Prevalence of vitamin D insufficiency among children in southern China
A cross-sectional survey

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Abstract
Vitamin D deficiency is associated with numerous public health issues. Limited data are available for children in southern China, a region that receives abundant sunlight. We aimed to estimate the 25-hydroxyvitamin D (25(OH)D) levels in children in that area, and to determine seasonal variations in serum 25(OH)D levels. A total of 16,755 children aged 0 to 6 years, who visited the Guangdong Women and Children’s Hospital for health examination between January 2016 and May 2017, were included in the present study. The serum 25(OH)D levels ranged from 10.5 to 307.4nmol/L (mean ± standard deviation: 78.5 ± 26.3nmol/L). The prevalence of vitamin D deficiency and insufficiency were 10.8% and 39.0%, respectively. The mean serum 25(OH)D level in spring (71.8 ± 24.9 nmol/L) was lower than that in other seasons. From January to April, we found a relatively high prevalence of vitamin D deficiency or insufficiency, both of which were also found to increase with age. Logistic regression analysis revealed that vitamin D deficiency and insufficiency were significantly associated with age and season. Deficiency and insufficiency of vitamin D are common among children in southern China, despite the area receiving sufficient sunlight.

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

Keywords: 25-Hydroxyvitamin D, children, deficiency, public health

1. Introduction
It is a well-established fact that vitamin D influences calcium and phosphorus homeostasis, as well as bone health. Increasing amounts of research on vitamin D metabolites in the serum reveal that the roles played by vitamin D have implications that reach beyond the health of skeletal tissue, and include the immune, nervous, and cardiovascular systems. Low serum concentrations of vitamin D are associated with numerous adverse health issues, and the corresponding public health consequences are enormous.

Serum 25-hydroxyvitamin D (25(OH)D) is the vitamin D metabolite that is measured clinically to assess vitamin D status. Despite disagreement surrounding the establishment of the minimal desirable serum concentration of 25(OH)D, with suggested cutoff levels ranging from 25 to >100nmol/L, the occurrence of vitamin D deficiency remains common worldwide, especially in children. A study conducted in the state of Alaska, in the United States, and based on infants aged 6 to 23 months, found that 11% of children had 25(OH)D level <32.5 nmol/L and 20% of children had 25(OH)D level between 32.5 to 62.5 nmol/L. The Canadian Health Measures Survey reported a prevalence of vitamin D insufficiency (<50nmol/L) of 13% in children aged 6 to 11 years from April to October. The Fourth Korea National Health and Nutrition Examination Survey found that 56.8% of males and 93.3% of females aged 10 years and older had a serum 25(OH)D level <75nmol/L, demonstrating that vitamin D insufficiency or deficiency was very common among Koreans. In addition, several studies have reported poor vitamin D status in children in China. A study in north China found that 45.2% of adolescent girls had 25(OH)D levels <12.5 nmol/L in the winter, and 5 studies conducted in southeast China (Shanghai, Nanjing, Wenzhou, Wuxi, and Huzhou) found that vitamin D deficiency and insufficiency were prevalent among infants, preschool children, school children, and adolescents.

Although inadequate vitamin D concentrations have been reported in different populations around the world, limited data are available on the vitamin D status among children in the southern regions of China, which receive abundant sunshine. This study aimed to describe the 25(OH)D status among children in southern China, and to determine the seasonal variations in serum 25(OH)D levels.

2. Materials and methods
2.1. Ethics statement
This study was approved by the Medical Research Ethics Board of Guangdong Women and Children’s Hospital, and written informed consent was obtained from the parents of each child.
The methods were carried out in accordance with the approved guidelines that conform to the Declaration of Helsinki.

2.2. Study design and participants

This large, hospital-based cross-sectional survey was conducted in Guangzhou district, which is located in South China (23°70’N latitude) and has a typical subtropical climate and receives plenty of sunshine. Children aged 0 to 6 years who visited the Department of Children’s Health Care at Guangdong Women and Children Hospital for a health examination between January 2016 and May 2017 were included in the present study. Subjects were excluded if they were diagnosed with known skeletal disease, genetic syndromes, or malabsorptive disorders. Information on the age, sex, date of visit, and concentration of 25(OH)D were extracted from the hospital Laboratory Information System.

2.3. Vitamin D measurement

Vitamin D status was assessed through the determination of concentration of 25(OH)D, the major circulating form of vitamin D. Fasting venous blood samples (2 mL) were collected and transported on ice to the laboratory. A biochemical analysis was performed within 24 h and serum was stored at −80°C for future analysis. Serum 25(OH)D concentrations were measured through electrochemiluminescence immunoassay using the Abbott ARCHITECT i4000 system (Abbott Laboratories, Lake Bluff, IL). The inter-assay and intra-assay coefficients of variation were <10%, and the coefficient of variation for the precision of the assay from Abbott was 6.2%. Quality controls were included in each assay batch. Vitamin D status was categorized as follows: deficiency (25(OH)D < 50 nmol/L), insufficiency (50 nmol/L ≤ 25(OH)D < 75 nmol/L), and sufficiency (25(OH)D ≥ 75 nmol/L), according to the Endocrine Society’s clinical practice guidelines.144

2.4. Statistical analysis

The seasons for blood sample collection were defined as: spring (March to May), summer (June to August), autumn (September to November), and winter (December to February).

The serum 25(OH)D levels were described using mean, standard deviations (SDs), medians, and interquartile ranges. Frequencies and percentages (%) were reported for categorical variables. Tests to determine differences in mean serum 25(OH)D levels, by sex, age, month, and season, were performed using analysis of variance. We used logistic regression to examine whether the prevalence of vitamin D deficiency or deficiency differed by sex, age, month, and season, as a predictor. P < .05 was considered statistically significant. Analyses were performed using the SPSS statistical software package (V20, IBM Corp, Armonk, NY) and R software (V3.1.2, R Core Team (2014). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. http://www.R-project.org).

3. Results

Data from 16,755 children, aged 0 to 6 years, were included in the analyses. The serum 25(OH)D levels ranged from 10.5 to 307.4 nmol/L (mean ± SD: 78.5 ± 26.3 nmol/L). The vitamin D statuses, stratified by the characteristics of the participants, are shown in Table 1. There were no significant differences between the male and female participants in terms of serum 25(OH)D level. Serum 25(OH)D concentrations varied with age, month, and season (Table 1; Fig. 1). Concentrations of serum 25(OH)D significantly decreased with age, and the serum 25(OH)D level in spring (71.8 ± 24.9 nmol/L) was lower than that observed in other seasons.

Overall, the prevalence of vitamin D deficiency, insufficiency, and sufficiency were 10.8%, 39.0%, and 50.3%, respectively. During certain months (from January to April), we found a relatively high prevalence of vitamin D deficiency or insufficiency. The prevalence of vitamin D deficiency was higher in spring (17.1%) than in summer (8.9%), autumn (5.6%), and winter (9.3%). The prevalence of vitamin D deficiency and insufficiency increased with age (Fig. 2). In addition, the logistic regression analysis revealed that vitamin D deficiency and insufficiency in children were significantly associated with age, month, and season (Table 2). Furthermore, the prevalence of deficiency or insufficiency (25(OH)D < 75 nmol/L) showed the same trends by month and season among the different age groups of children (Table 3).

4. Discussion

Although 25(OH)D levels are commonly used to define vitamin D status, there is no consensus on the cutoff levels for vitamin D deficiency and insufficiency. In the present study, we evaluated

| Table 1 | Serum 25(OH)D levels in children aged 0 to 6 years, stratified by participant characteristics. |
|---|---|---|---|---|---|
| Variables | N (%) | 25-Hydroxyvitamin D levels, nmol/L | 25-Hydroxyvitamin D levels, nmol/L | 25-Hydroxyvitamin D levels, nmol/L | 25-Hydroxyvitamin D levels, nmol/L |
| Sex | | | | | |
| Male | 9671 (57.7) | 78.2 ± 25.7 | 74.9 (61.2–92.0) | .093 |
| Female | 7084 (42.3) | 78.9 ± 27.1 | 75.3 (60.1–93.3) | |
| Age, y | | | | | |
| 0 | 6441 (38.4) | 86.0 ± 27.3 | 83.0 (68.0–100.5) | .001 |
| 1 | 4441 (26.5) | 82.5 ± 25.4 | 79.7 (65.9–96.3) | |
| 2 | 2060 (12.3) | 76.4 ± 23.7 | 73.4 (61.2–87.7) | |
| 3 | 1297 (7.7) | 65.9 ± 19.2 | 65.2 (54.0–76.4) | |
| 4 | 1086 (6.4) | 62.1 ± 16.4 | 61.9 (51.1–72.8) | |
| 5 | 793 (4.7) | 57.7 ± 17.3 | 56.9 (47.6–67.7) | |
| 6 | 657 (3.9) | 58.5 ± 16.1 | 59.2 (47.9–68.7) | |
| Month of the year | | | | | |
| January | 1234 (7.4) | 75.2 ± 26.3 | 72.0 (57.8–90.0) | .001 |
| February | 1229 (7.3) | 71.7 ± 25.7 | 68.4 (53.5–86.2) | |
| March | 1830 (10.9) | 73.0 ± 23.5 | 70.4 (57.6–84.5) | |
| April | 2018 (12.0) | 70.8 ± 25.7 | 67.4 (54.2–83.9) | |
| May | 2483 (14.8) | 79.4 ± 28.3 | 76.1 (61.2–93.8) | |
| June | 1187 (7.1) | 82.5 ± 25.7 | 79.3 (65.0–96.4) | |
| July | 1359 (8.1) | 85.6 ± 26.2 | 80.6 (67.5–99.7) | |
| August | 1283 (7.7) | 80.6 ± 25.1 | 75.2 (63.8–93.1) | |
| September | 985 (5.9) | 85.3 ± 25.5 | 81.5 (68.6–99.2) | |
| October | 1168 (7.0) | 83.4 ± 24.6 | 80.1 (66.1–97.1) | |
| November | 1092 (6.5) | 80.6 ± 24.7 | 76.9 (64.1–95.0) | |
| December | 977 (6.8) | 82.3 ± 26.0 | 79.4 (62.4–96.0) | |

Differences were tested using analysis of variance. IQR = interquartile range, SD = standard deviation.
vitamin D insufficiency on the basis of the conservative cutoff point suggested by the Endocrine Society. Our results showed that vitamin D insufficiency or deficiency is highly prevalent (49.8%) in southern Chinese children aged 0 to 6 years. The vitamin D levels were higher in infants than in children in the older age groups.

Vitamin D status is considered an important determinant of children’s health. Vitamin D is either obtained through the diet or synthesized in the skin in response to the sun’s ultraviolet B rays, and is metabolized in the liver to 25(OH)D, which plays an important role in bone and mineral metabolism. A deficiency of 25(OH)D is closely associated with osteomalacia and skeletal deformities in children.[6] The findings of the present study are in line with the current literature showing a high prevalence of vitamin D insufficiency or deficiency in young children. Various studies have reported on the prevalence of vitamin D deficiency in different parts of China. A study in Hangzhou reported that 33.6% and 5.4% of infants had serum 25(OH)D concentrations of <75 and 50nmol/L, respectively; deficiencies were also found in adolescents, with the corresponding concentrations found in 89.6% and 46.4% of subjects, respectively.[19] In Wuxi, the prevalence of vitamin D deficiency (<50nmol/L) was 16.1% among children aged 1 to 3 years. In Huzhou, 23.3% of children aged 0 to 18 years had a low vitamin D status (<75 nmol/L). In Beijing, 12.8% of children aged 12 to 35 months had a vitamin D deficiency,[20] and the prevalence of low 25(OH)D was 61% (<30 nmol/L) and 97% (<50 nmol/L) (mean 25(OH)D, 30 nmol/L) among adolescents.[21] The variations in the observed vitamin D status among studies could be attributed to differences in the study designs, the inclusion of different age groups, and the definition of insufficiency used, as well as the geographical differences.

A higher prevalence of vitamin D deficiency and insufficiency was observed in older children of the present study. These findings are in agreement with those of previously conducted studies that showed an association between lower levels of 25(OH)D and increasing age.[17,19,22,23] As serum vitamin D levels are determined by many factors, the cause of the age-related decline in 25(OH)D is multifactorial. Causes may include lack of vitamin D supplementation in older children, changes in diets and lifestyles, insufficient sun exposure, and spending less time on outdoor activities. A French study reported the lack of

Figure 1. Variations in serum vitamin D levels by month (A) and season (B) in children aged 0 to 6 years. A sufficient level of 75 nmol/L is indicated by the red line.

Figure 2. Percentage of vitamin D deficiency (25(OH)D < 50nmol/L), insufficiency (50nmol/L ≤ 25(OH)D < 75nmol/L), and sufficiency (25(OH)D ≥ 75nmol/L), stratified by sex, age, month, and season.
supplementation in older children; 53.4% of study participants did not have a prescription for vitamin D or had a prescription for supplementation below the recommended doses. [24] Although the Chinese Medical Association recommends that all children receive 400 IU vitamin D daily during the first 2 years of their lives, and that older children also receive vitamin D supplementation, the risk of vitamin D deficiency was found to increase with age in our study. This finding implies the development of an imbalance between nutritional intake and requirement with increasing age, and supplementation of 400 IU vitamin D daily may be ineffective in maintaining 25(OH)D levels at optimal concentrations (>75 nmol/L). The present study also revealed a

### Table 2

| Variables | Total numbers | Deficiency (25(OH)D < 50 nmol/L) | Deficiency/insufficiency (25(OH)D < 75 nmol/L) |
|-----------|---------------|---------------------------------|-----------------------------------------------|
|           |               | N (%)                          | OR (95% CI)                                   | N (%)                          | OR (95% CI)                                   |
| Sex       |               |                                |                                               |                               |                                               |
| Male      | 9671          | 1018 (10.5) Ref.               |                                               |                                |                                               |
| Female    | 7084          | 786 (11.1) 1.06 (0.96, 1.17) .240 |                                               |                                |                                               |
| Age, y    |               |                                |                                               |                               |                                               |
| 0         | 6441          | 418 (6.5) Ref.                 |                                               |                                |                                               |
| 1         | 4441          | 269 (6.1) 0.93 (0.79, 1.09) .362 |                                               |                                |                                               |
| 2         | 2060          | 199 (9.7) 1.54 (1.29, 1.84) <.001 |                                               |                                |                                               |
| 3         | 1297          | 241 (18.6) 3.29 (2.77, 3.90) <.001 |                                               |                                |                                               |
| 4         | 1066          | 238 (22.3) 4.14 (3.48, 4.93) <.001 |                                               |                                |                                               |
| 5         | 793           | 254 (32.0) 6.79 (5.68, 8.12) <.001 |                                               |                                |                                               |
| 6         | 657           | 185 (28.2) 5.65 (4.64, 6.88) .057 |                                               |                                |                                               |
| Month of the year | | | | | |
| January   | 1234          | 165 (13.4) Ref.               |                                               |                                |                                               |
| February  | 1229          | 235 (19.1) 1.53 (1.23, 1.90) <.001 |                                               |                                |                                               |
| March     | 1830          | 250 (13.7) 1.03 (0.85, 1.27) .818 |                                               |                                |                                               |
| April     | 2018          | 383 (19.0) 1.52 (1.24, 1.85) <.001 |                                               |                                |                                               |
| May       | 2483          | 303 (12.2) 0.90 (0.73, 1.10) .312 |                                               |                                |                                               |
| June      | 1187          | 90 (7.6) 0.53 (0.41, 0.70) .001 |                                               |                                |                                               |
| July      | 1359          | 53 (3.9) 0.26 (0.19, 0.36) .001 |                                               |                                |                                               |
| August    | 1283          | 78 (6.1) 0.42 (0.32, 0.56) .001 |                                               |                                |                                               |
| September | 965           | 53 (5.4) 0.37 (0.27, 0.51) .001 |                                               |                                |                                               |
| October   | 1168          | 60 (5.1) 0.35 (0.26, 0.49) .001 |                                               |                                |                                               |
| November  | 1002          | 79 (7.9) 0.50 (0.42, 0.64) <.001 |                                               |                                |                                               |
| December  | 977           | 55 (5.6) 0.39 (0.28, 0.53) .001 |                                               |                                |                                               |
| Season    |               |                                |                                               |                               |                                               |
| Spring    | 6331          | 936 (14.8) Ref.               |                                               |                                |                                               |
| Summer    | 3629          | 221 (5.8) 0.35 (0.30, 0.41) .001 |                                               |                                |                                               |
| Autumn    | 3155          | 192 (6.1) 0.37 (0.32, 0.44) .001 |                                               |                                |                                               |
| Winter    | 3440          | 455 (13.2) 0.88 (0.76, 0.99) .055 |                                               |                                |                                               |

CI = confidence interval, OR = odds ratio.

### Table 3

| Variables | 0 | 1 | 2 | 3 | 4 | 5 | 6 |
|-----------|---|---|---|---|---|---|---|
| Month of the year | | | | | | | |
| January   | 41.4 | 42.5 | 62.7 | 80.2 | 83.7 | 88.2 | 84.8 |
| February  | 44.4 | 47.0 | 66.0 | 82.8 | 94.0 | 93.2 | 94.4 |
| March     | 44.4 | 51.7 | 65.7 | 86.6 | 94.4 | 93.8 | 98.5 |
| April     | 48.0 | 60.8 | 73.0 | 87.7 | 83.3 | 83.5 | 90.5 |
| May       | 33.3 | 43.4 | 50.0 | 70.9 | 73.9 | 86.4 | 91.2 |
| June      | 31.2 | 32.1 | 44.8 | 63.6 | 67.2 | 80.8 | 83.7 |
| July      | 26.2 | 27.8 | 36.4 | 57.6 | 62.4 | 70.3 | 78.8 |
| August    | 33.0 | 33.3 | 47.3 | 68.5 | 78.3 | 78.6 | 86.8 |
| September | 23.8 | 31.1 | 37.3 | 58.8 | 67.9 | 81.3 | 90.0 |
| October   | 31.5 | 33.2 | 42.1 | 64.1 | 77.9 | 78.0 | 72.7 |
| November  | 35.8 | 37.0 | 52.1 | 62.9 | 82.4 | 87.0 | 93.8 |
| December  | 33.9 | 36.4 | 41.9 | 64.6 | 78.8 | 90.7 | 82.6 |
| Season    | | | | | | | |
| Spring    | 41.2 | 51.4 | 62.1 | 80.6 | 83.0 | 91.4 | 93.2 |
| Summer    | 30.0 | 30.9 | 42.7 | 63.4 | 69.7 | 76.2 | 83.5 |
| Autumn    | 30.6 | 33.6 | 43.5 | 62.3 | 76.2 | 82.4 | 84.0 |
| Winter    | 40.1 | 41.9 | 57.9 | 77.7 | 87.4 | 90.8 | 88.6 |
relatively high prevalence of vitamin D deficiency or insufficiency in certain months. Seasonal changes in serum 25(OH)D levels may reflect the synthesis of whole-body irradiation. There were significant variations in the prevalence of vitamin D deficiency during the 12 months of the year. The prevalence of vitamin D insufficiency or deficiency was higher from January to April than in the other months. This time period coincides with changes in relative humidity and the onset of more humid period in Guangzhou; these factors may lead to inadequate sun exposure. The present study evaluated the prevalence of vitamin D deficiency and insufficiency in children aged 0 to 6 years in South China. Nevertheless, the study had several limitations. First, this was a single-center study and the participant sample does not represent the general population. Second, detailed information on obesity status, lifestyle factors, and dietary composition (such as vitamin D supplementation) was not available. These factors might affect the vitamin D status of young children. Third, we did not investigate the amount of sunlight to which every participant was exposed. Thus, we could not estimate how the degree of sun exposure differed among the participants, leading to seasonal variations. Fourth, the current study lacked the gold-standard liquid chromatography–mass spectrometry measure of vitamin D. Serum 25(OH)D concentrations were determined by electrochemiluminescence immunoassay, which could be performed in a rapid, high throughput manner and offered excellent sensitivity; however, it was unable to distinguish between the various forms of vitamin D such as 25(OH)D₃ and 25(OH)D₂. Fifth, we did not assess the potential contribution of vitamin D axis gene polymorphisms, which could explain some of the observed differences. Furthermore, owing to the cross-sectional nature of the study, we cannot draw inferences regarding the key contributors to vitamin D deficiency, or the changes in vitamin D status over time.

5. Conclusions
Vitamin D deficiency and insufficiency are common among children in South China, despite the presence of sufficient sunlight in the region. Vitamin D status is worse in older children and in the winter.

Author contributions
Yong Guo and Jie-Ling Wu conceived and designed the study; Hai-Jin Ke, Ying Liu, Min Fu, Jing Ning, Li Yu, and Yu Xiao performed the experiments; Yong Guo, Di Che, Xiao-Yan Chen, and Yu-Hong Deng analyzed the data; Yong Guo and Jie-Ling Wu wrote the paper. All authors have seen and approved the final version of the manuscript.

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