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RESEARCH ARTICLE

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Influence of the COVID-19 pandemic on the vitamin D status of children: A cross-sectional study

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Abstract

Coronavirus disease 2019 (COVID-19), as well as its prevention and control measures, seriously affected people's livehood, which may have affected the body's level of vitamin D (VD). This study aimed to investigate the effect of the COVID-19 pandemic on the VD status of children in Zhengzhou, China. In this study, we included 12 272 children in 2019 (before the COVID-19 pandemic) and 16 495 children in 2020 (during the COVID-19 pandemic) to examine the changes in VD levels and deficiency rates among children before and during the COVID-19 pandemic. Total VD levels in 2020 were significantly higher than those in 2019 (26.56 [18.15, 41.40] vs. 25.98 [17.92, 40.09] ng/ml, $p < 0.001$). Further analysis revealed that during the COVID-19 pandemic control period in 2020, the VD levels in February, March, and April were lower than those in the same months of 2019, while the VD deficiency rates were significantly higher. Additionally, our data revealed that VD levels decreased significantly with age. Among children older than 6 years, the VD deficiency rate exceeded 50%. These results indicate that we should pay close attention to VD supplementation during the COVID-19 pandemic control period and in children older than 6 years of age.

KEYWORDS

children, COVID-19, vitamin D

1 | INTRODUCTION

Vitamin D (VD) is an essential vitamin for the human body that aids in the regulation of calcium and phosphorus balance as well as bone metabolism.[1] However, only a few foods naturally contain VD. It is primarily produced in the human body by skin self-synthesis following sun exposure. When exposed to sunlight, 7-dehydrocholesterol in the skin absorbs UVB radiation and is converted to previtamin D3, which isomerizes into vitamin D3.[2,3] VD is known to have antioxidant, anti-inflammatory, and neuroprotective properties.[4] It has been linked to the occurrence and severity of infectious diseases in children.[5–7] Children with low VD levels were found to be more susceptible to infectious diseases.[8,9] All these findings indicate that adequate VD levels are necessary for the maintenance of a healthy body.

Coronavirus disease 2019 (COVID-19) is a global coronavirus outbreak caused by the severe acute respiratory syndrome coronavirus

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2 (SARS-CoV-2), which was first identified in Wuhan, China, in 2019.[10] The most common symptoms of COVID-19 are fever, dry cough, and shortness of breath.[11] The transmission of SARS-CoV-2 mainly have three models known as “contact,” “droplet,” and “airborne” transmission.[12] COVID-19 is a highly infectious disease that has resulted in numerous critical cases and deaths, particularly among high-risk groups.[13] According to the Health Commission of Henan Province, Henan had more than 3449 confirmed cases of COVID-19 in 2020. Meanwhile, children of all ages, particularly infants, were susceptible to SARS-CoV-2 infection. From January 16, 2020, to February 8, 2020, the Chinese Center for Disease Control and Prevention reported 2135 pediatric cases of COVID-19.[14]

In response to COVID-19, many countries have implemented strict interventions, such as maintaining social distance, wearing masks, limiting crowd gathering, and restricting outdoor activities.[15] During the COVID-19 pandemic, China took strict measures to reduce outdoor activities that severely impacted the people's lives. People are unable to be fully exposed to natural sunlight due to a decline in outdoor activities, and insufficient exposure to sunlight can impair the ability of the skin to synthesize VD. However, the impact of these interventions on the VD status of children is unclear. Therefore, we measured serum 25-hydroxyvitamin D (25(OH)D) concentrations and the VD deficiency rate before and during the COVID-19 pandemic to investigate the effect of COVID-19-induced human lifestyle changes on VD status in children.

2 | METHODS

2.1 | Patient selection

This was a retrospective, single-center, cross-sectional observational study conducted at Henan Children's Hospital (Children's Hospital Affiliated to Zhengzhou University). Between January 2019 and December 2020, a total of 28 767 children who visited Henan Children's Hospital for VD detection were enrolled in this study. The inclusion criteria for this study were: (1) children younger than 18 years of age; and (2) children without malignancies, hematological system diseases, major congenital malformations, or infectious diseases. The study protocol complied with the Declaration of Helsinki and was approved by the hospital's ethics review board. All procedures in this study were performed as a part of routine clinical practice, and the data were anonymized. Given the retrospective nature of the study, the requirement for informed consent was waived.

2.2 | Data collection and VD measurements

The demographic and laboratory data, including age, gender, and VD concentrations, were obtained from electronic medical records. Serum VD concentrations in children were determined using the Elecsys® Vitamin D total kit (Roche Diagnostics) in the Cobas® 8000 modular analyzer (Roche Diagnostics). The general experimental steps were as follows: (1) serum samples were incubated with the pretreatment regent for 9 min to denature VD binding protein (VDBP) and release the bound VD; (2) samples were further incubated with a recombinant ruthenium-labeled VDBP to form a complex of VD and the ruthenium-labeled VDBP; (3) with the addition of a biotinylated VD, a complex consisting of the ruthenium-labeled VDBP and the biotinylated VD was formed; (4) the entire complex was bound to the solid phase, and the unbound substances were removed; (5) voltage was applied to the electrode to induce chemiluminescent emission, which was measured using a photomultiplier. The results were determined using an instrument-specific calibration curve generated by 2-point calibration and a calibration master curve provided via the regent barcode. According to the 2011 Institute of Medicine report, VD deficiency was defined as VD levels less than 20 ng/ml.[16]

2.3 | Statistical analysis

Continuous variables with nonnormal distributions are presented as medians (interquartile range). The Mann–Whitney *U*-test was utilized to compare two groups with nonnormal distributions. The Kruskal–Wallis test was utilized when comparing samples from more than two nonnormally distributed groups. Data were analyzed using SPSS version 24.0. The figures were created with GraphPad Prism 9 software (GraphPad Software Inc.). A two-sided *p*-value of less than 0.05 was considered statistically significant.

3 | RESULTS

3.1 | Patient characteristics

From January 1, 2019, to December 31, 2020, a total of 28 767 children were enrolled in this study, with 12 272 children (42.7%) in 2019 and 16 495 children (57.3%) in 2020 (Figure 1). As shown in Table 1, there were more boys than girls in both years. The proportion of boys in 2019 was higher than that in 2020 (57.6% vs. 53.9%, $p < 0.001$). In addition, there were more children of all ages in 2020 than that in 2019, with the majority of children aged more than 6 years of age (in 2019 and 2020, the proportion of children aged more than 6 years was 49.4% and 55.2%, respectively).

3.2 | Influence of epidemic prevention and control measures on VD levels

The median and quartile levels of VD among children in 2019 and 2020 are shown in Table 1. VD levels were significantly higher in 2020 than in 2019. Children were grouped by month to investigate the difference in VD levels between different months before and during the COVID pandemic. As shown in Table 2, the level of VD in February, March, April, August, and November of 2020 was significantly lower than in 2019 ($p < 0.001$). When compared to the

VD levels in June and July 2019, the VD level in children in June and July 2020 significantly increased ($p < 0.001$). There was no significant difference in VD levels between January, May, September, and October of 2019 and 2020. Meanwhile, children were divided into four age groups: <1, 1–3, 3–6, and >6 years. As shown in Table 3, the VD levels of children in all age groups in 2020 were significantly higher than those of children of the same age in 2019 ($p < 0.001$). Further analysis revealed that VD levels gradually decreased in the <1, 1–3, 3–6, and 6-year groups in both years ($p < 0.001$).

3.3 | Influence of epidemic prevention and control measures on the VD deficiency rate

There were 9003 children with VD levels of less than 20 ng/ml, accounting for 31.3% of all samples, including 3916 (31.9%) and 5087 children (30.8%) in 2019 and 2020, respectively. The VD deficiency rate was higher in 2019 than in 2020. Figure 2 shows the monthly VD deficiency numbers and rates for 2019 and 2020. Figure 2A shows the number of VD-deficient children in January, April, May, August, October, November, and December 2020 was higher than in the same months in 2019, whereas the number of VD-deficient children in February 2020 was lower than in February 2019. Figure 2B shows that the VD deficiency rates in February, March, April, and November 2020 were significantly higher than in the same months in 2019 ($p < 0.05$), whereas the VD deficiency rates in June and July 2020 were significantly lower than in the same months in 2019 ($p < 0.05$). The VD deficiency rates did not vary significantly between January, May, August, September, October, and December in 2019 and 2020. Further analysis revealed that the number of VD-deficient children aged more than 6 years in 2020 was higher than that of children of the same age in 2019, whereas there was no significant difference in the VD deficiency rates across all age groups between 2019 and 2020 (Figure 3).

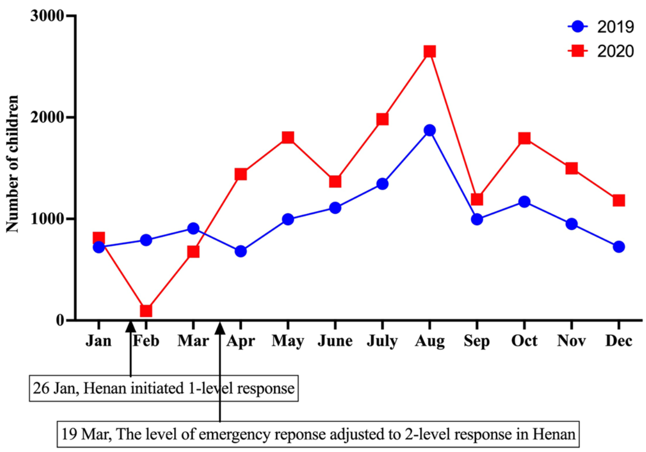

FIGURE 1 The number of children with VD detection in Henan Children's Hospital before and during the COVID-19 pandemic. COVID-19, coronavirus disease 2019; VD, vitamin D.

4 | DISCUSSION

COVID-19 is a highly infectious disease caused by SARS-CoV-2 that may result in life-threatening complications.[17] SARS-CoV-2 spreads rapidly via the respiratory tract. During the first 2 months of the COVID-19 pandemic outbreak, COVID-19 spread rapidly spread throughout China and caused varying degrees of illness.[18] Due to the high infectivity of coronavirus, countries have implemented stringent control measures to reduce the prevalence of COVID-19. Limiting outdoor activities is one of the most important interventions for preventing the spread of COVID-19. However, it reduced the amount of time people spent in sunlight. Lansiaux et al.[19] reported that there was a negatively correlation between sunlight exposure and COVID-19 mortality. In addition, because a reduction in sunlight exposure time

TABLE 1 Characteristics of study subjects in the year 2020 (during the COVID-19 pandemic) compared to 2019 (before the COVID-19 pandemic)

Variables	2019 (*n* = 12 272)	2020 (*n* = 16 495)	χ^2	*p* Value
Gender, *n* (%)				
Male	7074 (57.6%)	8899 (53.9%)	38.88	<0.001
Female	5198 (42.4%)	7596 (46.1%)		
Age (years), *n* (%)				
<1	1072 (8.7%)	1192 (7.2%)	22.10	<0.001
1–3	2844 (23.2%)	3174 (19.2%)	65.78	<0.001
3–6	2293 (18.7%)	3020 (18.3%)	0.66	0.416
>6	6063 (49.4%)	9109 (55.2%)	95.55	<0.001
VD (ng/ml)	25.98 (17.92, 40.09)	26.56 (18.15, 41.40)		<0.001
VD status (ng/ml), *n* (%)				
<20	3916 (31.9%)	5087 (30.8%)	3.75	0.053
≥20	8356 (68.1%)	11 408 (69.2%)		

Abbreviations: COVID-19, coronavirus disease 2019; VD, vitamin D.

TABLE 2 VD concentrations in each month of 2020 (during the COVID-19 pandemic) compared to 2019 (before the COVID-19 pandemic)

Years	Percentages (%)	January	February	March	April	May	June	July	August	September	October	November	December
2019	25	13.00	11.68	14.03	14.36	16.98	18.78	20.60	22.59	24.00	20.55	18.13	16.35
	50	18.73	16.55	20.47	21.63	25.11	26.96	27.57	29.99	33.88	26.78	24.67	25.26
	75	30.79	28.99	35.55	36.37	38.84	39.67	42.13	44.23	48.98	40.96	39.35	40.73
2020	25	12.65	7.89	11.78	12.94	16.06	22.53	22.90	21.20	24.17	24.17	16.02	16.76
	50	17.92	11.25	16.40	18.97	25.88	34.10	31.29	27.95	32.78	32.78	23.33	23.93
	75	29.76	14.62	26.35	34.32	41.42	50.20	48.42	42.24	50.69	50.69	35.86	38.67
	Z	−1.176	−7.136	−7.346	−3.612	−0.293	−9.922	−7.343	−3.483	−0.683	−0.221	−3.751	−0.239
	p Value	0.240	<0.001	<0.001	<0.001	0.769	<0.001	<0.001	<0.001	0.495	0.825	< 0.001	0.811

Note: The concentration unit of VD was ng/ml.

Abbreviations: COVID-19, coronavirus disease 2019; VD, vitamin D.

reduces the body's ability to synthesize VD, the body's VD level is reduced.[2] Therefore, VD is also referred to as "sunshine vitamin."[20]

For decades, VD has been recognized as a necessary nutrient for regulating calcium homeostasis, which aids in the development, function, and maintenance of healthy bones throughout life.[21] In addition, VD plays an important role in the nervous system,[22] the immune system,[23–25] and the cardiovascular system.[26,27] VD deficiency can increase the risk of various diseases, such as rickets osteoporosis,[28] aches weakness,[29] multiple sclerosis,[30] coronary heart disease,[31] asthma,[32] and various infectious diseases.[33] Adequate levels of VD in the host could inhibited the release of pro-inflammatory cytokines, thereby lowering the risk of cytokine storm.[34] Carpagnano et al.[35] reported that COVID-19 patients had a high prevalence of hypovitaminosis D and that COVID-19 patients with severe VD deficiency had a significantly increased risk of mortality. Meanwhile, numerous studies have shown that VD supplementation can help prevent respiratory infections and can lower ICU admission rates, mortality rates, and RT-PCR-positive rates in patients with COVID-19, while having no effect on the risk of COVID-19 infection.[36–43]

Henan is the birthplace of Han Chinese civilization, with over 3200 years of recorded history, and was China's cultural, economic, and political center until about 1000 years ago. Henan is located at latitude 34.7°N, and longitude 113.7°E, with abundant sunlight. Meanwhile, as the economy improves, Henan children's food, including beans, meat, eggs, fruits, and vegetables, becomes more abundant every day.[44] However, Henan is a populous province with a population of 114.44 million in 2020, of which 26.48 million are children under the age of 14, accounting for 23% of the total population. With a large number of children and strict control measures during the COVID-19 pandemic, more children may have insufficient VD. Therefore, it is necessary to investigate the effect of control measures on children's VD status during the COVID-19 pandemic.

In this study, we found that COVID-19 had no effect on the number of children who visited the hospital for VD detection and that total VD levels in 2020 were significantly higher than in 2019. This might be due to people's increased understanding of the importance of VD functions and daily VD supplementation. We also examined the change in VD levels and deficiency rates in different months and found that during the COVID-19 epidemic prevention and control period, VD levels in children decreased significantly in February, March, and April 2020 compared to the same months in 2019. Meanwhile, the VD deficiency rate increased significantly in February, March, and April 2020. We also examined the changes in VD levels in different age groups before and after the COVID-19 epidemic. The results revealed that VD levels in 2020 were significantly higher than those in 2019 for all age groups. In addition, we found that as age increased, the level of VD decreased significantly in 2019 as well as in 2020, while the VD deficiency rate increased significantly. The VD deficiency rate reached more than 50% in children over the age of 6 years. This may be related to the pediatrician's recommendation of daily VD supplementation for children under the age of 2 years. These results indicate that parents

TABLE 3 VD concentrations in different age groups in 2020 (during the COVID-19 pandemic) compared to 2019 (before the COVID-19 pandemic)

Variables	Percentages (%)	2019 (*n* = 12 272)	2020 (*n* = 16 495)	*Z*	*p* Value
Age (years)					
<1	25	36.68	41.14	−8.286	<0.001
	50	46.01	52.29		
	75	56.56	62.43		
1–3	25	37.12	41.59	−14.988	<0.001
	50	45.69	51.29		
	75	55.48	63.03		
3–6	25	22.58	24.73	−9.748	<0.001
	50	29.23	32.28		
	75	36.91	40.41		
>6	25	14.31	14.71	−6.904	<0.001
	50	18.87	19.78		
	75	24.07	25.58		
p Value		<0.001	<0.001		

Note: The concentration unit of VD was ng/ml.

Abbreviations: COVID-19, coronavirus disease 2019; VD, vitamin D.

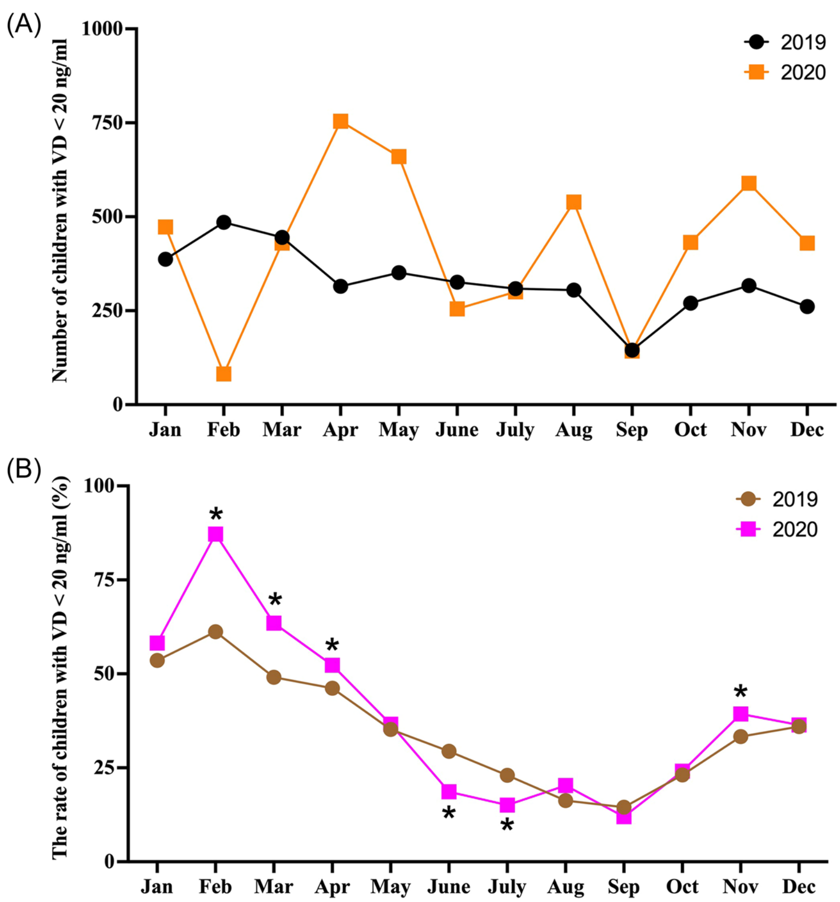

FIGURE 2 The monthly VD deficiency numbers and rates for 2019 and 2020. (A) The number of children with VD < 20ng/ml; (B) The rate of children with VD < 20ng/ml. VD, vitamin D.

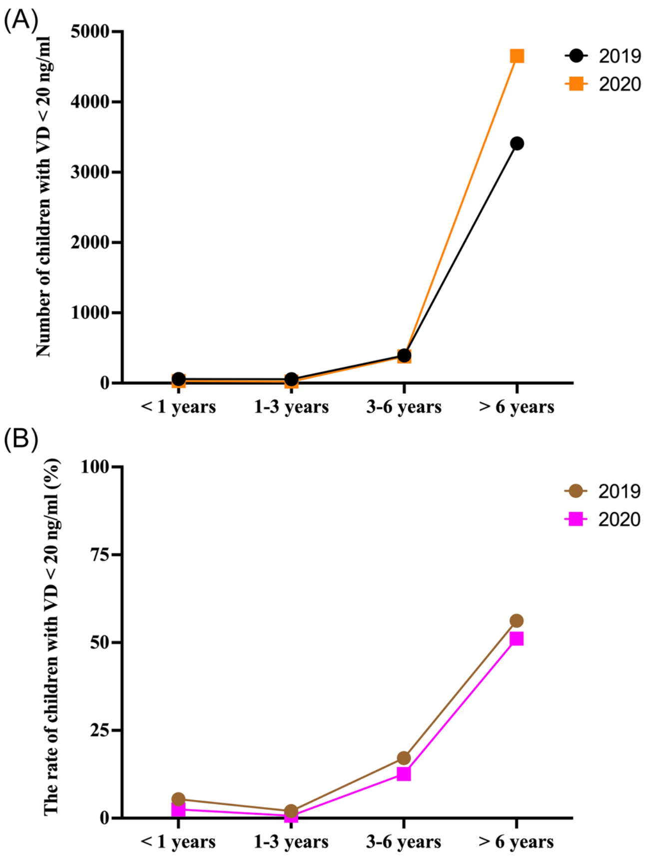

FIGURE 3 The VD deficiency numbers and rates in different age groups in 2019 and 2020. (A) The number of children with VD < 20ng/ml; (B) The rate of children with VD < 20ng/ml. VD, vitamin D.

or child guardians should focus on the nutritional supplementation of children's VD during the COVID-19 epidemic control period, as well as for children over 3 years old.

This is the first observational study to investigate the VD level and deficiency rate among nearly 30 000 children in China during the COVID-19 pandemic. However, this study also has some limitations. First, this study was a cross-sectional study, and we did not track future clinical outcomes. Therefore, we could not evaluate the association between VD deficiency and the risk of related diseases, such as rickets, osteoporosis, asthma, and infectious diseases (COVID-19). Second, this was a single-center study conducted in Henan, China. The research results may differ in other regions due to differences in sunlight exposure time and eating habits. Second, we did not collect data on children's diet structure, outdoor time, or VD supplementation, so there may be some biases.

5 | CONCLUSIONS

During the COVID-19 epidemic prevention and control period, VD levels decreased significantly, while VD deficiency rates increased. These findings indicate that we should pay more attention to VD supplementation during the COVID-19 epidemic control period.

AUTHOR CONTRIBUTIONS

Tiewei Li, Xiaojuan Li, Junmei Yang, and Lijun Bi contributed to the study design and methods. Tiewei Li, Xiaojuan Li, Nan Chen, and Jianli Yang were responsible for data collection and statistical analysis. Tiewei Li and Xiaojuan Li wrote the original draft of the manuscript. Junmei Yang provided overall guidance and managed the project. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Owing to ethical constraints, the data cannot be made freely available in the manuscript or a public repository because the study involved human participants. The corresponding author can provide the data used to support the study's findings upon request.

ETHICS STATEMENT

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Hospital Ethics Review Board of Henan Children's Hospital. All procedures in this study were performed as a part of routine clinical practice. Given the retrospective nature of the study, the requirement for informed consent was waived.

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