few foods are fortified with vitamin D in China. Thus, the vitamin D status of the participants was insufficient, as expected.

It is noteworthy that vitamin D status in females was significantly worse than in males. The result of multiple linear regression analysis indicated that female gender was negatively associated with vitamin D sufficiency. This was also reported in some previous studies [21,28,36,37], but not in others [38,39]. Differences in the amount of subcutaneous fat between males and females could be one of main reasons for the gender difference in serum vitamin D levels. It was well known that women on average have more subcutaneous fat than men [40,41]. Vitamin D is fat soluble and subcutaneous adipose tissue can store large amounts of it [42]. Therefore, the greater subcutaneous fat in women takes up more vitamin D molecules produced from skin, which leads to fewer vitamin D molecules entering the blood circulation in women than in men. However, BMI was not significantly associated with vitamin D concentration in multiple linear regression analysis in the present study (p=0.08), suggesting that the greater subcutaneous fat in women, which is closely related with estrogen, has more influence than visceral fat tissue on serum vitamin D concentration.

The associations between gender hormones and vitamin D are complicated and there have been few studies published on this topic. However, Jassen et al. showed that body estradiol concentration was negatively associated with vitamin D status in healthy postmenopausal women [30], while testosterone level was reported to be significantly and positively correlated with vitamin D concentration [43,44]. Those reports help explain our findings of differences in vitamin D levels between males and females.

Moreover, some studies found that vitamin D insufficiency is associated with some autoimmune diseases with obvious female predominance, such as multiple sclerosis, rheumatoid arthritis, type 1 diabetes, and systemic lupus erythematosus [45]. The finding suggests potential interactions among vitamin D, sex hormones, and some gender-related factors. Together with the immunoregulation effects of vitamin D, it could be expected that vitamin D supplementation would be one of potential treatments for those autoimmune diseases with female predominance, and this warrants further research.

In addition, lifestyle differences between Chinese men and women could contribute to the gender difference in vitamin D status. For example, female urban dwellers tend to adhere to the traditional Chinese aesthetic opinion that values paler skin. Women often intentionally avoid sunshine or use sun screen when they are outdoors. It was reported that using the amount of sun cream recommended by World Health Organization exponentially suppresses vitamin D synthesis in the skin [46].

It is interesting that younger women (under age 40) had the worst vitamin D status among all age groups in both men and women. Their average vitamin D concentration was even significantly less than that of elderly women. This finding is contrary the accepted observation that vitamin D photosynthesis markedly declines with age [47]. This is most likely due to lifestyle differences between young and middle-aged women *vs.* older women. In China, especially in urban areas, women younger than 40 years old generally are office workers and do not have time to do physical exercise in the daytime, which directly affects their sun exposure and vitamin D synthesis. By contrast, many women older than age 60 have retired and have more time to do outdoor activities when weather is good, increasing their sun exposure and vitamin D synthesis.

Our findings and those of others discussed above suggests the need for public health education on vitamin D, especially for young women. They should appropriately adjust their lifestyle, such as decreasing use of sun protection and increasing outdoor activities, as well as taking vitamin D supplements, to prevent vitamin D insufficiency. Vitamin D and/or its body metabolites have appealing potential as treatment for some autoimmune diseases with female predominance. Further research is needed on the relationships among vitamin D, estrogen, and other female-specific factors, as well as the possible underlying mechanisms.

A strength of the present study is the use of HPLC-MS/MS in measuring vitamin D concentration, which increased the accuracy of vitamin D testing. A limitation of our study is the failure to measure some gender-related factors, such as sex hormones concentration and use of estrogen contraceptives, in female participants.

Conclusions

Vitamin D insufficiency was highly prevalent in Jinzhong residents in China during the winter season. We found significant differences between males and females in vitamin D concentrations. Compared to males, females were more likely to have vitamin D insufficiency, and female gender appears to be a risk factor for vitamin D insufficiency.

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Conflict of interests

None.

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