



Effects of the COVID-19 pandemic on serum vitamin D concentration in Korean children

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Purpose: Social distancing policies and school closures in South Korea induced by coronavirus disease 2019 have raised concerns about a lower chance of exposure to sunlight in children and adolescents. This study investigates changes in the vitamin D status of children and adolescents following the pandemic.

Methods: This retrospective study includes healthy children aged 3–18 years who visited Hanyang University Hospitals in Seoul or Guri during pre-coronavirus disease 2019 (COVID-19) and post-COVID-19 pandemic periods. August 2017 to July 2019 is defined as the pre-COVID-19 pandemic period, while the period from July 2020 to July 2021 is defined as post-COVID-19 or "during the pandemic." Propensity scores were used to match the prepandemic and pandemic groups 1:1 based on age, sex, season of blood collection, and body mass index z-score to compare vitamin D status among subjects.

Results: Among 786 eligible children, 506 were matched using propensity scores. There were no significant differences in mean serum 25-hydroxyvitamin D (25(OH)D) levels (20.1 ± 6.5 ng/mL vs. 19.9 ± 6.3 ng/mL, $P > 0.05$) or vitamin D deficiency rates (53.0% vs. 54.9%, $P > 0.05$) between the prepandemic and pandemic groups. Seasonal analysis revealed lower mean serum 25(OH)D levels during the pandemic in winter/spring seasons in comparison to these levels in subjects in prepandemic winter/spring seasons (19.1 ± 3.8 ng/mL vs. 17.2 ± 3.7 ng/mL, $P = 0.006$).

Conclusion: During the COVID-19 pandemic, Korean children and adolescents showed similar serum 25(OH)D levels and vitamin D status to the prepandemic period, with a significant decrease in these measures observed in winter/spring seasons only. Prolonged confinement, such as in pandemic circumstances, underscores the need for vigilant monitoring of vitamin D status and supplementation, particularly in high-risk seasons.

Keywords: Vitamin D, COVID-19, Propensity score, Child, Adolescent

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Highlights

- Coronavirus disease 2019 pandemic did not significantly alter overall serum vitamin D levels in Korean children.
- Seasonal analysis revealed significant declines in winter/spring vitamin D levels.
- Study underscores the need for vigilant vitamin D monitoring during extended indoor periods in high-risk seasons.

Introduction

Recent studies reveal that, in addition to regulating calcium metabolism, vitamin D plays a crucial role in the human body.¹⁾ The coronavirus disease 2019 (COVID-19) pandemic increased researchers' interest in the role of vitamin D in immunomodulatory effects and the

pathogenesis of infectious diseases.^{2,3)}

Vitamin D is primarily synthesized via cutaneous exposure to ultraviolet B radiation.⁴⁾ Today, vitamin D deficiency (VDD) is an important public health challenge in children and adolescents worldwide, probably due to decreased exposure to sunlight. Modern lifestyle habits, including sedentary habits and increased indoor time, have increased VDD in adults and children.⁵⁾

The COVID-19 pandemic led to prolonged restrictions that may significantly impact the health of children and adolescents.⁶⁾ Since the World Health Organization declared the COVID-19 pandemic in March 2020, Korea has implemented a national social distancing campaign to reduce the transmission of COVID-19.⁷⁾ Following the first school closure on February 23, 2020, the country transitioned to expanding remote learning. Additionally, social distancing restrictions have limited children's access to regular physical activity,⁸⁾ which has reduced overall exposure time to sunlight. Accordingly, prolonged confinement has raised concerns about an increased risk of VDD due to reduced opportunities for sun exposure.

Several epidemiological studies have explored changes in the vitamin D status of pediatric patients in the context of the COVID-19 pandemic. One study in Korea reports decreased 25-hydroxyvitamin D (25(OH)D) concentrations after 6 months of school lockdown when accounting for seasonality despite increased obesity in subjects.⁹⁾ Another study in Turkey reveals that mean 25(OH)D concentrations in school-aged children during the first year of the pandemic were similar to those during the prepandemic period, but the study did not account for age, sex, and seasonal differences.¹⁰⁾ Heterogeneous results suggest that these studies do not simultaneously consider factors that may influence vitamin D status, such as age, sex, adiposity, seasonality, and the use of dietary supplements. Accordingly, this study uses propensity score matching to balance the range of variables that can affect vitamin D status. Our approach makes it possible to assess the direct or indirect influence of social distancing and school closures during the COVID-19 pandemic on vitamin D status and serum 25(OH)D concentrations in pediatric subjects.

Materials and methods

1. Study design and population

This is a retrospective cohort study of children and adolescents who visited the Division of Pediatric Endocrinology at Hanyang University Hospitals in Seoul or Guri for initial growth and development assessment. Patients who underwent a survey recording medication or who had taken nutrient supplements within the preceding year, those with perinatal history, and patients with underlying diseases who had undergone a measurement of serum 25(OH)D concentrations at the visit were included. Excluded from our study were (1) children under 3 years of age, (2) patients with underlying diseases that could influence their height and weight status or bone metabolism, such as endocrine disorders (growth hormone deficiency,

diabetes mellitus, and thyroid disease) and severe illnesses affecting general nutritional status, such as hemato-oncologic, neurologic, and chronic kidney diseases, and (3) patients who reported taking other medications, hormonal drugs, vitamin or dietary supplements, or growth-promoting herbal medicine within the preceding year. We classified study groups based on the date of social distancing and the declaration of nationwide lockdown in Korea (February 29, 2020). The "prepandemic" group comprised patients who visited the hospitals before the enforcement of social distancing and school closure from August 2017 to July 2019, and the "pandemic" group comprised those who visited after enforcement of these pandemic circumstances from July 2020 to July 2021. In further analyses, participants were categorized into 2 groups based on blood sampling season—namely, "summer/fall" and "winter/spring."

2. Study definitions

Vitamin D status was measured using 25(OH)D concentration levels. Accordingly, patients were grouped into VDD (25(OH)D < 20 ng/mL), insufficiency (25(OH)D ≥ 20, < 30 ng/mL), or sufficiency (25(OH)D > 30 ng/mL) groups.¹¹⁾ To adjust for seasonal variability, patients were divided according to seasons during which blood sampling had occurred: patients with samples collected from June to November were defined as the summer/fall group, and patients with samples collected from December to May were defined as the winter/spring group.

3. Anthropometric measurements

Medical records of study participants were reviewed for the following objective parameters: birth date, sex, date of first visit, height, and weight. Height (cm) was measured to the nearest 0.1 cm using a Harpenden stadiometer (Holtain Ltd., Crymch, Wales, UK), and weight (kg) was measured to the nearest 0.1 kg using a digital scale. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared and expressed as kg/m². Age-specific and sex-specific z-scores for height, weight, and BMI were assessed using the 2017 Korean National Growth Charts.

4. Statistical analysis

All calculations were performed using R ver. 4.2.3 (R Foundation for Statistical Computing, Vienna, Austria). Quantitative variables are expressed as mean ± standard deviation and were analyzed using Student *t*-test. Qualitative variables are expressed as frequencies and percentages and were analyzed using chi-square test. Statistical significance was set at *P* < 0.05.

As nonrandomized studies, observational studies are needed to reduce the effects of selection bias on conclusions. To address these potential biases, propensity score matching was performed to ensure homogeneity between the prepandemic and pandemic groups using the nearest neighbor matching method. A multivariate logistic regression model was constructed to

predict propensity scores based on age, sex, BMI z-score, and season of blood collection. Subsequently, patients were matched in a 1:1 ratio with a caliper of 0.3 times the standard deviation of the logit propensity score. The matching process was conducted using the MatchIt function in R software. The standardized mean difference (SMD) was calculated to assess the balance of variables between the daily and monthly groups, with an SMD <0.25 indicating a negligible covariate imbalance between the 2 groups.

5. Ethical statement

The study protocol was approved by the Institutional Review Board of Hanyang University Hospital (2022-07-054). Requirement for informed consent was waived due to the

retrospective nature of the study.

Results

1. Baseline characteristics

In this study, 1,460 patients were initially analyzed. We included 786 patients after excluding 8 patients under 3 years of age; 2 patients with an underlying disease; and 664 patients who had taken hormonal drugs, vitamin or dietary supplements, growth-promoting herbal medicine, or other medications within the year preceding the survey. The prepandemic group (n=292, males=59 [20.2%]); mean age, 8.5 ± 2.0 years) and pandemic group (n=494, 217 males [43.9%]; mean age, 9.5 ± 2.3 years) were matched at 1:1 (253 patients in each cohort; Fig. 1). Absolute values of the standard differences in season, sex, age,

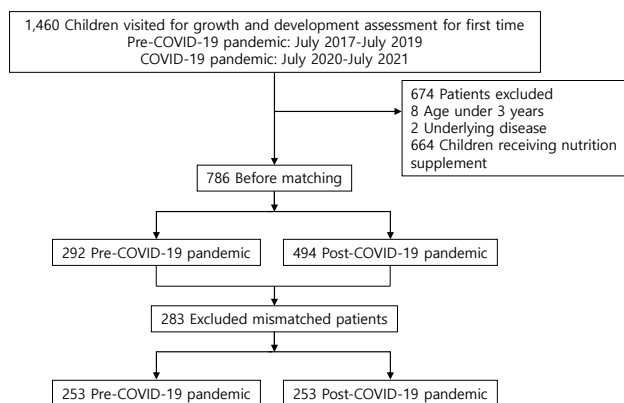


Fig. 1. Schematic diagram of the research. COVID-19, coronavirus disease 2019.

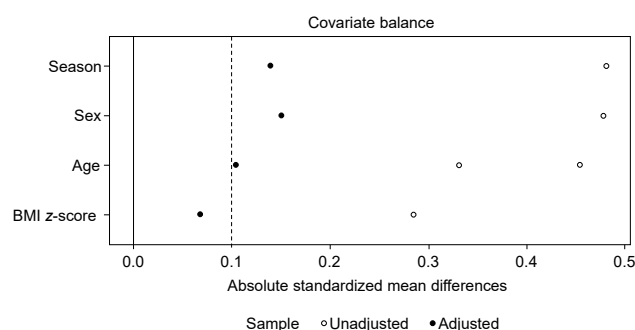


Fig. 2. Comparison of the absolute standardized mean difference before and after nearest neighbor matching. BMI, body mass index.

Table 1. Comparison of demographic characteristics between prepandemic and pandemic groups before and after propensity score matching

Variable	Full cohort				Propensity-score matched cohort			
	Prepandemic (n=292)	Pandemic (n=494)	P-value	SMD	Prepandemic (n=253)	Pandemic (n=253)	P-value	SMD
Age (yr)	8.5 ± 2.0	9.5 ± 2.3	<0.001*	0.454	8.6 ± 1.9	8.8 ± 2.1	0.177	0.104
Sex			<0.001*	0.478			0.069	0.151
Male	59 (20.2)	217 (43.9)			57 (22.5)	76 (30.0)		
Female	233 (79.8)	277 (56.1)			196 (77.5)	177 (70.0)		
Height z-score	0.0 ± 1.6	0.2 ± 1.1	0.088		0.1 ± 1.6	0.1 ± 1.1	0.806	
Weight z-score	0.2 ± 1.5	0.5 ± 1.2	<0.001*		0.2 ± 1.5	0.3 ± 1.1	0.570	
Body mass index z-score	0.2 ± 1.3	0.6 ± 1.3	<0.001*	0.285	0.3 ± 1.3	0.4 ± 1.2	0.421	0.068
Season			<0.001*	0.481			0.155	0.140
Summer/fall	118 (40.4)	314 (63.6)			117 (46.2)	134 (53.0)		
Winter/spring	174 (59.6)	180 (36.4)			136 (53.8)	119 (47.0)		
Serum 25(OH)D (ng/mL)	20.1 ± 6.4	20.0 ± 6.4	0.759		20.1 ± 6.5	19.9 ± 6.3	0.719	
Vitamin D status			0.988				0.859	
Deficiency	155 (53.1)	260 (52.6)			134 (53.0)	139 (54.9)		
Insufficiency	116 (39.7)	199 (40.3)			99 (39.1)	93 (36.8)		
Sufficiency	21 (7.2)	35 (7.1)			20 (7.9)	21 (8.3)		

Values are presented as mean $\pm$ standard deviation or number (%). SMD, standardized mean difference; 25(OH)D, 25-hydroxyvitamin D.

* $P < 0.05$, statistically significant differences.

and BMI z-score before and after matching are shown in Fig. 2. Demographic characteristics of the patients before matching are presented in Table 1. Mean 25(OH)D concentration showed no significant difference between prepandemic and pandemic groups (20.1 ± 6.4 ng/mL vs. 20.0 ± 6.4 ng/mL, respectively). Additionally, proportions of subjects with VDD (53.1% in the prepandemic group vs. 52.6% in the pandemic group), vitamin D insufficiency (39.7% in the prepandemic group vs. 40.3% in the pandemic group), and sufficiency (7.2% in the prepandemic group vs. 7.1% in the pandemic group) were similar between the 2 groups ($P > 0.05$). Weight and BMI z-scores were higher in the pandemic group than in the prepandemic group (weight z-score: 0.2 ± 1.5 in the prepandemic group vs. 0.5 ± 1.2 in the pandemic group; BMI z-score: 0.2 ± 1.3 in the prepandemic group vs. 0.6 ± 1.3 in the pandemic group, $P < 0.001$), while the height z-score was comparable ($P > 0.05$). Table 2 shows that winter/spring seasons had significantly higher weight and BMI z-scores in the pandemic group than in the prepandemic group (weight z-score: 0.1 ± 1.4 in the prepandemic group vs. 0.6 ± 1.2 in the pandemic group; BMI z-score: 0.2 ± 0.5 in the prepandemic group vs. 0.7 ± 1.2 in the pandemic group, $P < 0.001$).

2. Comparison of vitamin D status between prepandemic and pandemic subjects after propensity score matching

Table 1 also shows baseline characteristics of the 2 groups after nearest neighbor matching based on age, sex, season, and BMI z-score. No significant difference was found in mean 25(OH)D concentrations between the 2 groups (20.1 ± 6.5 ng/mL in the prepandemic group vs. 19.9 ± 6.3 ng/mL in the pandemic group, $P > 0.05$). Furthermore, the proportion of subjects with VDD did not differ significantly between the prepandemic and pandemic groups (53.0% in the prepandemic group vs. 54.9% in the pandemic group, $P > 0.05$). However, after propensity score matching based on age, sex, and BMI z-scores in each patient group for summer/fall and winter/spring seasons of blood sampling (Table 3), concentrations of serum 25(OH)D were significantly lower in the pandemic group compared to the prepandemic group only during winter/spring (19.1 ± 3.8 in the prepandemic group vs. 17.2 ± 3.7 ng/mL in the pandemic group, $P = 0.006$). Additionally, during the winter/spring seasons, the proportion of subjects with VDD in the pandemic group was significantly higher than in the prepandemic group (55.2%

Table 2. Comparison of demographic characteristics between prepandemic and pandemic groups divided by season before propensity score matching

Variable	Summer/fall			Winter/spring		
	Prepandemic (n=118)	Pandemic (n=314)	P-value	Prepandemic (n=174)	Pandemic (n=180)	P-value
Age (yr)	8.4 ± 2.1	9.4 ± 2.2	$<0.001^*$	8.5 ± 1.9	9.8 ± 2.4	$<0.001^*$
Sex			$<0.001^*$			$<0.001^*$
Male	21 (17.8)	121 (38.5)		38 (21.8)	96 (53.3)	
Female	97 (82.2)	193 (61.5)		136 (78.2)	84 (46.7)	
Height z-score	0.3 ± 1.7	0.3 ± 1.2	0.95	0.1 ± 1.6	0.2 ± 1.1	0.07
Weight z-score	0.3 ± 1.5	0.5 ± 1.3	0.17	0.1 ± 1.4	0.6 ± 1.2	$<0.001^*$
Body mass index z-score	0.3 ± 1.3	0.5 ± 1.3	0.07	0.2 ± 1.2	0.7 ± 1.2	$<0.001^*$

Values are presented as mean $\pm$ standard deviation or number (%)

* $P < 0.05$, statistically significant differences.

Table 3. Comparison of demographic characteristics between prepandemic and pandemic groups divided by season after propensity score matching

Variable	Summer/fall			Winter/spring		
	Prepandemic (n=118)	Pandemic (n=118)	P-value	Prepandemic (n=116)	Pandemic (n=116)	P-value
Age (yr)	8.1 ± 1.4	8.7 ± 1.4	0.008	8.6 ± 1.5	8.8 ± 1.4	0.820
Sex			1.000			1.000
Male	21 (17.8)	22 (18.6)		36 (31.0)	37 (31.9)	
Female	97 (82.2)	96 (81.4)		80 (69.0)	79 (68.1)	
Height z-score	0.6 ± 1.1	0.2 ± 1.0	0.833	-0.1 ± 1.6	0.1 ± 1.1	0.179
Weight z-score	0.3 ± 1.5	0.6 ± 1.3	0.106	0.2 ± 1.5	0.4 ± 1.2	0.156
Body mass index z-score	0.2 ± 1.1	0.5 ± 0.9	0.066	0.2 ± 1.1	0.5 ± 0.9	0.268
Serum 25(OH)D (ng/mL)	19.3 ± 4.2	20.1 ± 3.9	0.529	19.1 ± 3.8	17.2 ± 3.7	0.006*
Vitamin D status			0.802			0.017*
Deficiency	61 (51.7)	57 (48.3)		64 (55.2)	81 (69.8)	
Insufficiency	47 (39.8)	52 (44.1)		46 (39.7)	26 (22.4)	
Sufficiency	10 (8.5)	9 (7.6)		6 (5.2)	9 (7.8)	

Values are presented as mean $\pm$ standard deviation or number (%)

25(OH)D, 25-hydroxyvitamin D.

* $P < 0.05$, statistically significant differences.

in the prepandemic group vs. 69.8% in the pandemic group, $P=0.017$).

Discussion

Since declaration of the COVID-19 pandemic, several studies have explored changes in the vitamin D status of children and adolescents. However, no studies have compared vitamin D status after adjusting for factors that may influence vitamin D concentrations in this population. This study uses propensity score matching to balance covariates that can influence serum 25(OH)D concentrations and explores the effects of COVID-19 pandemic-induced indoor confinement on vitamin D status in children and adolescents. Retrospective data demonstrate no significant changes in serum 25(OH)D concentrations during the COVID-19 pandemic in comparison to the prepandemic period among a specific sample of children and adolescents.

Because vitamin D is mainly synthesized through sunlight exposure, stay-at-home orders and lockdown measures implemented to prevent the spread of COVID-19 may have influenced the vitamin D status in both children and adolescents.^{10,12} Beyazgül et al.¹⁰ explored changes in vitamin D concentrations of children residing in Turkey during the first year of the pandemic. Their study revealed that mean vitamin D concentrations did not change in overall study groups following the COVID-19 pandemic but decreased only in adolescent and school-aged children. Another study conducted in Italian children and adolescents showed that mean concentrations of 25(OH)D during the COVID-19 pandemic period were similar to those in the prepandemic period, but the prevalence of VDD increased in comparison to the prepandemic period.¹² That study, however, did not consider other covariates that could influence 25(OH)D concentrations.

Previous studies indicate that factors other than sunlight exposure are associated with serum 25(OH)D concentration. First, it is well known that children and adolescents with obesity have a higher risk of VDD.¹³⁻¹⁵ This vulnerability is explained by the decreased bioavailability of vitamin D₃ due to the sequestration of vitamin D in the adipose tissue and the volumetric dilution of 25(OH)D into greater tissue volume.¹⁶ Second, sex differences may affect serum 25(OH)D concentrations in children and adolescents.¹⁷ One study explained that differences in time spent outdoors, physical activity, and exposure to sunlight can lead to a higher prevalence of VDD in girls. In addition, considerable variations in body composition (i.e., muscle tissue and adiposity) and body fat distribution might contribute to differences in vitamin D status between the sexes.¹⁸ Furthermore, previous studies have shown a decrease in serum 25(OH)D concentrations with advancing age in children, with the lowest levels during and after puberty.¹⁹ Considering these factors, the current study controls for age, sex, BMI *z*-score, and season of blood withdrawal and conducts propensity score matching to compare 25(OH)D concentrations between prepandemic and pandemic groups of children and adolescents. Our results show no significant differences in

vitamin D status between the 2 groups.

Another finding of this study is increased weight and BMI *z*-scores between study groups after the COVID-19 pandemic. It has been reported that the COVID-19 pandemic resulted in increased prevalence of obesity in the pediatric population.²⁰ Social isolation and school closures led to reduced physical activity and increased sedentary time, increasing fat accumulation in younger subjects. An excess increase in BMI of 0.24 kg/m² per year over the previous prepandemic period has been reported in the United States.²¹ Furthermore, Kang et al.⁹ revealed that the prevalence of overweight or obese increased from 23.9% to 31.4% following the COVID-19 pandemic lockdown in Korea, which is supported by the results of our study. Herein, no significant changes in BMI *z*-scores were observed after the pandemic during summer/fall seasons. However, a notable increase in BMI *z*-scores was observed during winter/spring seasons in subjects.

In Korea, located between latitudes of 33°N and 38°N, sunlight is effective in synthesizing vitamin D from April to October during the hours of 10 AM and 3 PM daily. As a result, 25(OH)D concentrations tend to be lower from winter to spring, owing to low solar exposure.^{22,23} Consequently, we categorized patients into winter/spring and summer/fall groups. After adjusting for covariates of age, sex, and BMI *z*-scores using propensity score matching, we found that serum 25(OH)D concentrations during the pandemic were similar to prepandemic levels in the summer/fall seasons. In contrast, during the winter/spring period, serum 25(OH)D levels were lower and the incidence of VDD was higher in comparison to the same period before the pandemic. These results indicate that, during winter and spring seasons in the pandemic period, children and adolescents likely experienced reduced opportunities for outdoor activities and sunlight exposure due to stay-at-home orders and school closures, increasing their risk of hypovitaminosis D. In early 2020, Seoul (where our study was conducted) accounted for 23.5% of total cases of COVID-19 in Korea, a lower rate than other regions.^{24,25} Social distancing policies relaxed around March 2020, and daily activities of living gradually resumed, indicating a minimal impact of isolation on vitamin D status in subjects during the summer/fall seasons. However, a later COVID-19 surge in Seoul led to stricter distancing in late 2020. Combined with limited school attendance until early 2021, these factors likely reduced outdoor activities and sunlight exposure among subjects in the winter/spring seasons of the postpandemic.

One strength of this study is our use of propensity score matching to investigate the impact of COVID-19 pandemic-induced changes on the vitamin D status in children and adolescents. This method allowed us to account for other variables that could influence vitamin D status. Second, through survey data on the history of medication or nutrition supplement intake across the preceding year, we excluded patients who had taken dietary supplements, vitamins, herbal medicines, or other medications.

The current study has some limitations. First, it is a retrospective study, and other factors that could influence serum 25(OH)

D concentrations, including lifestyle, diet, and physical activity,²⁶⁾ were not considered. Second, different cohorts of children before and after the COVID-19 pandemic were compared, indicating the likelihood of conflicting variables. Further prospective studies are required to confirm and extend our findings.

In conclusion, among children and adolescents, the concentration of 25(OH)D and vitamin D status was similar between prepandemic and postpandemic groups, despite an increase in weight and BMI z-scores following COVID-19. However, when we conducted separate analyses divided by seasons, our study revealed significantly lower 25(OH)D concentrations during the winter/spring seasons of the pandemic period. During extended periods of confinement, such as during the COVID-19 pandemic, obesity prevention and vitamin D status should be monitored in children and adolescents, especially during high-risk seasons of lower solar exposure.

Notes

Conflicts of interest: No potential conflict of interest relevant to this article was reported.

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Data availability: The data that support the findings of this study can be provided by the corresponding author upon reasonable request.

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