

Meteorological Condition and Air Pollution Exposure Associated with Vitamin D Deficiency: A Cross-Sectional Population-Based Study in China

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Objective: The aim of this study was to investigate the status of Vitamin D deficiency and the effect of environmental factors on Vitamin D levels so as to provide theoretical support for public health promotion in this region.

Methods: A total of 22,387 subjects who underwent a physical examination at the center in the West China Hospital, Sichuan University, between April, 2018 and May, 2020 were enrolled in this study. Their data on gender, age, inspection date, serum 25 hydroxyvitamin D (25-(OH) D), parathyroid hormone (PTH), and total calcium were retrospectively reviewed. Next, the percentage of Vitamin D status was compared in different sex and age groups, and the fluctuation of Vitamin D level was described in relation to the change of environment. Finally, the univariable and multivariable linear regression analyses were performed to explore the risk and protective factors of Vitamin D deficiency.

Results: The proportion of Vitamin D deficiency in this area was 42.17%, and it was significantly higher among women and young people. The fluctuation trend of 25-(OH) D levels are consistent with temperature and solar radiation, and opposite to air quality, in the whole year. There was a positive relationship between 25-(OH) D levels with temperature and solar radiation; however, parathyroid hormone, female and AQI were negatively correlated with Vitamin D levels.

Conclusion: Vitamin D deficiency is common in subtropic areas, such as Sichuan Basin, which is related to solar radiation and air pollution.

Keywords: Vitamin D deficiency, 25 hydroxyvitamin D, environmental factors, air quality index

Introduction

Vitamin D is beneficial for the human body as it participates in the intake and use of calcium and phosphorus. Also, it has a critical role in regulating immunity and cell growth.¹ Vitamin D deficiency (VDD) is related to the general mortality of the population and the vast majority of illnesses, including osteoporosis, fractures, rickets in children, osteomalacia in adults, cardiovascular disease, inflammation, cancers, and so on.²⁻⁴ Serum total 25-(OH) D, a stable and abundant metabolite, is commonly used to assess the levels of Vitamin D in humans.⁵ Zhang et al reported that although vitamin D supplementation was not significantly associated with a reduction in all-cause mortality, it can reduce the risk of cancer death.⁶

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Currently, most existing studies have focused on the elderly, suggesting that low levels of Vitamin D are negatively correlated with all-cause mortality. However, there is a lack of research on the relationship between Vitamin D deficiency and all-cause mortality in young people in relation to all important confounding factors.⁷

Many diseases have been recognized to occur as the results of environmental factors. Personal health status is threatened by the growing urbanization, intercity automobile use, climate change, and air pollutants.^{8,9} It has been demonstrated that exposure to a harmful environment increases mortality and morbidity, outpatient visits, and hospitalizations and decreases the life expectancy of the influenced population.^{10,11} Based on the relationship between 25-(OH) D levels and environmental factors, we aimed to determine whether the meteorological condition and air pollution exposure contribute to or accelerate the progression of VDD. In this study, we evaluated the situation of VDD in Western China and the impact of environmental factors on the levels of Vitamin D in this population so as to provide theoretical support for public health promotion in this region.

Materials and Methods

Study Subjects

A total of 22,387 subjects who underwent a physical examination at the center in the West China Hospital, Sichuan University, between April, 2018 and May, 2020 were included in this study. All subjects were between 18 and 60 years old with complete records of essential information and laboratory results. All the subjects suffering from cancers, organ failure, abnormal liver and kidney function, osteoporosis/fractures, cardiovascular diseases, and endocrine and metabolic diseases were excluded. The data on gender, age, inspection date, serum 25-(OH) D, parathyroid hormone (PTH), and total calcium (TCa) were collected from the laboratory information system (LIS). Also, exceptional data were treated as missing values (Figure S1). The study received approval from the Ethics Committee on Biomedical Research, West China Hospital of Sichuan University (Approval No: 977 (2019)). At the same time, the Ethics Committee accordance with the principles stated in the Declaration of Helsinki approved the waiver of informed consent because of the following reasons. Firstly, we obtained the medical records in this study from previous clinical diagnosis and treatment of repository in the laboratory information

system, and consent would be impossible or impracticable to obtain for such research. Secondly, the waiver of informed consent did not adversely affect the rights and health of the subjects. Thirdly, the privacy and data of the subjects are confidentiality. Finally, this study does not involve medical records that the subjects have explicitly refused before.

Laboratory Testing

All the serum samples were collected from the elbow vein after 8~12 hour fasting and separated after centrifuging at 3500 rpm for 8 minutes. Serum 25-(OH) D and PTH were measured by electrochemiluminescence method and run in the Roche Cobas e601 (Mannheim, Germany). Serum total calcium (TCa) was measured by O-cresolphthalein ketone colorimetric method and analyzed using Roche Cobas c702 (Mannheim, Germany). The coefficient of variation for low-quality control and high-quality control of 25 (OH)-D was 6.32% and 4.86%, PTH was 3.72%, and 3.33%, and TCa was 1.39% and 1.04%, respectively. All tests were completed by Roche original reagents and calibrators and were used for an external quality assessment accredited by the College of American Pathologists (CAP) and National Center for Clinical Laboratories (NCCL) of China with the bias of 6.3% for 25-(OH) D, 5.8% for PTH and 0.8% for TCa that indicated that the test results were accurate and reliable.

Environment Factors

Daily total radiation and net radiation (2018.04–2019.11) were downloaded from the China Meteorological Data Network (<http://data.cma.cn/site/index.html>). Daily Air Quality Index (AQI) (2018.04–2020.05) was downloaded from the air quality online monitoring and analysis platform (<https://www.aqistudy.cn/>). According to the recommendations, there are six levels of AQI (Table S1).^{9,12}

Statistical Analysis

The Kolmogorov–Smirnov statistic, histogram, and quantile-quantile plot (Q-Q plot) were used to test for the normality of variables. Abnormal 25-(OH) D, PTH, and TCa values were excluded by the criteria of more than three times the interquartile range. Chinese experts suggested that Chinese health practitioners should adopt the same views as those accepted by the American Academy of Medical Sciences, the British Osteoporosis Society, and the Australian Bone Mineral Association. Accordingly, subjects were divided into three groups with the 25-(OH)

D values: less than 29.9 nmol/L (deficient), 30–49.9 nmol/L (insufficient), greater than 50 nmol/L (sufficient).¹³ We compared the percentage of the three groups in relation to different sex and age by using the Chi-square test. We also compared the three groups in quantile of total radiation, net radiation, season, and AQI groups. Univariable and multivariable linear regression and the collinear diagnosis were used to explore the potential influence factors of Vitamin D status. Independent variables included sex, age, season, AQI, and total radiation. We also calculated the median of 25-(OH) D, PTH, TCa, temperature, total radiation, and AQI per month and drew a time variation curve to show how variables fluctuate over time. All analyses were performed by the R software (version 3.6.3). A *P*-value of <0.05 was considered statistically significant.

Results

Prevalence of Vitamin D Deficiency

We investigated the serum 25-(OH) D levels to evaluate the VDD in this area, where the normality test showed that the level of 25-(OH) D in this area was an approximately normal distribution (Figure S2). There were 42.17% of subjects who had Vitamin D deficiency or insufficient levels of Vitamin D. The results showed that the morbidity rates of VDD and Vitamin D insufficiency were significantly higher in females (51.6%) than in males (34.1%). The proportion of Vitamin D sufficiency was significantly lower in females compared to males. Moreover, there were differences in the ratio of VDD among different age groups. The most challenging situation was found among people aged 20 to 30 years old, 48.7% of whom were Vitamin D insufficient, and 10.7% had VDD. People aged 50 to 60 years old showed to have the most favorable condition since 67.4% of them were Vitamin D sufficient. Their morbidity rates of Vitamin D insufficiency and deficiency were 29.4% and 3.2%, respectively. The details of Vitamin D deficiency across different gender and age are shown in Table 1.

Factors Influencing Serum 25-(OH) D Levels

We analyzed the fluctuations of serum 25-(OH) D levels in the crowd. The average levels of 25-(OH) D were 53.2 nmol/L, and the levels in males were higher than those in females. Besides, with reference to Vitamin D sufficiency,

Table 1 The Prevalence of Vitamin D Deficiency in West China

	Deficient N (%)	Insufficient N (%)	Sufficient N (%)	P
All subjects	1159 (5.18)	8282 (36.99)	12,946 (57.83)	—
Sex				
Males	366 (3.0)	3773 (31.1)	7980 (65.8)	<0.001
Females	793 (7.7)	4509 (43.9)	4966 (48.4)	
Age				
(17,20)	18 (11.3)	64 (40.3)	77 (48.4)	<0.001
(20,30)	211 (10.7)	958 (48.7)	797 (40.5)	
(30,40)	296 (5.9)	2108 (42.1)	2607 (52.0)	
(40,50)	427 (4.8)	3274 (37.0)	5157 (58.2)	
(50,60)	207 (3.2)	1878 (29.4)	4308 (67.4)	

insufficiency, and deficiency, 25-(OH) D levels increased with age. The details are shown in Table 2.

The line graph demonstrated the fluctuations in 25-(OH) D levels over a year in West China. According to the chart, the 25-(OH) D levels significantly increased from January to October, when they reached the peak. Although it was sometimes fluctuating, the overall trend was upward. The 25-(OH) D levels decreased between October and December, and the lowest point of the year was in January. In contrast, the yearly

Table 2 The 25-OH-Vitamin D Levels (Nmol/L) in Different Groups

	All	Deficient	Insufficient	Sufficient
All subjects	53.2 (42.5–66.1)	26.4 (23.5–28.4)	41.8 (36.9–46.1)	63.6 (56.3–74.6)
Sex				
Males	56.9 (45.8–69.8)	26.9 (24.0–28.6)	42.7 (37.6–46.4)	65.0 (57.1–76.4)
Females	49.3 (39.1–61.2)	26.2 (23.3–28.2)	41.1 (36.3–45.7)	61.7 (55.3–71.5)
Age				
(17,20)	49.0 (38.8–59.9)	25.7 (24.1–27.7)	40.8 (37.4–46.2)	60.0 (55.6–69.8)
(20,30)	46.4 (36.8–58.1)	26.4 (23.5–27.9)	40.0 (36.1–45.3)	61.1 (55.2–69.8)
(30,40)	50.7 (40.9–62.5)	26.5 (23.9–28.7)	41.7 (36.7–45.9)	62.0 (55.3–72.0)
(40,50)	53.4 (42.7–66.0)	26.3 (23.2–28.2)	41.8 (36.9–46.1)	63.6 (56.4–74.2)
(50,60)	57.6 (46.3–71.1)	26.6 (24.2–28.5)	42.9 (37.8–46.5)	65.7 (57.3–78.1)

trend of PTH was opposite to 25-(OH) D, and the overall fluctuation range of PTH was relatively small. The overall fluctuation trend of serum total calcium was similar to that of Vitamin D, and the peak value occurred slightly later than that of Vitamin D. Next, to explore the factors impacting on the VDD, we evaluated the relationships between environment and 25-(OH) D levels. Based on the time variation curve, we found that the fluctuation of 25-(OH) D is also related to AQI and radiation. 25-(OH) D was the lowest in January, which was the valley value of temperature and total radiation and the peak value of AQI (Figure 1). For AQI, summer is unique in this area. Every year, AQI reaches a second peak in August.

Finally, we described the time variation curve of specific pollutants and 25-(OH) D levels. In August, the primary pollutant was O₃. Although stratospheric ozone

can absorb ultraviolet rays and reduce solar radiation, ozone pollution had relatively little effect on Vitamin D levels at that time (Figure S3).

Prevalence of Vitamin D Deficiency in Different Environments

The proportion of Vitamin D sufficient was highest in summer and lowest in winter; on the contrary, the percentage of Vitamin D deficiency and insufficiency was lowest in summer and most elevated in winter (Figure 2A). The proportion of Vitamin D sufficiency grows with the increase of total radiation. In contrast, the percentage of Vitamin D insufficiency and deficiency decreased, just as the effects of net radiation (Figure 2B and C). Besides, the impact of air pollution on VDD was slightly different. The proportion of varying Vitamin D status

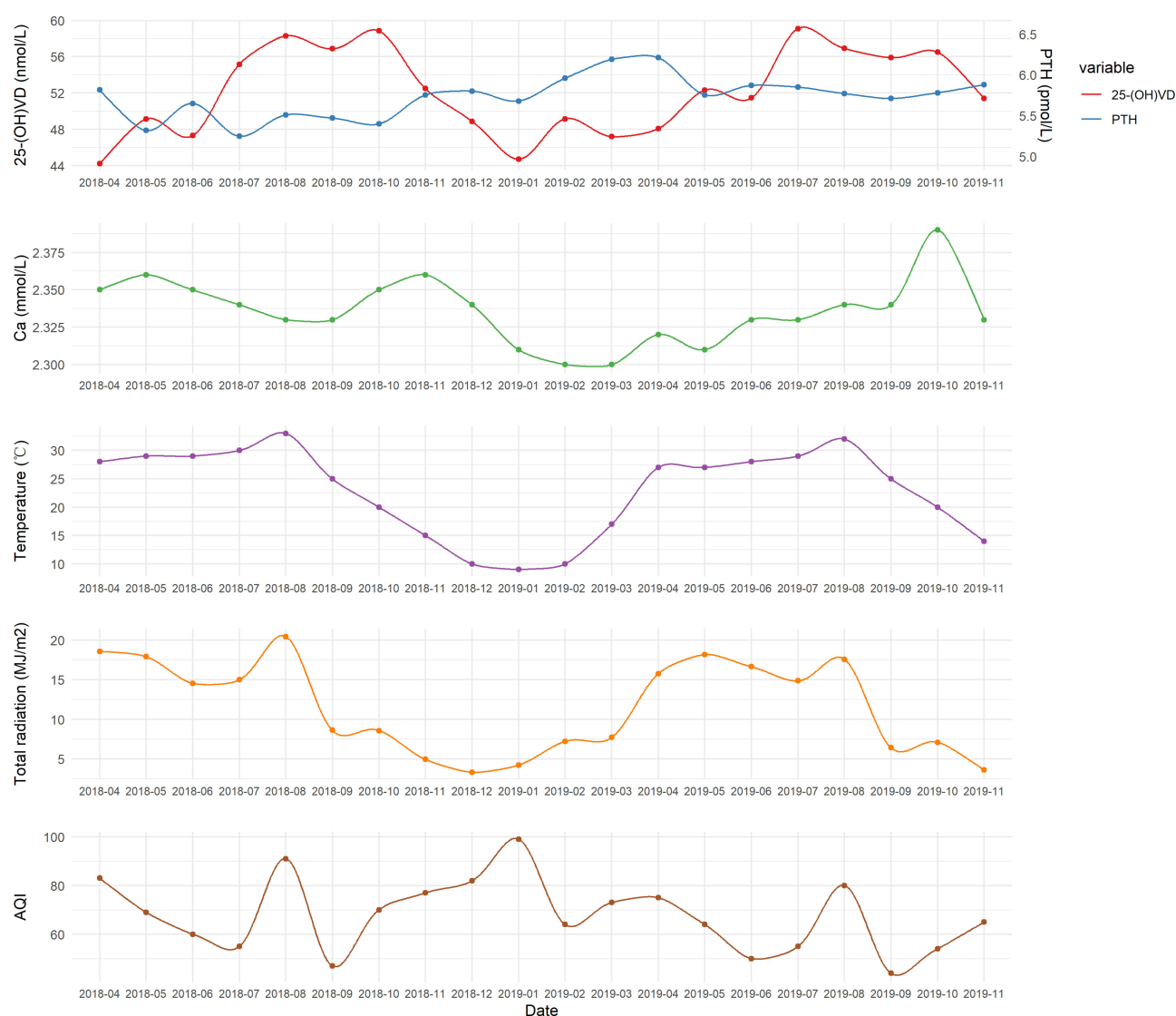


Figure 1 The fluctuations of Vitamin D levels throughout a year with different environmental factors.

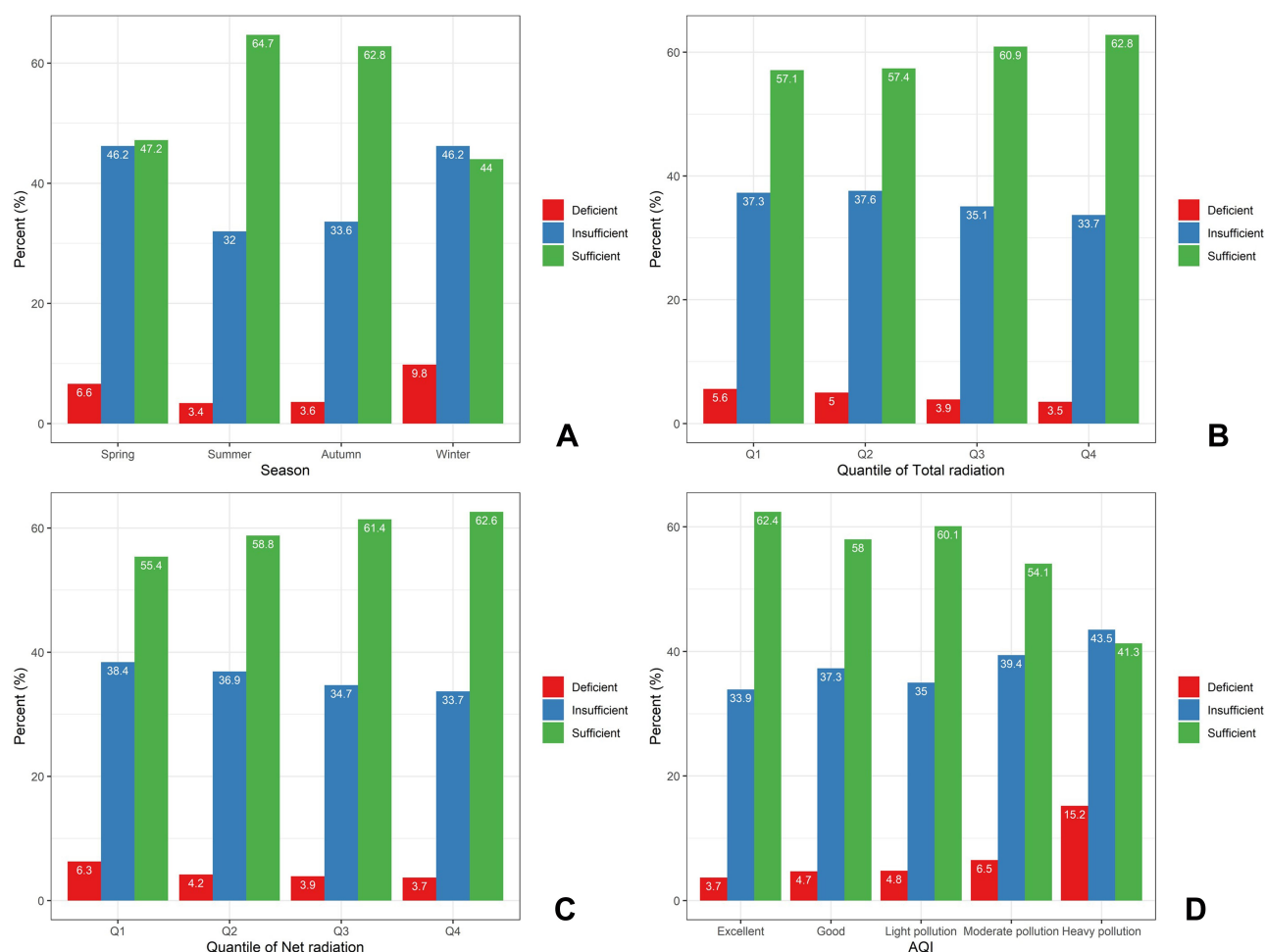


Figure 2 The prevalence of VDD in a different environment. **(A)** Vitamin D deficiency is the lowest in summer and autumn. **(B, C)** With the increase of total radiation and net radiation, the sufficient proportion of Vitamin D increased, while the percentage of insufficient and deficiency decreased. **(D)** In the heavy pollution, Vitamin D deficiency was worst, while in the excellent AQI, the status of sufficient Vitamin D was the best.

in the AQI of good and light pollution was similar. Besides, with the aggravation of AQI, the portion of VDD increased (Figure 2D).

Risk Factors of Vitamin D Deficiency

Univariable and multivariable linear regression showed that males had higher levels of 25-(OH) D than women and 25-(OH) D levels increased with age. With reference to the seasons, there was a negative relationship with 25-(OH) D levels in spring and winter compared with summer, but a positive relationship with autumn. Besides, 25-(OH) D levels were negatively correlated with AQI and positively correlated with total radiation (Table 3).

Discussion

Vitamin D deficiency is a common occurrence worldwide and a public health problem that is especially evident in

low and lower-middle-income countries.¹⁴ According to the World Bank Group's per capita gross national income, China is classified as a developing economy, which is especially evident in the western region of China, where the average level is lower than that of the whole country.¹⁵ Over recent years, the attempts to promote economic development have been inevitably accompanied by some environmental damage. Environmental factors, including climatic conditions, solar radiation, and environmental pollution, have been given serious attention considering their impact on human health.¹⁶ Some epidemiological studies showed that air pollution might be the potential risk factor for Vitamin D deficiency.¹⁷ In this study, we analyzed the time variation curve of 25-(OH) D levels under different conditions and the constituent ratio of VDD. We also explored the environmental factors that impact VDD in this region.

Table 3 Univariable and Multivariable Linear Regression of VD

Variables	Univariable		Multivariable	
	Coef (95% CI)	P	Coef (95% CI)	P
Sex (males)	7.46 (6.99–7.94)	<0.001	7.80 (7.32–8.27)	<0.001
Age	0.38 (0.35–0.41)	<0.001	0.38 (0.35–0.40)	<0.001
Season				
Summer (reference)				
Spring	−7.60 (−8.31–6.90)	<0.001	−8.69 (−9.44–7.94)	<0.001
Autumn	0.26 (−0.30–0.82)	0.36	0.82 (0.21–1.43)	0.009
Winter	−8.51 (−9.28–7.74)	<0.001	−6.51 (−7.53–5.50)	<0.001
AQI	−5.22 (−6.54–3.90)	<0.001	−1.32 (−2.82–0.18)	0.08
Total radiation	2.24 (1.41–3.06)	<0.001	2.39 (1.36–3.43)	<0.001

It has been previously reported that females and young populations have an increased prevalence of VDD.¹⁸ Other studies^{19,20} have suggested that if older people are excluded from taking Vitamin D supplements, their average level of 25-(OH) D is lower, and VDD is more severe.²¹ Because of the decreased concentrations of 7-dehydrocholesterol, the ability to make Vitamin D through the skin decreases in older people. However, our results confirmed that the female gender and younger age were the risk factors of Vitamin D insufficiency and deficiency. In subtropic areas, young people have a higher rate of Vitamin D intake;¹⁸ yet, their Vitamin D levels were still low, which may be related to sun exposure. In these areas, the young tend to spend more time working, studying, and even exercising indoor, while the elderly prefer outdoor sports. Further, young girls like to use sunscreen and other cosmetics to reduce sun exposure, which results in less exposure to the sun.^{22,23}

The findings of our research on Vitamin D deficiency in the population of Sichuan Province, Western China indicated that about 42.17% of the population had insufficient levels of vitamins in the body, and the average levels were 53.22 nmol/L, which is comparable to the national level.^{24–26} However, China has a vast territory, and environmental factors are entirely different across different regions, even at the same latitude or longitude. Sichuan Basin is located in the upper reaches of the Yangtze River in Southwest China. Because of the plateau mountains, its topography is unique, and the height difference is significant, the climate is more complicated than in other regions, with substantial regional climate characteristics. The subjects included in this study mainly live in the subtropical monsoon humid climate, which is

characterized by early spring, hot summer, cool autumn, and warm winter. Consistent with most studies, our findings showed that with the decrease in temperature and solar radiation, the level of 25-(OH) D decreased. As temperature and radiation levels rise, 25-(OH) D levels increase.^{27,28}

The particular geographical factors and specific climate characteristics led to the environmental pollution of this region being different from that of other areas.^{29,30} The prevalence of VDD is highest in winter, which is related to lower temperatures, radiation, and severe air pollution. The 25-(OH) D levels were positively related to temperature and radiation. Nevertheless, they were negatively associated with AQI. The multivariable linear regression also showed that winter and air pollution were the risk factors for Vitamin D insufficiency and deficiency. Hoseinzadeh et al reviewed the literature and suggested that air pollutants inhibit the absorption of Vitamin D by affecting solar radiation, which eventually leads to VDD in the population.¹⁷ Yet, in this area, due to the unique geographical conditions of the basin, air pollution peaks every summer. During this period, the annual temperature and radiation levels are the highest. However, Vitamin D levels are still slightly affected, showing a downward trend and returning to the peak level in October. Therefore, we thought that the impact of air pollution is not immediate, and there may be a potential mechanism through which Vitamin D levels get directly affected by air pollution.³¹ Similarly, the regression analysis also showed that compared with summer, the Vitamin D levels in autumn were higher, which may also be related to the severe ozone pollution in August, considering the radiation and temperature in this month are the highest throughout the year.

Conclusion

Vitamin D deficiency is common in the subtropics areas such as Sichuan Basin. The prevalence of Vitamin D deficiency tends to vary from season to season due to variations in temperature, solar radiation, and air pollution. Different pollutants have different effects on Vitamin D levels, and further multicenter studies are needed to prompt public health efforts.

Abbreviations

VDD, Vitamin D deficiency; 25-(OH) D, 25 hydroxyvitamin D; PTH, parathyroid hormone; TCa, total calcium;

AQI, Air Quality Index; PM_{2.5}, fine particulate matter; PM₁₀, inhalable particles; SO₂, sulfur dioxide; NO₂, nitrogen dioxide; O₃, Ozone; CO, carbon monoxide.

Data Sharing Statement

Daily total radiation and net radiation (2018.04-2019.11) were downloaded from the China Meteorological Data Network (<http://data.cma.cn/site/index.html>). Daily Air Quality Index (AQI) (2018.04-2020.05) was downloaded from the air quality online monitoring and analysis platform (<https://www.aqistudy.cn/>). The data, including gender, age, inspection date, serum 25-(OH) D, and PTH, were collected from the laboratory information system (LIS), and it can be obtained with the consent of the corresponding author.

Compliance with Ethical Standards

The study received approval from the Ethics Committee of West China Hospital, Sichuan University (Approval No: 977 (2019))

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Disclosure

The authors report no conflict of interest.

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