Status and influential factors of vitamin D among children aged 0 to 6 years in a Chinese population

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Abstract

Background Vitamin D insufficiency and deficiency in childhood are common, and they are closely related to bone development. However, the status and influential factors of vitamin D during different ages are not clear. This study aimed to survey vitamin D status in children aged 0 to 6 years and explore its influential factors.

Materials and methods: A total of 6953 children were recruited in Wuxi City of East China from January to December 2016. Enzyme-linked immunosorbent assay was used to determine the serum concentrations of 25-hydroxyvitamin D [25(OH)D].

Results: The median vitamin D level in the infancy group (0-1 years of age) was 69.40 nmol/L, which was higher than that in both the toddlerhood group (1-3 years of age; 62.30 nmol/L) and the preschool group (3-6 years of age; 50.85 nmol/L) ($P < 0.001$). In addition, the median vitamin D level was 71.70 nmol/L in summer, which was higher than that in spring (64.25 nmol/L), autumn (62.95 nmol/L) and winter (64.10 nmol/L; $P < 0.001$). However, no difference was observed between genders ($P = 0.974$). Furthermore, the prevalence of vitamin D deficiency (< 50 nmol/L) was 48.1% in the preschool group (3-6 years of age), which was higher than the 21.2% vitamin D deficiency in the toddlerhood group (2-3 years of age) and the 17.9% vitamin D deficiency in the infancy group (0-1 years of age). Interestingly, a nonlinear association between 25(OH)D and air temperature was observed.

Conclusions: A high prevalence of vitamin D deficiency was common in a Chinese population of children 0-6 years old, especially in the preschool-aged group. Season and air temperature were related to vitamin D status. Therefore, we suggest that the recommendation for vitamin D supplementation in the Chinese pediatric population should be revised to include older children and adolescents.

Introduction

Vitamin D, including vitamin D₂ and D₃, is a class of fat-soluble vitamins and steroid hormones synthesized when the skin is exposed to sunlight. In the human body, vitamin D is mainly produced through ultraviolet irradiation of the skin [1]. Vitamins D₂ and D₃ are catalyzed by 25-hydroxylase in the liver to produce 25(OH)D, which is further catalyzed by 1- α hydroxylase to produce 1, 25(OH)₂D in the kidney. 25(OH)D is the main form of vitamin D in the body and is also the best indicator to evaluate the level of vitamin D, while 1, 25(OH)₂D is the main active vitamin D compound in the body [1, 2]. Vitamin D has a classic effect on calcium and phosphorus metabolism that impacts bone health. Vitamin D mainly plays a biological role by binding to vitamin D receptors in organs or tissues in the body. In addition, a growing number of studies have linked Vitamin D to extraosseous conditions, including autoimmune diseases, asthma, cardiovascular diseases and infections [3–6], because Vitamin D receptors widely exist in various organ systems of the human body.

Most scholars recognize the definition of vitamin D levels from the American Institute of Medicine (IOM). A 25(OH)D level < 20 ng/mL (50 nmol/L) is defined as deficiency, $20 \sim 29$ ng / mL (50 $\sim$ 75 nmol/L) is

defined as inadequacy, and ≥ 30 ng/mL (≥ 75 nmol/L) is defined as sufficient [7]. Only 5–10% of vitamin D throughout the body is obtained from dietary intake, while more than 90% of vitamin D is derived from cutaneous production [8]. With the increasing air pollution and corresponding decline of outdoor activities, vitamin D deficiency has become increasingly common in humans, especially in children [9].

Vitamin D insufficiency and deficiency has become a public health problem. A study showed that in America, vitamin D insufficiency in children aged 6–11 years (73%) was higher than that aged 1–5 years (63%) [10]. In addition, the rate of vitamin D deficiency (25(OH)D levels < 50 nmol/L) was the lowest among infants (5.4%) and was the highest among adolescents (46.4%) [11]. A previous study focused on vitamin D status in children aged 0–3 years found that the prevalence of vitamin D deficiency was 16.1% among children aged 1–3 years [9]. However, the vitamin D status of children in the preschool period is seldom investigated, especially in Southeast China.

The purpose of this study was to evaluate vitamin D status among children aged 0 to 6 years old in Wuxi City of Southeastern China. Additionally, we also analyzed the influential factors of vitamin D deficiency and insufficiency.

Materials And Methods

Participants

Our participants were from Health Examination Centers at Wuxi Maternal and Child Health Hospital in Wuxi City, Jiangsu Province, China, from January to December 2016. The present study obtained ethics approval from the ethics committee of Wuxi Maternal and Child Health Hospital. All participants' parents or guardians agreed to this study. A total of 6,953 children aged 0–6 years old were recruited for this study.

Collect samples for determination of 25 (OH) D

Finger sticks were used to collect the blood samples from each participant. Within 10 min after collection, the blood sample was centrifuged for 15 min at 3500 rpm. All sera samples were collected for analysis and stored at -80°C . The concentrations of 25(OH)D were analyzed by Enzyme-linked immunosorbent assay following the manufacturer's instructions (IDS Ltd., Boldon Colliery, Tyne & Wear, UK) [9].

Statistical analysis

The distribution of serum 25(OH)D levels among the children was positively skewed; it approximated a normal distribution after being natural log-transformed. Therefore, percentiles and medians were used to describe the serum 25(OH)D concentrations. The season during which each serum sample was collected was classified as follows: spring (March to May); summer (June to August); fall (September to November); and winter (December to February) [9]. We conducted analyses of serum 25(OH)D concentrations stratified by age group, season and gender. The children were classified into the infancy group (0–1 years of age), toddlerhood group (1–3 years of age), and preschool group (3–6 years of age).

A logistic regression model was used to examine odds ratios (ORs) and 95% confidence intervals (95% CIs) in the relationship between vitamin D deficiency and age group. We performed all statistical analyses with SPSS (version 16.0). A two-tailed P-value less than 0.05 was considered statistically significant. To further evaluate the possible association 25(OH)D with air temperature, a nonlinear curve fitting method was applied by using BStudio.

Results

Status of vitamin D in children aged 0–6 years old

A population of 6,953 children (3,749 boys and 3,204 girls) aged 0 to 6 years was recruited in this study. The median (P₅-P₉₅) concentration of serum 25(OH)D was 65.40 (51.65–81.50 nmol/L) in the total population (Table 1).

Table 1
Comparison of serum 25(OH)D levels in 6953 young children stratified by age, season or gender.

Variables	Number	Median (IQR)	P ₅ –P ₉₅	P value
Total population	6953	65.40 (51.65–81.50)	34.00-102.70	
Age group (years)				
Infant (0–1 years)	4603	69.40 (55.00-85.30)	34.50-106.70	< 0.001
Early childhood (2–3 years)	1546	62.30 (51.70–77.20)	38.60-94.87	
Pre-school (4–6 years)	804	50.85 (40.65–62.70)	30.60–80.70	
Season				
Spring	2150	64.25 (50.30–80.50)	33.10-100.80	< 0.001
Summer	1727	71.70 (55.70–87.30)	37.30-107.60	
Autumn	1392	62.95 (49.42–78.80)	34.36–104.70	
Winter	1684	64.10 (51.10–78.40)	33.50–100.00	
Gender				
Boy	3749	65.60 (51.30–81.50)	34.25–102.30	0.974
Girl	3204	65.20 (52.00-81.57)	33.90-103.95	
Abbreviation: IQR, interquartile range.				

The median level of 25(OH)D in the infancy group (0–1 years of age) was 69.40 nmol/L, which was higher than that in toddlerhood group (1–3 years of age; 62.30 nmol/L) and that in preschool group (3–

6 years of age; 50.85 nmol/L) ($P < 0.001$) (Table 1). Meanwhile, the median level of vitamin D was 71.70 nmol/L in summer, which was higher than that in spring (64.25 nmol/L), autumn (62.95 nmol/L) and winter (64.10 nmol/L; $P < 0.001$). However, no difference in median vitamin D between the genders was observed within the different age groups ($P = 0.974$) (Table 1).

In addition, there was a high prevalence of vitamin D deficiency (22.1%) and insufficiency (43.2%) among children aged 0–6 years old in the Chinese population (Table 2). The prevalence of vitamin D deficiency was 48.1% in the infancy group (0–1 years of age), which was higher than that in the toddlerhood group (1–3 years of age; 21.2%) and that in the preschool group (3–6 years of age; 17.9%) (Table 2).

Table 2
The groups of vitamin D concentrations stratified by age, season and gender.

Variables	Vitamin D groups			P value
	Deficiency (< 50 nmol/L)	Insufficient (50–74.9 nmol/L)	Sufficient (≥ 75 nmol/L)	
Total population	22.1	43.2	34.7	
Age group (years)				
Infant (0–1 years)	17.9	40.8	41.3	< 0.001
Early childhood (2–3 years)	21.2	50.6	28.2	
Pre-school (4–6 years)	48.1	42.2	9.7	
Season				
Spring	24.4	42.7	32.9	< 0.001
Summer	15.8	39.1	45.1	
Autumn	26.0	43.4	30.6	
Winter	22.4	47.7	29.9	
Gender				
Boy	22.7	42.2	35.1	0.167
Girl	21.4	44.3	34.3	

Factors influencing vitamin D deficiency

The logistic regression analysis revealed that child age was strongly associated with vitamin D deficiency and insufficiency (Table 3). Compared to serum 25(OH)D ≥ 75 nmol/L, the OR for vitamin D deficiency (< 50 nmol/L) in the toddlerhood group (1–3 years of age) and the preschool group (3–6 years of age) were 1.73 (95% CI: 1.47, 2.04) and 11.5 (95% CI: 8.87, 14.81), respectively. The ORs for vitamin D insufficiency

(50–74.9 nmol/L) in the toddlerhood group children (1–3 years of age) and preschool group children (3–6 years of age) were 1.82 (95% CI: 1.59, 2.08) and 4.40 (95% CI: 3.41, 5.67), respectively. After adjustment for confounding factors, the association remained (Table 3).

Table 3

Odds ratios (95% CIs) of vitamin D deficiency and vitamin D insufficient associated with age group.

Vitamin D deficiency (< 50 nmol/L) ^a			Vitamin D insufficient (50–74.9 nmol/L) ^a	
	Univariate OR (95% CI)	Adjusted ^b OR (95% CI)	Univariate OR (95% CI)	Adjusted ^b OR (95% CI)
Age group				
0–1 years	1.00	1.00	1.00	1.00
2–3 years	1.73 (1.47, 2.04)***	1.76 (1.49, 2.08)***	1.82 (1.59, 2.08)***	1.83 (1.60, 2.10)***
4–6 years	11.5 (8.87, 14.81)***	12.22 (9.42, 15.84)***	4.40 (3.41, 5.67)***	4.60 (3.56, 5.94)***
^a The reference group was serum 25(OH)D ≥ 75 nmol/L.				
^b Adjusted for season and genders.				
*** P < 0.001				

The trends in 25(OH)D, together with the average monthly air temperature variation, are shown in Fig. 1. The results showed that the changes in vitamin D levels were not entirely consistent with the changes in air temperature. In Fig. 2, the nonlinear curve for the association between 25(OH)D and air temperature is shown. With increasing air temperatures, the 25(OH)D levels first decreased at air temperature in the range of 0–10°C, then increased to a high level at air temperature in the range of 10–24°C, and then again declined slightly at air temperature over 24°C.

Discussion

Vitamin D deficiency and insufficiency are global problems [12–15]. Our present study found a high prevalence of vitamin D deficiency and insufficiency among children aged 0–6 years old in a Chinese population. For serum 25(OH)D concentration, only 34.7% of children were sufficient, 43.2% were insufficient, and 22.1% were deficient in the total population. The prevalence of vitamin D deficiency (< 50 nmol/L) was increased by age, with 17.9%, 21.2% and 48.1% in the infancy (0–1 years of age), toddlerhood (1–3 years of age) and preschool (3–6 years of age) groups, respectively. Consistent with our findings, the prevalence of vitamin D deficiency increased by age in American children, with a

deficiency prevalence of 14%, 20%, and 28.8% in children aged 2–5 years, children aged 6–11 years, and adolescents, respectively [10, 16]. In addition, a dramatic seasonal variation of vitamin D deficiency and insufficiency was observed in our present study; the levels were very low in autumn, increased gradually in spring and winter, and reached a peak in summer. This is consistent with the results reported in other studies [11, 17–19]. There are many reasons for vitamin deficiency and insufficiency. It is known that the content of vitamin D in the skin of the human body exceeds 90%, and the vitamin D obtained from dietary intake for only about 5–10% [8]. The origin of Vitamin D in infants is mainly from milk and exogenous supplementation; the Pediatrics Branch of Chinese Medical Association recommends that all children receive no less than 400 IU/day of vitamin D from two weeks to two years after birth [20]. However, when the children reach ages older than 2 years, milk is no longer the main food, and the origin of Vitamin D is mainly from outdoor activities. Studies have shown that children have lower levels of vitamin D due to less time in outdoor activities [21–23].

The condition of UVB on skin radiation determines the effect of temperature on vitamin D status [24–25]. For most people, the majority (80–90%) of the 25 (OH) D in the circulation is produced by the skin's 7-dehydrocholesterol by ultraviolet B radiation [26]. A few studies have investigated the association between 25(OH)D levels and air temperature and revealed that the 25(OH)D levels were fairly consistent with the changes in air temperature [9]. Interestingly, our research found a nonlinear curve for the association between 25(OH)D levels and air temperature in the pediatric population. Our research showed that the 25(OH)D levels decreased quickly with increasing air temperatures in the temperature range of 0–10°C. This may be because children spent less time in outdoor activities during the transition from winter to spring (0–10°C). The 25(OH)D levels increased to a high level when the air temperature increased from 10°C to 24°C. It is probable that the children had increased outdoor activities in this more comfortable temperature range. However, when the air temperature exceeded 24°C, the 25(OH)D levels again declined slightly with rising air temperatures. Children spent less time outdoors with the highest air temperatures, which is a probable reason for the decreasing vitamin D levels.

There were some limitations of our study that need to be mentioned. The socioeconomic status of the participants has not been provided in this study. Additionally, our study did not collect information regarding the children's dietary intake, vitamin D supplements, body mass index, time of physical activities or amount of sunlight exposure. These factors might affect the vitamin D status of young children.

Conclusions

A high prevalence of vitamin D deficiency was common in this population of Chinese children between 0 and 6 years old, especially in the preschool group. Taking into consideration the lack of vitamin D in children and adolescents, the American Academy of Pediatrics has issued a new recommendation that all children receive 400 IU / day of vitamin D daily from the first day of life to adolescence [19].

Therefore, we suggest that the current recommendation for vitamin D supplementation in the Chinese pediatric population should be extended to include preschool children and adolescents. Additionally, our study also suggested that we should pay more attention to vitamin D supplementation in children through all seasons of the year except summer, especially for children over 3 years old.

Declarations

Acknowledgements

Not applicable.

Authors' contributions

All authors contributed to the conceptualization, design, and interpretation of the study. HZ, ZJL, JYF, YLF and YRW collected data and conducted statistical analyses. HZ and ZJL wrote the manuscript. DZC and DXX revised the manuscript. All authors reviewed and approved the final manuscript.

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Ethics approval and consent to participate

All participants' parents or guardians consented in writing to their children's participation, and the above protocols were approved by the ethics committee of Wuxi Maternal and Child Health Hospital.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

- [1] Marino R, Misra M. Extra-Skeletal Effects of Vitamin D. *Nutrients*, 2019; 27: 11(7).
- [2] Li YC. Molecular mechanism of vitamin D in the cardiovascular system. *Investig Med*, 2011; 59(6):868-871.
- [3] Zerofsky M, Ryder M, Bhatia S, Stephensen CB, King J, Fung EB. Effects of early vitamin D deficiency rickets on bone and dental health, growth and immunity. *Matern Child Nutr*, 2016; 12(4): 898-907.
- [4] Zhang HQ, Teng JH, Li Y, Li XX, He YH, He X, Sun CH. Vitamin D status and its association with adiposity and oxidative stress in schoolchildren. *Nutrition*, 2014; 30: 1040–1044.
- [5] Litonjua AA. Vitamin D deficiency as a risk factor for childhood allergic disease and asthma. *Curr Opin Allergy Clin Immunol*, 2012; 12: 179–185.
- [6] Thornton KA, Marín C, Mora-Plazas M, Villamor E. Vitamin D deficiency associated with increased incidence of gastrointestinal and ear infections in school-age children. *Pediatr Infect Dis J*, 2013; 32: 585–593.
- [7] Calvo MS, Whiting SJ, Barton CN. Vitamin D intake: a global perspective of current status. *J Nutr*, 2005; 135: 310–316.
- [8] Holick MF. Sunlight, UV-radiation,. vitamin D and skin cancer: how much sunlight do we need? *Adv Exp Med Biol*, 2008; 624: 1–15.

- [9] Zhao X, Xiao J, Liao X, Cai L, Xu F, Chen D, Xiang J, Fang R. Vitamin D Status among Young Children Aged 1-3 Years: A Cross-Sectional Study in Wuxi, China. *PLoS One*. 2015; 10(10):e0141595.
- [10] Mansbach JM, Ginde AA, Camargo CA Jr. Serum 25-hydroxyvitamin D levels among US children aged 1 to 11 years: do children need more vitamin D. *Pediatrics*, 2009;124: 1404-1410.
- [11] Zhu Z, Zhan J, Shao J, Chen W, Chen L, Li W, Ji C, Zhao Z. High prevalence of vitamin D deficiency among children aged 1 month to 16 years in Hangzhou, China. *BMC Public Health*, 2012; 12: 126.
- [12] Quah SW, Abdul Majid H, Al-Sadat N, Yahya A, Su TT, Jalaludin MY. Risk factors of vitamin D deficiency among 15-year-old adolescents participating in the Malaysian Health and Adolescents Longitudinal Research Team Study (MyHeARTs). *PLoS One*, 2018; 13(7):e0200736.
- [13] Al-Musharaf S, Fouda MA, Turkestani IZ, Al-Ajlan A, Sabico S, Alnaami AM, Wani K, Hussain SD, Alraqebah B, Al-Serehi A, Alshingetti NM, Al-Daghri N, McTernan PG, Wimalawansa SJ, Saravanan P. Vitamin D Deficiency Prevalence and Predictors in Early Pregnancy among Arab Women. *Nutrients*, 2018; 10(4).
- [14] Liu X, Baylin A, Levy PD. Vitamin D deficiency and insufficiency among US adults: prevalence, predictors and clinical implications. *Br J Nutr*, 2018; 8, 928- 936.
- [15] Kubota T, Nakayama H, Kitaoka T, Nakamura Y, Fukumoto S, Fujiwara I, Hasegawa Y, Ihara K, Kitanaka S, Koyama S, Kusuda S, Mizuno H, Nagasaki K, Oba K, Sakamoto Y, Takubo N, Shimizu T, Tanahashi Y, Hasegawa K, Tsukahara H, Yorifuji T, Michigami T, Ozono K. Incidence rate and characteristics of symptomatic vitamin D deficiency in children: a nationwide survey in Japan. *Endocr J*. 2018; 65(6):593-599.
- [16] Wagner CL, Greer FR. Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. *Pediatrics*, 2008; 122:1142-1152.
- [17] Gu Y, Zhu Z, Luan X, He J. Vitamin D status and its association with season, depression in stroke. *Neurosci Lett*, 2019; 690:99-105.
- [18] Gu Y, Luan X, Ren W, Zhu L, He J. Impact of seasons on stroke-related depression, mediated by vitamin D status. *BMC Psychiatry*, 2018; 18(1):359.
- [19] Hansen L, Tjønneland A, Køster B, Brot C, Andersen R, Cohen AS, Frederiksen K, Olsen A. Vitamin D Status and Seasonal Variation among Danish Children and Adults: A Descriptive Study. *Nutrients*, 2018; 20, 10(11).
- [20] Editorial Committee of *Zhonghua Er Ke Za Zhi*, Child Health Group of Chinese Academy of Pediatrics, National Scientific Group of Prevention and Cure of Rickets. Recommendation for prevention and treatment of rickets of vitamin D deficiency in childhood. *Zhonghua Er Ke Za Zhi*, 2008, 46:190-191, (in Chinese).

[21] Voortman T, van den Hooven EH, Heijboer AC, Hofman A, Jaddoe VW, Franco OH. Vitamin D deficiency in school-age children is associated with sociodemographic and lifestyle factors. *J Nutr*, 2015; 145:791–798.

[22] Yao Y, Fu S, Li N, Hu F, Zhang H, Zhu Q, Luan F, Zhang F, Zhao Y, He Y. Sex, Residence and Fish Intake Predict Vitamin D Status in Chinese Centenarians. *J Nutr Health Aging*. 2019; 23(2):165-171.

[23] Ten Haaf DSM, Balvers MGJ, Timmers S, Eijsvogels TMH, Hopman MTE, Klein Gunnewiek JMT. Determinants of vitamin D status in physically active elderly in the Netherlands. *Eur J Nutr*. 2018; 6.

[24] Holick MF. Vitamin D deficiency. *N Engl J Med*, 2007; 357:266-281.

[25] Marwaha RK, Sreenivas V, Talwar D, Yenamandra VK, Challa A, Lakshmy R, Sharma VK, Sethuraman G. Impact of solar ultraviolet B radiation (290-320 nm) on vitamin D synthesis in children with type IV and V skin. *Br J Dermatol*. 2015;173(2):604-606.

[26] Greenfield JA, Park PS, Farahani E, Malik S, Vieth R, McFarlane NA, Shepherd TG, Knight JA. Solar ultraviolet-B radiation and vitamin D: a cross-sectional population-based study using data from the 2007 to 2009 Canadian Health Measures Survey. *BMC Public Health*. 2012; 12:660.

Figures

Figure 1

Trends in 25(OH)D results and in average monthly air temperature variation. From January december to 2016, the 25(OH)D levels and average monthly air temperature values showed variation and the shapes of the curves.

Figure 2

The possible non-linear association between 25(OH)D and air temperature.