
Variation Trend of Vitamin D Status in Wintertime Among Infants: A Cross-sectional Study

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Abstract: Background The requirement of vitamin D in different stage may be diverse, but research on the variation trend of vitamin D status during infancy is scarce. Objective This study aimed to explore the variation trend of vitamin D status and influencing factors of vitamin D deficiency and insufficiency during wintertime among infants. Methods A cross-sectional study was conducted. A total of 500 infants were included in our study during January to March 2017. The serum 25(OH)D was performed by chemiluminescent assay. Multivariate Logistic regression was conducted to evaluate the influencing factors of vitamin D deficiency and vitamin D insufficiency. Results The older infants had a higher concentration of vitamin D than younger infants ($r=0.62$, $P<0.0001$). And the overall prevalence of vitamin D deficiency and insufficiency were 33.80% and 18.00%, respectively. With the increase of month age, the risk of vitamin D deficiency (OR=0.63, 95%CI: 0.57-0.70) and insufficiency (OR=0.69, 95%CI: 0.62-0.77) were both declined. In addition, the infant with low birthweight, breastfed, living in rural area were correlated with a higher risk of vitamin D deficiency and insufficiency ($P<0.05$). Conclusion Vitamin D deficiency and insufficiency prevalence changed with month age, routine monitoring of vitamin D levels is necessary for infant.

Keywords: Vitamin D Status, Vitamin D Deficiency, Vitamin D Supplementation, Infant, Wintertime, Breastfed

1. Introduction

Vitamin D, which can enhance intestinal calcium and phosphate absorption and promote bone mineralization, has been identified as one of the key nutrients that contributes to the development and maintenance of optimum bone mass from the very early stage. [1] Without controversy, vitamin D deficiency with or without calcium deficiency, can lead to nutritional rickets, calcium

homeostasis disturbance and osteomalacia. [2, 3] In addition, over the last two decades, with the discovery of vitamin D receptors in other body tissues and cells, the associations between vitamin D and several health outcomes, such as birthweight, dental caries, myopia and so on, have also been confirmed [4]. Vitamin D nutritional status has attracted more and more researchers' attention

nowadays.

Infancy period is the fastest growth stage that needs a great dose of calcium and phosphate for osteogenesis. The infant has a relative high demand for vitamin D. In humans, the source of vitamin D mainly depends on skin exposure to ultraviolet B radiation. But for infant, the body surface area and frequency of exposure to sunlight are not enough to produce adequate vitamin D, especially in winter. In addition, the concentration of vitamin D in breast milk is low, hence the dietary sources vitamin D become more limited. Vitamin D deficiency or insufficiency is vulnerable in infant [5].

Multiple guidelines or public health policies on vitamin D supplementation have been published in the last decade [6]. In 2008, American Academy of Pediatrics recommended that all infants should have a minimum intake of 400IU/day vitamin D supplement beginning soon after birth [7]. And in China, this recommendation has been in place since 2010 [8]. But with the aggravation of air pollution, urbanization, over-crowding, the endogenous synthesis of vitamin D might be less and less because of the reduced ultraviolet B radiation exposure time and frequency in recent years [9]. Seasonal variation of sunlight is one of critical factors in the determination of human vitamin D, and endogenous synthesis of vitamin D is even worse in winter. The implementation effect needs to be evaluated in the current environment, especially in winter. In addition, the requirement of vitamin D in different stage may be diverse, but research on the variation trend of vitamin D status during infancy is scarce [10]. We conducted a cross-sectional study to measure the wintertime vitamin D status of infant. The aim of our study was conducted to (1) explore the variation trend of vitamin D status with month of age (2) explore the influencing factors of the vitamin D deficiency and insufficiency.

2. Materials and Methods

2.1. Study Participants

Our study was designed as a cross-sectional study. A total of 500 infants were consecutively recruited in department of pediatrics, Tongji Hospital of Huazhong University of Science & Technology, Wuhan city, central China, during January to March 2017. Exclusion criteria were: age > 12 months; birth defects; chronic disease; use of medications known to affect vitamin D metabolism. The study was approved by the institutional review boards of Tongji Medical College, Huazhong University of Science & Technology, and parents or guardians provided written informed consent at study enrollment.

2.2. Demographic Indices

The demographic data (including sex, month age, birthweight, region of residence, feeding patterns and so on) were collected from the parents or guardians (most preferably from the mother) during the first visit to the hospital. All interviews were conducted by the trained nurses with the use of a standardized questionnaire.

2.3. Laboratory Measurements

2mL blood sample was obtained for each participant accompany with the routine blood drawing. Serum 25(OH)D test was performed in the hospital laboratory using chemiluminescent assay. The infants were divided into 3 groups using the cut-off values proposed by the Endocrine Society: vitamin D deficiency (serum 25(OH)D concentrations ≤ 20 ng/mL), vitamin D insufficiency (serum 25(OH)D concentrations > 20 but < 30 ng/mL) and optimal vitamin D status (serum 25(OH)D concentrations ≥ 30 ng/mL).

2.4. Statistical Analysis

Normality of distribution for continuous variables was tested by the Kolmogorov-Smirnov test. Normal distribution data were presented as mean \pm SD, and the differences among groups were compared by analysis of variance (ANOVA). For categorical data, the difference between groups were tested using the chi-square test. Spearman rank correlation was used to calculate correlations between serum 25(OH)D level and month age. The multivariate Logistic regression with stepwise selection was performed to evaluate the influencing factors of vitamin D deficiency and vitamin D insufficiency. $P < 0.05$ was accepted as statistically significant. Analyses were performed with SPSS Software, Version 18.0 for Windows (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Variation Trend of Vitamin D Status by Month of Age

As shown in Figure 1A, the older infants had a higher concentration of vitamin D than younger infants ($r = 0.62$, $P < 0.0001$). In addition, the overall prevalence of vitamin D deficiency and insufficiency were 33.80% and 18.00%, respectively. There was a declining trend between vitamin D deficiency prevalence and month age ($r = -0.91$, $P < 0.0001$), so was vitamin D insufficiency ($r = -0.83$, $P = 0.0004$). Moreover, the prevalence of optimal vitamin D status was increased with the month age ($r = 0.91$, $P < 0.0001$) (Figure 1B).

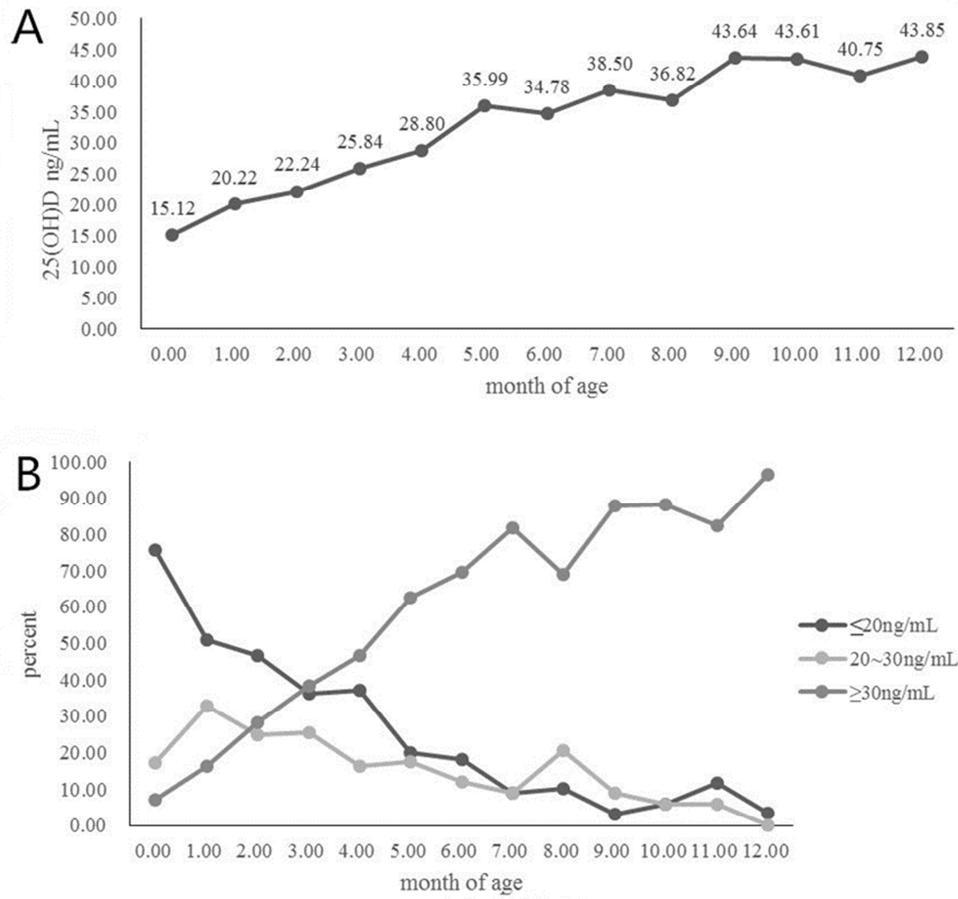


Figure 1. Vitamin D status by month of age.

3.2. Influence Factors of Vitamin D Deficiency and Insufficiency

Table 1 summarized the descriptive characteristics of the study population by vitamin D deficiency, insufficiency and optimal vitamin D status. There was no significant difference in sex distribution among groups ($P>0.05$). Compared with the optimal vitamin D status group, the proportions of infant who resided in rural was significantly higher in vitamin D

deficiency group ($P<0.05$). In addition, there was a higher rate of the infant who were low birthweight, premature, breastfed in vitamin D deficiency group than optimal vitamin D status group ($P<0.05$). Vitamin D deficiency group also had a higher parity and gravidity ($P<0.05$). The distribution of vitamin D insufficiency infant was in accordance with the vitamin D deficiency group.

Table 1. Descriptive characteristics of study participants by Vitamin D status. N (%).

	Vitamin D deficiency (n=169)	Vitamin D insufficiency (n=90)	optimal vitamin D (n=241)	P
sex				0.75
Boys	105(62.13)	60(66.67)	156(64.73)	
Girls	64(37.87)	30(33.33)	85(35.27)	
Region of residence				<0.0001
Rural	82(48.52)	49(54.44)	77(31.95)	
urban	87(51.48)	41(45.56)	164(68.05)	
Birthweight				<0.0001
<2500g	75(44.38)	16(17.78)	24(9.96)	
$\ge 2500\text{g}$	94(55.62)	74(82.22)	217(90.04)	
Gestational age				<0.0001
premature	82(48.52)	25(27.78)	30(12.45)	
Term infant	87(51.48)	63(72.22)	210(87.55)	
Gravidity				<0.0001
1	85(50.30)	47(52.22)	151(62.66)	
2	37(21.89)	27(30.00)	70(29.05)	
≥ 3	47(27.81)	14(15.56)	18(7.47)	
Parity				0.03

	Vitamin D deficiency (n=169)	Vitamin D insufficiency (n=90)	optimal vitamin D (n=241)	P
1	91(53.85)	52(59.09)	160(66.67)	
≥2	78(46.15)	36(40.91)	80(33.33)	
Feeding patterns				<0.0001
breastfeeding	59(34.91)	35(38.89)	63(26.14)	
Mixed feeding	46(27.22)	28(31.11)	115(47.72)	
Artificial feeding	17(10.06)	17(18.89)	60(24.90)	
Not start feeding	34(20.12)	5(5.56)	2(0.83)	
Maternal health in pregnant				
Pregnancy induced hypertension	19(11.24)	4(4.44)	4(1.66)	<0.001
Gestational diabetes mellitus	8(4.73)	5(5.56)	10(4.15)	0.84

In our study, 41 infants were enrolled immediately after birth before feeding. Among them 34 (82.93%) were diagnosed with vitamin D deficiency, and only 2 (4.88%) were with optimal vitamin D status.

The selected influencing factors of vitamin D deficiency and insufficiency in infant were presented in Table 2. Based on this data, with the increase of month age, the risk of vitamin D deficiency (OR=0.63, 95%CI: 0.57-0.70) and insufficiency (OR=0.69, 95%CI: 0.62-0.77) were both declined. In addition, the infants resided in rural were found

to be 2.29 (95%CI: 1.34-3.93) and 2.55 (95%CI: 1.45-4.50) times more likely to be vitamin D deficiency and insufficiency respectively, compared with the infants resided in urban. Moreover, the low birthweight infants had a high odds for vitamin D deficiency (OR=4.04, 95%CI: 1.93-8.47). The artificial fed infant had the lowest odds for vitamin D deficiency (OR=0.10, 95%CI: 0.04-0.22) and insufficiency (OR=0.24, 95%CI: 0.11-0.54), compare with breastfed infants.

Table 2. Multivariate logistic regression analyses examining the influencing factors of vitamin D deficiency and insufficiency in infant.

	Vitamin D deficiency		Vitamin D insufficiency	
	OR(95%CI)	P	OR(95%CI)	P
month of age	0.63(0.57-0.70)	<0.0001	0.69(0.62-0.77)	<0.0001
Region of residence				
urban	1.00		1.00	
Rural	2.29(1.34-3.93)	0.002	2.55(1.45-4.50)	0.001
Birthweight				
<2500g	4.04(1.93-8.47)	0.002	1.15(0.48-2.80)	0.75
≥2500g	1.00		1.00	
Feeding patterns				
breastfeeding	1.00			
Mixed feeding	0.32(0.17-0.59)	<0.001	0.34(0.18-0.66)	0.002
Artificial feeding	0.10(0.04-0.22)	<0.0001	0.24(0.11-0.54)	<0.001

4. Discussion

To our knowledge, this was the first study reported the variation trend of vitamin D status with month age among infants. And our results showed an increased concentration of vitamin D and decreased prevalence of vitamin D deficiency and insufficiency with month age, among infants in China, during winter. This might account for the cumulative effect of routine vitamin D supplementation, increased breast milk or formula intake, the induction of complementary food and the increased ability of vitamin D synthesize and so on. Hence, along with the daily 400IU supplementation of vitamin D, routine monitoring of vitamin D levels was very necessary, especially for infants under 4 months of age. According to the monitoring results, the vitamin D supplementary dosage would be conducted personalized and effectively.

The overall prevalence of vitamin D deficiency was 33% in our infant group during winter, which was relatively lower compared with other age groups. In Greek primary schoolchildren, the prevalence of vitamin D lower than 20ng/mL was 52.5% [11], and it was 45.9% in Italian children and adolescents (range 2.0-21.0 years) wintertime

[12]. The results from the occupied Palestinian territory also showed that vitamin D deficiency was more common in children older than 1 years than in children aged 1 year or younger [13]. However, 82.39% newborns at birth were vitamin D deficiency in our study, similar with the 75% in Iranian population and 84.0% in New Zealand population [14]. Another study conducted in an environment with abundant sunshine (Doha, Qatar during summer months) also found that 83% breastfed infant without vitamin D supplementation at 1 month of age were deficient [15]. Many studies had confirmed the positive relationship between maternal late pregnancy vitamin D concentration and newborn vitamin D store or cord vitamin D concentration [14, 16-18]. In addition, the results of our study also concluded that the breastfed infants owned a higher risk of vitamin D deficiency and insufficiency, consistent with the published results in other populations [15]. A double-blind randomized placebo controlled trial showed that maternal orally supplemented with 60000IU of vitamin D daily in the early postpartum period could increase the concentration of 25(OH)D in exclusively breastfed infants at 6 months of age [19]. So for breast-fed infants, vitamin D supplementation combined with maternal postpartum supplement might have

a better effect on vitamin D deficiency prevention. Above all, maternal prenatal to postpartum vitamin D supplementation might be an effective intervention to promote optimal vitamin D status in newborns and infants [20]. The serum 25(OH)D concentration in lactating mothers should at least up to the recommended target value of >50 nmol/L.

Our results also concluded that the low birth weight infant was the risk group for vitamin D deficiency. The vitamin D deficiency of low birth weight might be the subsequent effect of maternal vitamin D deficiency. Many studies concluded that maternal vitamin D insufficiency is independently associated with low birth weight [21-23]. Hence, for low birth weight infant, might be a higher dose of vitamin D supplement was effectible for vitamin D deficiency prevention, and further studies were needed to explore.

Published literature presented that vitamin D deficiency was more likely in girls than in boys, because of the lower dietary intake of vitamin D and lower levels of physical activity executed outdoors [11, 13, 24, 25]. But for infant, the dose of vitamin D supplementation was the same between different sex. In addition, during winter, the body surface area of exposure to sunlight was rare and most of the infant had no capacity for autonomous activity. Hence, there were no sex difference observed in the present study.

In spring, summer and autumn season, the urbanization degree differences on vitamin D status was concerned [11, 26]. These differences mainly be attributed to the particularities of the physical environment which could be more supportive of increased outdoor physical activity levels and consequently greater sun exposure in rural area [27]. But in winter months (January or March), as the subjects both urban and rural regions usually spent more time indoors, due to the colder weather conditions and shorter daytime, sun exposure during this period was not efficient enough in stimulating endogenous vitamin D synthesis [28]. Manios et al did not find the regional differences on vitamin D status during winter [11]. But in the present study, the infant living in rural region were more at risk for vitamin D deficiency than those live in urban areas, consistently with the results from Chinese children and adolescents [29]. The quality of formula and vitamin D supplements might explain these difference.

The findings of the current study should be interpreted in light of its strengths and limitations. Regarding strengths, the current study presented the variation trend of vitamin D status with month age, focused on the infant in wintertime. For limitations, first was the absence of the measurement of dietary vitamin D intake. Secondly, our study was a hospital-based studies which might skew the results. The longitudinal investigations with a larger sample size, involving all seasons should be conducted in further researches.

5. Conclusion

In summary, in wintertime, the concentration of vitamin D for infant was increased with month age. And low birthweight, breastfed, living in rural area might be predictors of vitamin D

deficiency and insufficiency. Hence, except for infant vitamin D supplementation strategies, maternal prenatal to postpartum vitamin D supplementation might be an effective intervention to promote optimal vitamin D status in infants.

Author Contributions

Wei Li, Qiong Dai and Yongying Qiu written the initial draft and revised it. Jianqiong Liu collected the data and analyzed. Yan Guo conducted the vitamin D detection, Bin Wang was the project leadership and designed the work.

Conflicts of Interest Statement

The authors report no conflict of interest.

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