#### ORIGINAL RESEARCH

# Effect of Pandemic-Related Confinement on Vitamin D Status Among Children Aged 0–6 Years in Guangzhou, China: A Cross-Sectional Study

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**Purpose:** Pandemic-related confinement helps to contain the transmission of the novel coronavirus disease (COVID-19) but restricts children's exposure to sunlight, thereby possibly affecting their 25-hydroxyvitamin D [25(OH)D] levels. This study aimed to examine the effect of COVID-19 measures on 25(OH)D levels in children.

**Patients and Methods:** This study included children who underwent health checks between March 1 and June 30, 2020, and those over the equivalent period during 2017–2019 (N = 3600). Children's 25(OH)D levels and the proportion of children with vitamin D deficiency were compared between different observation periods.

**Results:** The mean serum 25(OH)D level was  $84 \pm 25$ nmol/L. The overall proportion of children with vitamin D deficiency (25(OH)D level <50 nmol/L) was 4.6%. Home confinement led to an increase in the proportion of children aged 3–6 years with vitamin D deficiency during March 1–June 30, 2020 compared with the same months in previous years, and the most noticeable increase was found in March 2020. In children aged 3–6 years, 25(OH)D levels were lower in 2020 (65 ± 17nmol/L) than during 2017–2019, and the proportion of those with vitamin D deficiency was higher in 2020 (19.0%) than in previous years. Among children aged 0.5–1 and 1–3 years, 25(OH)D levels were higher (97 ± 25 nmol/L, 91 ± 27 nmol/L), while the proportion of children with vitamin D deficiency was lower in 2020 (2.3%, 3.0%) than during 2017–2019.

**Conclusion:** The 25(OH)D levels tended to decrease gradually with increasing age. Reduced sunlight exposure during confinement is associated with lower 25(OH)D levels among children aged 3–6 years. Therefore, vitamin D supplementation for children aged >3years is recommended.

Keywords: 25-hydroxyvitamin D, coronavirus disease, deficiency, sunlight exposure

### Introduction

The novel coronavirus disease (COVID-19) pandemic has been spreading worldwide since December 2019. To reduce the rate of virus transmission, the Chinese government implemented a series of social distancing policies, restricting travel and movement and requiring a greater physical distance between people in public spaces.<sup>1,2</sup> Levels 1 and 2 of public health response, including the shutdown of public transportation systems, travel restrictions, and temperature measurement of people entering public spaces, were initiated in Guangdong Province between January 23 and May 8, 2020. Residents were encouraged to work from home and leave home only for essential activities. Moreover, the Spring Festival holiday was

extended, and return to work and school was postponed. Libraries, factories, and government agencies were temporarily closed.<sup>3</sup> Although these measures helped to reduce COVID-19 transmission rates,<sup>4</sup> they were associated with short- and long-term consequences. Indeed, reduced physical activity due to confinement is likely to increase the adoption of unhealthy lifestyles, thereby increasing the prevalence of risk factors for noncommunicable diseases and exacerbating existing clinical problems.<sup>5</sup> In addition, an online survey of Canadian parents evaluated changes in children's play and exercise patterns during pandemic-related confinement and showed that up to 95.2% of children and 99.4% of youth did not get the recommended amount of physical activity.<sup>6</sup> These findings suggest that pandemic-related confinement affects children's well-being and health.

The prevalence of vitamin D deficiency is increasing globally. The Endocrine Society's clinical practice guidelines recommend that vitamin D status should be divided into deficiency, insufficiency, and sufficiency, corresponding to 25-hydroxyvitamin D [25(OH)D] levels of <50, 50–75, and  $\geq$ 75 nmol/L, respectively.<sup>7</sup> Sources of vitamin D include cutaneous synthesis from cholecalciferol upon exposure to ultraviolet-B light, specific foods, and dietary supplements. Notably, even among individuals who have a high intake of vitamin D-containing products and those who live in higher than mid-latitude regions, sunlight exposure remains an essential factor in maintaining sufficient 25(OH)D levels.<sup>8</sup> Consistently, our previous studies also have shown that in Guangzhou, a city in southern China with a subtropical climate and sufficient sunlight exposure, children and pregnant women tend to have vitamin D deficiency or insufficiency.9,10

Pandemic-related confinement reduces the amount of time spent outdoors, particularly among children. It is likely that 25(OH)D levels in children were lower during the period of confinement than otherwise. To verify our hypothesis, we conducted a retrospective cross-sectional study to compare 25(OH)D levels among children before and after pandemic-related confinement in the Guangzhou area of southern China (23°70 N, 113°15 E).

### **Patients and Methods**

This study included children who underwent a routine physical examination between March 1 and June 30 during 2017–2020. Children were excluded if they had a medical history of vitamin D-associated metabolic disorders, such as skeletal or gastrointestinal system diseases, liver or

kidney diseases, genetic syndromes, obesity, malnutrition, or malabsorption disorders. We extracted data on date of birth, sex, date of hospital visits, and 25(OH)D levels, which were stored in the Hospital Information System. Plasma 25(OH)D levels were determined using an electrochemiluminescence immunoassay (Abbott Laboratories, Lake Bluff, IL, USA) with an intra/inter-assay coefficient of variation of <10.0%. Vitamin D deficiency and insufficiency were defined as 25(OH)D levels of <50 and 50–75 nmol/L, respectively, according to the Endocrine Society's clinical practice guidelines.<sup>7</sup>

Children were examined between March 1 and June 30, 2020 (ie, during the period when confinement measures were introduced from January 23 to May 8, 2020), and their 25(OH)D levels were compared with those in children examined over the equivalent quarter during 2017–2019. The 2020 children included 150 boys and 150 girls aged 3–6 years, 300 infants aged 0.5–1 year, and 300 toddlers aged 1–3 years. Age- and sex-matched children examined during 2017–2019 were also included. A total of 300 children were included in each age group per year, and in total, 3600 children were included in the study.

Serum 25(OH)D levels are presented as means and standard deviations, and categorical variables are presented as absolute values and relative frequencies. Mean serum 25(OH)D levels were compared between different observation periods (from March to June), age groups, and observation groups (2017–2019 and 2020) using the ANOVA test. Pearson's chi-square test was used for comparisons of categorical variables. P-values <0.05 were considered statistically significant. SPSS statistical software version 23 (IBM Corp, Armonk, NY, USA) was used for statistical analysis.

### Results

The mean age of participants was  $29 \pm 23$  (range, 6–84) months. The mean serum 25(OH)D level was  $84 \pm 25$  (range, 28–247) nmol/L. The overall proportion of children with vitamin D deficiency (25(OH)D level <50 nmol/L) was 4.6%. The overall average 25(OH)D level in 900 children evaluated from March to June 2020 was  $84 \pm 27$  nmol/L. The proportion of children with vitamin D deficiency recorded between March and June 2020 (8.1%) was higher than that recorded during the same period in previous years (2017, 2018, and 2019: 4.9%, 2.2%, and 43.1%, respectively) (p < 0.05). Notably, the proportion of children with vitamin D sufficiency (25(OH)D  $\geq$  75 nmol/L) recorded in

Table I	Characteristics	of the	Participants	(N =	3600)
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	2020 (N=900)	2019 (N=900)	2018 (N=900)	2017 (N=900)	P value
Mean of age (Mean ± SD, months)	28 ± 23	29 ± 23	28 ± 22	29 ± 22	0.96 <sup>b</sup>
Month of blood collection, n (%)		·		·	
March	95 (10.6%)	204 (22.7%)	231 (25.7%)	194 (21.6%)	<0.001ª
April	183 (20.3%)	208 (23.1%)	230 (25.6%)	207 (23.0%)	
May	316 (35.1%)	256 (28.4%)	224 (24.9%)	233 (25.9%)	
June	306 (34.0%)	232 (25.8%)	215 (23.9%)	266 (29.6%)	
25(OH)D level (Mean $\pm$ SD, nmol/L)	84 ± 27	86 ± 25	84 ± 24	82 ± 25	0.03 <sup>b</sup>
25(OH)D categories, n (%)					
Deficiency (<50 nmol/L)	73 (8.1%)	28 (3.1%)	20 (2.2%)	44 (4.9%)	<0.001ª
Insufficiency (50–75 nmol/L)	290 (32.2%)	326 (36.2%)	372 (41.3%)	383 (42.6%)	
Sufficiency (≥75 nmol/L)	537 (59.7%)	546 (60.7%)	508 (56.4%)	473 (52.6%)	

Notes: <sup>a</sup>Differences between groups were tested using the chi-square test. <sup>b</sup>Differences between groups were tested by the ANOVA test.

Abbreviations: SD, standard deviation; 25(OH)D, serum 25-hydroxyvitamin D.

2020 (59.7%) was higher than that recorded in 2017 (52.6%) and 2018 (56.4%) but lower than that recorded in 2019 (60.7%) (p < 0.05). Baseline characteristics of participants are reported in Table 1.

Between 2017 and 2020, 25(OH)D levels showed a consistent and gradual downward trend with increasing age. Meanwhile, the proportion of participants with vitamin D deficiency increased with age; 25(OH)D levels in participants aged 0.5-1 years were higher in 2020 than during 2017-2018 but lower than in 2019 (p = 0.03), and 25(OH) D levels in participants aged 1-3 years in 2020 were higher than those observed in the same age groups during 2017–2019 (p < 0.001). Moreover, the proportion of participants with vitamin D deficiency observed in these two age groups (aged 0.5-1 years and aged 1-3 years) was lower than that observed in the same age groups in previous years (p = 0.01 and p = 0.003, respectively). However, opposite trends in 25(OH)D levels were observed among participants aged 3-6 years; 25(OH)D levels among children aged 3-6 years were lower in 2020 than during 2017–2019 (p <0.001), and the proportion of children aged 3-6 years with vitamin D deficiency was higher in 2020 than in previous years (p < 0.001) (Table 2; Figure 1). Between 2017 and 2020, 25(OH)D levels gradually increased from March to June. The proportion of children with vitamin D deficiency gradually decreased from March to June, and 25(OH)D levels among participants who visited the study site in March 2020 were lower than those observed in the same month during 2017–2019 (p < 0.001). Consistently, the proportion of children with vitamin D deficiency reported in March 2020 was higher than that observed in the same month during 2017-2019 (p < 0.001) (Table 3; Figure 1).

### Discussion

To our knowledge, this study is the first to explore changes in 25(OH)D levels in children due to COVID-19 pandemic-related confinement. The present study found that 25(OH)D levels before and after confinement were lower among children aged 3–6 years than among children aged <3 years. Consistently, Zhang et al analyzed 25(OH)D levels in 6953 children aged 0–6 years and revealed that the rates of vitamin D deficiency among children aged 0–1, 1–3, and 3–6 years were 17.9%, 21.2%, and 48.1%, respectively,<sup>11</sup> and Isa et al found a decrease in 25(OH)D levels of 2.164 nmol/L per year of age and showed that 25 (OH)D levels were negatively associated with increasing age.<sup>12</sup> Taken together, these findings suggest that 25(OH)

The present findings are related to public health policies in China. Lack of regular vitamin D supplementation, reduced intake of dietary products fortified with vitamin D, insufficient sunlight exposure, and reduced amounts of outdoor activities contribute to vitamin D deficiency in older children. Prolonged confinement is associated with reduced exposure to sunlight, which is associated with a lower rate of cutaneous vitamin D synthesis. As expected, in the present study, 25(OH)D levels measured in 2020 among children aged 3–6 years were lower than those measured in previous years among children at the same age, while the proportion of children with vitamin D deficiency was higher in 2020 than in previous years. To

Age Group		2020 (N=900)	2019 (N=900)	2018 (N=900)	2017 (N=900)	P value		
0.5–Iy	25(OH)D level (Mean ± SD, nmol/L)	97 ± 25	98 ± 26	94 ± 29	92 ± 29	0.03 <sup>b</sup>		
	25(OH)D categories, n (%)							
	Deficiency (<50 nmol/L)	7 (2.3%)	8 (2.7%)	10 (3.3%)	13 (4.3%)	0.01ª		
	Insufficiency (50–75 nmol/L)	55 (18.3%)	49 (16.3%)	76 (25.3%)	79 (26.3%)			
	Sufficiency (≥75 nmol/L)	238 (79.3%)	243 (81.0%)	214 (71.3%)	208 (69.3%)			
Ι3γ	25(OH)D level (Mean ± SD, nmol/L)	91 ± 27	89 ± 24	84± 24	84 ± 24	<0.001 <sup>b</sup>		
	25(OH)D categories, n (%)							
	Deficiency (<50 nmol/L)	9 (3.0%)	7 (2.3%)	10 (3.3%)	14 (4.7%)	0.003 <sup>a</sup>		
	Insufficiency (50–75 nmol/L)	73 (24.3%)	79 (26.3%)	106 (35.3%)	109 (36.3%)			
	Sufficiency (≥75 nmol/L)	218 (72.7%)	214 (71.3%)	184 (61.3%)	177 (59.0%)			
3—6у	25(OH)D level (Mean ± SD, nmol/L)	65 ± 17	70 ± 16	73 ± 13	70 ± 14	<0.001 <sup>b</sup>		
	25(OH)D categories, n (%)							
	Deficiency (<50 nmol/L)	57 (19.0%)	13 (4.3%)	0 (0.0%)	17 (5.7%)	<0.001ª		
	Insufficiency (50–75 nmol/L)	162 (54.0%)	198 (66.0%)	190 (63.3%)	195 (65.0%)			
	Sufficiency (≥75 nmol/L)	81 (27.0%)	89 (29.7%)	110 (36.7%)	88 (29.3%)			

Table 2 Vitamin D Status of Different Age Groups from 2017 to 2020

**Notes:** <sup>a</sup>Differences between groups were tested using the chi-square test. <sup>b</sup>Differences between groups were tested by the ANOVA test. **Abbreviations:** SD, standard deviation; 25(OH)D, serum 25-hydroxyvitamin D.

prevent vitamin D-related rickets, vitamin D at a dose of 400 IU/day is administered to infants up to 2 years of age. As children aged <3 years took daily vitamin D supplements, their 25(OH)D levels were not affected by pandemic-related confinement. In fact, 25(OH)D levels of children aged <3 years in 2020 were higher than those

of their peers measured during the same period in previous years.

In addition to the cutaneous synthesis of vitamin D, vitamin D fortified diets and supplements are also important sources of vitamin D. During home confinement, access to food and medication was not significantly

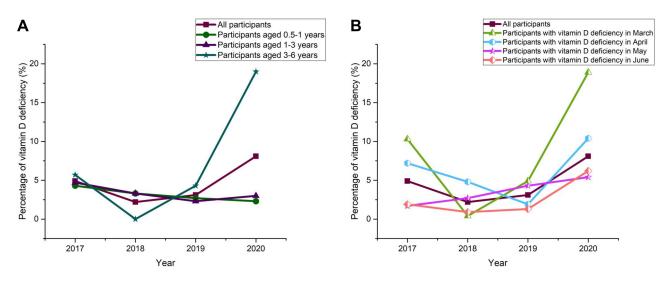


Figure I The percentage of vitamin D deficiency (25(OH)D < 50 nmol/L) in 2017–2019, stratified by age group (A) and month (B).

Month		2020 (N=900)	2019 (N=900)	2018 (N=900)	2017 (N=900)	P value		
March	25(OH)D level (Mean ± SD, nmol/L)	76 ± 29	85 ± 24	84 ± 23	77 ± 23	<0.001 <sup>b</sup>		
	25(OH)D categories, n (%)							
	Deficiency (<50 nmol/L)	18 (18.9%)	10 (4.9%)	I (0.4%)	20 (10.3%)	<0.001ª		
	Insufficiency (50–75 nmol/L)	32 (33.7%)	70 (34.3%)	91 (39.4%)	91 (46.9%)			
	Sufficiency (≥75 nmol/L)	45 (47.4%)	124 (60.8%)	139 (60.2%)	83 (42.8%)			
April	25(OH)D level (Mean ± SD, nmol/L)	82 ± 24	84 ± 24	81 ± 23	80 ± 25	0.39 <sup>b</sup>		
	25(OH)D categories, n (%)							
	Deficiency (<50 nmol/L)	19 (10.4%)	4 (1.9%)	(4.8%)	15 (7.2%)	0.001ª		
	Insufficiency (50–75 nmol/L)	56 (30.6%)	85 (40.9%)	96 (41.7%)	94 (45.4%)			
	Sufficiency (≥75 nmol/L)	108 (59.0%)	119 (57.2%)	123 (53.5%)	98 (47.3%)			
May	25(OH)D level (Mean ± SD, nmol/L)	85 ± 25	85 ± 25	85± 24	86 ± 26	0.98 <sup>b</sup>		
	25(OH)D categories, n (%)							
	Deficiency (<50 nmol/L)	17 (5.4%)	(4.3%)	6 (2.7%)	4 (1.7%)	0.25 <sup>a</sup>		
	Insufficiency (50–75 nmol/L)	109 (34.5%)	94 (36.7%)	91 (40.6%)	93 (39.9%)			
	Sufficiency (≥75 nmol/L)	190 (60.1%)	151 (59.0%)	127 (56.7%)	136 (58.4%)			
June	25(OH)D level (Mean ± SD, nmol/L)	88 ± 29	89 ± 27	86 ± 27	86 ± 25	0.34 <sup>b</sup>		
	25(OH)D categories, n (%)							
	Deficiency (<50 nmol/L)	19 (6.2%)	3 (1.3%)	2 (0.9%)	5 (1.9%)	<0.001 <sup>a</sup>		
	Insufficiency (50–75 nmol/L)	93 (30.4%)	77 (33.2%)	94 (43.7%)	105 (39.5%)			
	Sufficiency (≥75 nmol/L)	194 (63.4%)	152 (65.5%)	119 (55.3%)	156 (58.6%)			

Table 3	Vitamin	D St	atus in	Different	Months	from	2017	to	2020
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**Notes:** <sup>a</sup>Differences between groups were tested using the chi-square test. <sup>b</sup>Differences between groups were tested by the ANOVA test. **Abbreviations:** SD, standard deviation; 25(OH)D, serum 25-hydroxyvitamin D.

restricted. During the COVID-19 pandemic, many medical centers have shifted from person-to-person appointments to providing telemedicine and online services. Some medical centers provide online drug-related services, including placing orders, making payments, and arranging drug prescription and delivery.<sup>13,14</sup> A study of the dietary diversity of China's residents indicates that online services have likely helped residents maintain a diversified diet during pandemic-related confinement.<sup>15</sup> This finding suggests that internet access and online services can help ensure that people continue to receive vitamin D supplements and fortified dietary products during pandemic-related confinement.

Although the vitamin D supplementation policy is aimed to prevent rickets, the rate of compliance among children remains very low. Daily intake over extended periods of time is a common cause of therapeutic dropout.<sup>16</sup> The COVID-19 pandemic has both positive and negative effects on lifestyle choices.<sup>17</sup> For example, during confinement, patients with type 1 diabetes had more time to manage their disease and achieve better glycemic control.<sup>18</sup> Similarly, more time at home might have increased the extent of parental supervision of children, thereby improving vitamin D supplementation compliance among children aged <3 years.

Seasonal variations in 25(OH)D levels have been previously reported and are associated with seasonal variations in sunlight. For example, Chaoimh et al showed that the proportion of children with vitamin D deficiency who lived in Cork, Ireland (51°N) was 45.2% between November and April and 10.4% between May and October,<sup>19</sup> and Nakano et al examined seasonal fluctuations in serum 25(OH)D levels among children who lived in Shizuoka (35.2°N, 138.4°E) and Tokyo (35.4°N, 139.4°E) and found that serum 25(OH)D levels were lower in winter and spring than in summer and autumn.<sup>20</sup> Home confinement led to an increase in the proportion of children with vitamin D deficiency between March and June 2020 compared to the same month in previous years. Public health responses were initiated in Guangdong Province on January 23, 2020. Reduced sunlight exposure led to lower 25(OH)D levels, and consequently, the proportion of children with vitamin D deficiency in March 2020 was higher than that during 2017–2019 (p < 0.001). After restrictions were lifted, sunlight exposure and children's outdoor activities increased during the summer months. Between April and June 2020, the impact of home confinement on children's 25(OH)D levels gradually decreased.

The present study is associated with the following limitations. First, in China, the preventive use of vitamin D is common among healthy children aged <3 years; however, similar preventive supplementation is rare among older children. As this study included participants from both groups, the present findings are unlikely to be representative in the general population. Second, due to lack of participant dietary information, including details of daily vitamin D intake, we were unable to control for the effect of vitamin D intake on the present findings; these factors might have resulted in biased estimates. Third, this retrospective study did not account for the amount or duration of sunlight exposure among participants. Variations in sunlight exposure between participants might have biased our findings. Fourth, the present study was based on a single measurement of 25(OH)D levels and did not account for its longitudinal changes. In addition, there was no detailed information on parathyroid hormone in this study. Therefore, we cannot assess the associations between parathyroid hormone and 25(OH)D levels in children. Finally, the diversity of vitamin D receptors might also affect individual 25(OH)D levels; however, this aspect was outside the scope of the present study.

### Conclusion

Pandemic-related confinement had different effects on 25 (OH)D levels among different ages of children. Serum vitamin D levels decreased with increasing age, and the decline in 25(OH)D levels among children aged 3–6 years was related to reduced sunlight exposure. However, no

decline in 25(OH)D levels among children aged <3 years was observed, likely due to regular vitamin D supplementation. These findings can inform future policy on preventive vitamin D supplementation among older children.

## Abbreviations

25(OH)D, 25-hydroxyvitamin D (vitamin D); COVID-19, coronavirus disease.

# Ethics Approval and Informed Consent

Ethics approval was obtained from the Medical Research Ethics Committee of Guangdong Women and Children Hospital, Guangdong, China (No.202,001,183). This study was conducted in accordance with the principles stated in the Declaration of Helsinki. The requirement for informed consent was waived due to the retrospective nature of the study. Data were processed anonymously to ensure the privacy of patients.

### **Author Contributions**

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; drafted the article or revised it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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# Disclosure

The authors declare that they have no competing interests.

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