Vitamin D deficiency among healthy infants in Hong Kong: a pilot study

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KEY MESSAGES

1. This pilot study suggests that vitamin D deficiency is prevalent among Chinese infants in Hong Kong.
2. Exclusive breastfeeding is an important factor associated with vitamin D deficiency.
3. More studies are needed to evaluate the health implications of vitamin D deficiency during early infancy.

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Introduction

A suboptimal vitamin D level has been associated with various disease conditions, although whether a causal relationship exists remains uncertain.[1] Vitamin D insufficiency among children has become a worldwide issue.[2] In infants, it could be attributed to exclusive breastfeeding and limited sunlight exposure.[3] 25-Hydroxyvitamin D, also known as 25(OH)D, is the main circulating form of vitamin D and is used to define vitamin D status. A consensus on the serum 25(OH)D concentration that should define vitamin D deficiency for infants and children has not yet been reached. If bone health is used as the clinical outcome, vitamin D deficiency is generally defined as a serum 25(OH)D concentration of <50 nmol/L, at which bone adverse outcomes are observed. In Hong Kong, efforts to promote breastfeeding have successfully boosted the rate at 3 months from 10% in 1997-2000 to 37% in 2010.[4] Although more children benefit from the advantages of breast milk, there may be a growing risk of vitamin D deficiency among exclusively breastfed children. There is no local recommendation about postnatal vitamin D supplementation, and updated local data on this issue are needed. This pilot study aimed to explore the prevalence of vitamin D deficiency among healthy infants in Hong Kong.

Methods

Healthy Chinese newborns were recruited in the postnatal wards of the Prince of Wales Hospital with convenience sampling. Mothers of eligible infants were asked to participate and written informed consent was obtained. When the infants reached 3 months of age, they and their parents were invited to return for the measurement of infants' serum vitamin D level and completion of questionnaires. Infants were excluded from analysis if they had congenital anomalies, renal or hepatic diseases, feeding problems and/or malabsorption, metabolic bone disease or calcium disorder, rickets, or hypocalcaemia; if they were taking medications known to affect plasma 25(OH)D concentration; or if the mother had been treated with vitamin D within 6 months of the current pregnancy.

Anthropometric measurements of infants' recumbent length and weight were made. For serum 25(OH)D measurement, 1 mL of blood was collected, centrifuged, aliquoted, and stored at -70°C until analysis. The sum of $25(OH)D_3$ and $25(OH)D_2$, hence the total serum 25(OH)D, was measured by tandem mass spectrometry after ultra-performance liquid chromatography separation using a pentafluorophenyl column (UPLC-Xevo TQ System; Waters Corporation, Milford [MA], USA). This method separated out the biologically inactive 3-epi-$25OHD_3$, which has been reported to be present in infants in a significant amount.[5]

Parametric, non-parametric, and categorical data were presented as mean with standard deviation (SD), median with interquartile range (IQR), and percentage, respectively. The prevalence of vitamin D deficiency was calculated. The vitamin D sufficient and deficient groups were compared using the chi-square test for categorical variables and Mann-Whitney *U* test and *t* test for non-parametric and parametric variables, respectively. Spearman's rho was used to test the correlation of serum 25(OH)D level with breastfeeding duration, growth variables at 3 months, and plasma alkaline phosphatase, calcium, and phosphorous concentrations. A P value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS (Windows version 20.0; IBM Corp, Hong Kong).

Results

Of 269 infants enrolled, 155 (of whom 75 were male) completed the study, giving a response rate of 57.6%. Baseline characteristics between those who completed the study and those who dropped out did not differ significantly in terms of sex distribution, gestational age, birthweight, season at birth, maternal age, maternal smoking status, or feeding practice at recruitment (Table 1).

Serum 25(OH)D concentration was determined at a mean age of 98.3 (SD, 9.7) days. No infant received vitamin D supplementation. The median serum 25(OH)D concentration at 3 months was 58 (IQR, 32-75) nmol/L. Of 155 infants, 52 (33.5%) had vitamin D deficiency defined as a serum 25(OH)D concentration of <50 nmol/L; of these, 34 (21.9%) had a concentration of <25 nmol/L, indicating severe deficiency. The proportion of infants with a history of exclusive breastfeeding was higher in those with vitamin D deficiency than in those with vitamin D sufficiency (P<0.001, Table 2). The duration of exclusive breastfeeding was inversely correlated with the serum 25(OH)D concentration at 3 months of age (r= −0.605, P<0.001). Thirty eight (24.5%) of the infants were exclusively breastfed at 3 months, 37 (97.4%) had vitamin D deficiency, with a mean concentration of 19.7 (SD, 14.3) nmol/L. The serum 25(OH)D concentration was positively correlated with plasma phosphorous concentration (r=0.556, P<0.001). The serum 25(OH)D concentration was not correlated with infant exposure to sunlight, plasma calcium or alkaline phosphatase concentration, or growth at 3 months of age.

Discussion

Our pilot study suggests that vitamin D deficiency may be prevalent in local Chinese infants at 3 months of age. Exclusive breastfeeding is associated with vitamin D deficiency; the duration of exclusive breastfeeding is inversely correlated with the serum 25(OH)D concentration at 3 months of age. Among exclusively breastfed infants, 97.4% had vitamin D deficiency; the rate is higher than that reported in other studies (6% to 81%).[6-8] The difference may be due to variation among different localities and ethnicities; endogenous production of vitamin D may be influenced by ethnic, cultural, and environmental factors such as skin pigmentation, extent of sun exposure, and geographic latitude. The prevalence of vitamin D deficiency in our cohort at 3 months was 33.5%, which is higher than the 29.8% and 28.3% reported in studies that included older infants and defined vitamin D insufficiency as a serum 25(OH) D concentration of <75 nmol/L.[9,10] The differences indicate that serum 25(OH)D concentrations may vary during infancy, and infants at 3 months may be at a higher risk of vitamin D deficiency than older infants. Vitamin D obtained through transplacental passage from the mother stores in the newborn and lasts until around 3 months.[11] At 3 months, infants rely on breast milk and/or formula milk as their sole source of nutrients. It is also the age at which there is limited sunlight exposure. Exhaustion of the body's reserve of vitamin D and lack of solid food and sun exposure may explain why exclusively breastfed infants have a high prevalence of vitamin D deficiency. When children get older and have a

TABLE 1. Baseline characteristics of participants and dropouts

Characteristic	Participants (n=155)*	Dropouts (n=114)*	P value
Males:females, No.	75:80	50:64	0.54
Gestational age at birth, w	38.9±1.1	39.4±5.8	0.25
Birth weight, kg	3.1±0.33	3.1±0.34	0.61
Season at birth, No.			0.43
Winter	31	21	
Spring	57	40	
Summer	46	42	
Autumn	21	11	
Maternal age, y	30.6±4.4	30.2±3.9	0.27
Maternal smoking during pregnancy, No. (%)	7 (4.5)	3 (2.6)	0.35
Feeding practice at recruitment, No.			0.49
Breastfeeding	68	56	
Formula milk	20	15	
Mixed	67	43	

* Data are presented as mean ± standard deviation, unless otherwise indicated

TABLE 2. Comparison of participants with vitamin D sufficiency or deficiency

Characteristic	Participants (n=155)*	Vitamin D sufficiency (n=103)*	Vitamin D deficiency (n=52)*	P value
Serum 25-hydroxyvitamin D, nmol/L	58 (32-75)	70 (58-80)	18 (12-32)	<0.001
Males:females, No.	75:80	49:54	26:26	0.78
Age, d	98.3±9.7	97.4±8.8	100.1±11.2	0.13
Gestation at birth, w	38.9±1.1	38.8±1.1	39.0±1.2	0.35
Birth weight, kg	3.1±0.3	3.2±0.3	3.1±0.3	0.47
Season at birth, No.				0.57
Winter	31	18	13	
Spring	57	39	18	
Summer	46	30	16	
Autumn	21	16	5	
Season at sampling, No.				0.74
Winter	21	15	6	
Spring	32	19	13	
Summer	53	37	16	
Autumn	49	32	17	
History of exclusive breastfeeding, No. (%)	73 (47.1)	29 (28.2)	44 (84.6)	<0.001
Breastfeeding ever, No. (%)	108 (69.7)	-	-	-
Maternal age, y	30.5±4.2	30.6±4.4	30.2±3.9	0.27
Nutritional supplement during pregnancy, No. (%)	132 (85.2)	86 (83.5)	45 (86.5)	0.63
Nutritional supplement during lactation among mothers who ever breastfed, No./total (%)	82/108 (75.9)	25/64 (39.1)	22/44 (50.0)	0.17
Maternal smoking during pregnancy, No. (%)	7 (4.5)	6 (5.8)	1 (1.9)	0.48
Maternal sunlight exposure during pregnancy, h/w	1.5 (0.5-5.44)	1.75 (0.5-5.9)	1.3 (0.5-3.5)	0.36
Infant sunlight exposure, h/w	1 (0-3)	1 (0-2.8)	1.25 (0-4)	0.12
Sunblock use during pregnancy, No. (%)	68 (43.9)	42 (40.8)	25 (48)	0.49
Sunblock use for infants, No. (%)	6 (3.9)	3 (2.9)	3 (5.8)	0.41
Household income <HK$20 000, No. (%)	31 (20)	16 (15.5)	15 (28.8)	0.09
Body weight at 3 months, kg	6.1±0.7	6.1±0.7	6.1±0.7	0.70
Body height at 3 months, cm	61.5±2.3	61.4±2.4	61.7±2.0	0.50
Plasma calcium, mmol/L	2.6±0.1	2.6±0.1	2.6±0.1	0.12
Plasma phosphorous, mmol/L	1.8±0.2	1.9±0.1	1.7±0.2	<0.001
Plasma alkaline phosphatase, IU/L	283.8±75.5	283.6±71.0	284.2±84.6	0.96

* Data are presented as mean ± standard deviation or median (interquartile range), unless otherwise indicated

more diverse dietary intake and sunlight exposure, vitamin D status may improve. Longitudinal studies are required to evaluate the natural change in vitamin D status during infancy.

Exclusive breastfeeding is consistently associated with vitamin D deficiency.[12,13] The vitamin D content of breast milk is low, even in vitamin D–adequate lactating mothers.[12,13] The major source of vitamin D is from sun exposure and diet, so exclusively breastfed infants with limited sun exposure are at higher risk of vitamin D deficiency. In our study, there were no significant differences in growth or calcium and alkaline phosphatase levels in those who were vitamin D sufficient or deficient. Although plasma phosphorous level is associated with serum 25(OH)D concentration, its clinical significance remains uncertain. Studies to investigate the effect of vitamin D supplementation on bone health have not demonstrated any dose-response relationship between vitamin D concentration and bone mineral content or accretion.[14,15] Further Mendelian randomisation studies are needed to

investigate various clinical outcomes of vitamin D deficiency during pregnancy and early childhood and to define the optimal serum 25(OH)D concentration in infancy.

There are several limitations in our study. It was a single-centre pilot study with limited sample size and uncertain generalisability to the entire local population. The dropout rate was high. Vitamin D status was determined only at the age of 3 months. Maternal vitamin D status during pregnancy was not assessed and the clinical outcomes related to vitamin D deficiency were not studied. Nonetheless, this pilot study revealed a previously unrecognised proportion of infants with vitamin D deficiency. Interventional studies in infants to evaluate the clinical implications of vitamin D deficiency are needed to provide guidance for future studies and recommendations about vitamin D supplementation during pregnancy and infancy.

Conclusion

Vitamin D deficiency is prevalent in Hong Kong infants and is associated with exclusive breastfeeding. More studies are needed to evaluate the health implications of vitamin D deficiency during early infancy.

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Ethical Approval

This pilot cohort study was approved by the Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee (CRE-2012.436). Parental consent for participation was obtained.

Declaration

The authors have no conflicts of interest to disclose.

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