Observational Study

Medicine®

OPEN

Prevalence of vitamin D deficiency and insufficiency among 460,537 children in 825 hospitals from 18 provinces in mainland China

Chunsong Yang, MPH[a,b], Meng Mao, MD[c], Li Ping, MD[c], Dan Yu, MD[d,*]

Abstract

This study was conducted to estimate the 25-hydroxyvitamin D (25(OH)D) levels and explore factors related to vitamin D deficiency/insufficiency. This was a multicenter, hospital-based, cross-sectional observational study. Children admitted to hospitals for health examination were included for vitamin D measurement and the 25(OH)D concentration results were categorized into 3 groups: deficiency (<30 nmol/L), insufficiency (30–50 nmol/L), and sufficiency (>50 nmol/L). Four lakh sixty thousand five hundred thirty-seven children in 825 hospitals from 18 provinces participated in this study. The prevalence of vitamin D deficiency, insufficiency, and sufficiency were 6.69%, 15.92%, and 77.39%, respectively. Vitamin D deficiency was the most severe in the central region, followed by the north, and southwest regions; however, data for the western region were lacking.

Logistic regression showed that vitamin D status was worse in girls, newborns, and those visiting the hospital in the winter. In conclusion, the prevalence of vitamin D deficiency is high among Chinese children and adolescents. Studies on population estimates, cost-effective screening strategies, and interventions for high-risk cases are needed.

Abbreviation: DSRSC = Depression.

Keywords: 25-hydroxyvitamin D, children, deficiency, China

1. Introduction

Vitamin D is an essential nutrient for bone growth, mineralization, and other metabolic processes in the human body.[1] Serum 25-hydroxyvitamin D (25(OH)D) is the vitamin D metabolite that is measured clinically to assess vitamin D status.[2] The deficiency of vitamin D can be an important health issue in all stages of life; level of vitamin D concentration can not only influence the health of children and adolescents, but also the health of their adulthood. Such as, it is known to cause rickets in children and osteomalacia in adults.[3,4]

The deficiency of vitamin D has been reported widely all over the world; national-level epidemiological studies in Mexico showed that the prevalence of vitamin D insufficiency (<50 nmol/L) was 24%, 10%, and 8% in preschoolers, schoolchildren, and adolescents, respectively.[5] In western Europe, Akkermans et al[6] included 325 children and found the overall prevalence of vitamin D deficiency is 22.8%. Some studies conducted in China also showed that vitamin D deficiency and insufficiency were common. Fraser [7] reported that 45.2% of adolescent girls in north China had 25(OH)D levels <12.5 nmol/L in the winter.

Editor: Yoshihiro Shidoji.

This study was funded by Sichuan Health and Wellness Committee (18PJ528) and Science & Technology Department of Sichuan Province (No. 2018SZ0123). The sponsor had no role in the study design, writing of the manuscript, or decision to submit this or future manuscripts for publication.

This study was supported by the National Key Development Plan for Precision Medicine Research (2017YFC0910004), Wu Jieping Medical Foundation from Chinese Medical Association Clinical Pharmaceutical Branch: Construction of medication adherence Nomogram Prediction Model for Childhood with Epilepsy and Intervention Strategies Based on Risk Stratification and Sichuan Health and Wellness Committee: Study on association of medication compliance and seizures in children with epilepsy (18PJ532). The sponsor had no role in the study design, writing of the manuscript, or decision to submit this or future manuscripts for publication.

The authors declare that they have no competing interests.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

[a] Department of Pharmacy, Evidence-based Pharmacy Center, West China second hospital, Sichuan University, Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, [b] Department of Epidemiology, West China School of Public Health, and West China Fourth Hospital, [c] Department of Pediatrics, West China Second Hospital, Sichuan University, [d] Department of Children's Genetic Endocrinology and Metabolism, West China Second hospital, Sichuan University, Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, Chengdu, Sichuan, China.

[*] Correspondence: Dan Yu, Department of Children's Genetic Endocrinology and Metabolism, West China Second University Hospital, Sichuan University, No.16, Third Section, Renmin Nan Lu, Chengdu, Sichuan 610041, P. R. China (e-mail: yd540@126.com).

How to cite this article: Yang C, Mao M, Ping L, Yu D. Prevalence of vitamin D deficiency and insufficiency among 460,537 children in 825 hospitals from 18 provinces in mainland China. Medicine 2020;99:44(e22463).

Received: 18 May 2020 / Received in final form: 24 August 2020 / Accepted: 28 August 2020

http://dx.doi.org/10.1097/MD.0000000000022463

Yu et al[8] and Liang et al[9] reported that vitamin D deficiency and insufficiency were prevalent in children of all ages in Shanghai and Nanjing from southeast China. Guo et al[10] estimated the 25-(OH)D levels in children in southern China and included 16,755 children aged 0 to 6 years; the results showed that the prevalence of vitamin D deficiency and insufficiency were 10.8% and 39.0%, respectively, and they concluded that deficiency and insufficiency of vitamin D are common among children in southern China. However, all these studies are single-center study without good representation. In addition, the prevalence of vitamin D deficiency and insufficiency in children in mainland China is unknown; therefore, we conducted a multicenter, hospital-based, cross-sectional observational study to estimate the 25(OH)D levels and explore factors related to vitamin D deficiency/insufficiency.

2. Methods

2.1. Study design

This was a multicenter, hospital-based, cross-sectional observational study. Eight hundred twenty-five hospitals from 18 provinces participated in this study. The study period is between January 2016 and December 2018.

2.2. Participants

Participants aged 0 to 18 years admitted to hospitals for health examination in 18 provinces in mainland China were enrolled. Subjects were excluded if they had any underlying diseases with known skeletal diseases, genetic syndromes, or malabsorptive disorders.

2.3. Data collection

Basic characteristics of participants was collected, including gender, age, season, hospital nature, hospital level, and region. Age was divided into 6 groups: neonatal period (0–28 days), infant period (28 days–1 year), toddle period (1–3 years), preschool age (3–7 years), school age (7–10 years), and adolescence (10–18 years). Season was divided into 4 groups: spring (March, April, May), summer (June, July, August), autumn (September, October, and November), winter (December, January, February). Hospital nature was divided into 2 groups: nonmaternal and child, maternal and child. Hospital level was divided into 4 groups: first level, secondary level, third level, and other. According to the China Health Statistics Yearbook, region was divided into 3 groups: western (Inner Mongolia, Yunnan, Sichuan, Shaanxi, Guangxi), eastern (Beijing, Liaoning, Hebei, Shandong, Jiangsu, Zhejiang, Guangdong), and central China (Heilongjiang, Anhui, Hubei, Henan, Shanxi, Hunan).

2.4. Vitamin D measurement

25(OH)D, which is the main circulating form of vitamin D in vivo, was used to determine the level of vitamin D. All fasting venous blood samples were collected and use cold-chain transportation to the same laboratory. Samples were stored store in a light-proof and refrigeration environment. Concentration of 25(OH)D was determined by LC-MS/MS after pretreatment. Internal standard method was used to quantify 25(OH)D2 and 25(OH)D3. The correlation coefficient of the standard curve was <1%, and QC sample should be X ± 2SD. Vitamin D status was evaluated by determining the 25(OH)D concentration. The 25(OH)D concentration results were categorized into 3 groups: deficiency (<30 nmol/L), insufficiency (30–50 nmol/L), and sufficiency (>50 nmol/L).[11]

2.5. Statistical analyses

Frequencies and percentages (%) were reported for categorical variables. Categorical variables were analyzed using the Chi-square or Fisher exact test as appropriate.

Logistic regression determined the association between deficiency or insufficiency and covariates. All analyses were performed using SAS, v. 9.4 (SAS Institute, Inc., Cary, NC, USA., and the threshold for statistical significance was set at $P < .05$.

2.6. Ethical issues

The design of the study was in accordance with the Helsinki Declaration. The study began after the approval of the Office of Research Ethics Committees of West China Second Hospital. Informed consent was obtained from all caregivers, and consent was provided from children aged 8 years.

3. Results

3.1. Prevalence of vitamin D deficiency, insufficiency, and sufficiency

In total, 460,537 children aged 1 day to 18 years (median: 1.33 years) from 825 hospitals in 18 provinces were included. The mean 25(OH)D concentration was 72.18 ± 30.10 nmol/L. The prevalence of vitamin D deficiency, insufficiency, and sufficiency were 6.69%, 15.92%, and 77.39%, respectively (Table 1).

Chi-square test results showed that there was significant difference in the prevalence of vitamin D deficiency, insufficiency, and sufficiency in different sex, age, season, hospital nature, hospital level, and region group.

Figures 1 and 2 show the prevalence of vitamin D deficiency and insufficiency by region. In brief, the locations of vitamin D deficiency/insufficiency mainly included Beijing, Hebei Province, Henan Province, Shanxi Province, Shaanxi Province, Inner Mongolia Autonomous Region, and Shandong Province. Vitamin D deficiency was the most severe in the central region, followed by the north, and southwest regions; however, data for the western region were lacking.

3.2. Influencing factors of vitamin D deficiency and insufficiency in China

After adjustment, logistic regression showed that being female, being a neonate, visiting the hospital in the winter, visiting the maternal and child hospital, visiting a Tier 2 hospital, and living in eastern China were associated with vitamin D deficiency and insufficiency (Tables 2 and 3).

4. Discussion

We conducted a large sample size multicenter, hospital-based, cross-sectional observational study to investigate the prevalence of vitamin D deficiency, insufficiency; a total of 460,537 children

Table 1

Prevalence of vitamin D deficiency, insufficiency, and sufficiency in China.

Characteristic	Total number	Deficiency <30 nmol/L	Insufficiency 30–50 nmol/L	Sufficiency >50 nmol/L	χ^2	*P*
Overall	460,537	30,823 (6.69)	73,322 (15.92)	356,392 (77.39)		
Sex					578.04	<.001
Male	267,520	16,622 (6.21)	40,557 (15.16)	210,341 (78.63)		
Female	193,017	14,201 (7.36)	32,765 (16.98)	146,051 (75.67)		
Age					98,857.06	<.001
Neonatal period	13,321	7324 (54.98)	4410 (33.11)	1587 (11.91)		
Infant period	213,961	9981 (4.66)	17,818 (8.33)	186,162 (87.01)		
Toddle period	102,907	2170 (2.11)	12,242 (11.90)	88,495 (86.00)		
Preschool age	85,493	5320 (6.22)	23,634 (27.64)	56,539 (66.13)		
School age	25,607	2597 (10.14)	8398 (32.80)	14,612 (57.06)		
Adolescence	19,248	3431 (17.83)	6820 (35.43)	8997 (46.74)		
Seasons					26,177.50	<.001
Spring	102,305	8183 (8.00)	20,062 (19.61)	74,060 (72.39)		
Summer	135,886	3280 (2.41)	12,287 (9.04)	120,319 (88.54)		
Autumn	125,834	6170 (4.90)	17,857 (14.19)	101,807 (80.91)		
Winter	96,512	13,190 (13.67)	23,116 (23.95)	60,206 (62.38)		
Hospital nature					188.23	<.001
Nonmaternal and child	348,166	22,643 (6.50)	56,636 (16.27)	268,887 (77.23)		
Maternal and child	112,371	8180 (7.28)	16,686 (14.85)	87,505 (77.87)		
Hospital level					6037.04	<.001
Tier 1	4893	258 (5.27)	738 (15.08)	3897 (79.64)		
Tier 2	240,124	18,403 (7.66)	41,657 (17.35)	180,064 (74.99)		
Tier 3	176,862	11,597 (6.56)	28,645 (16.20)	136,620 (77.25)		
other	38,658	565 (1.46)	2282 (5.90)	35,811 (92.64)		
Region					330.39	<.001
Eastern	214,460	13,991 (6.52)	36,248 (16.90)	164,221 (76.57)		
Central	155,710	10,427 (6.70)	23,909 (15.35)	121,374 (77.95)		
Western	90,367	6405 (7.09)	13,165 (14.57)	70,797 (78.34)		

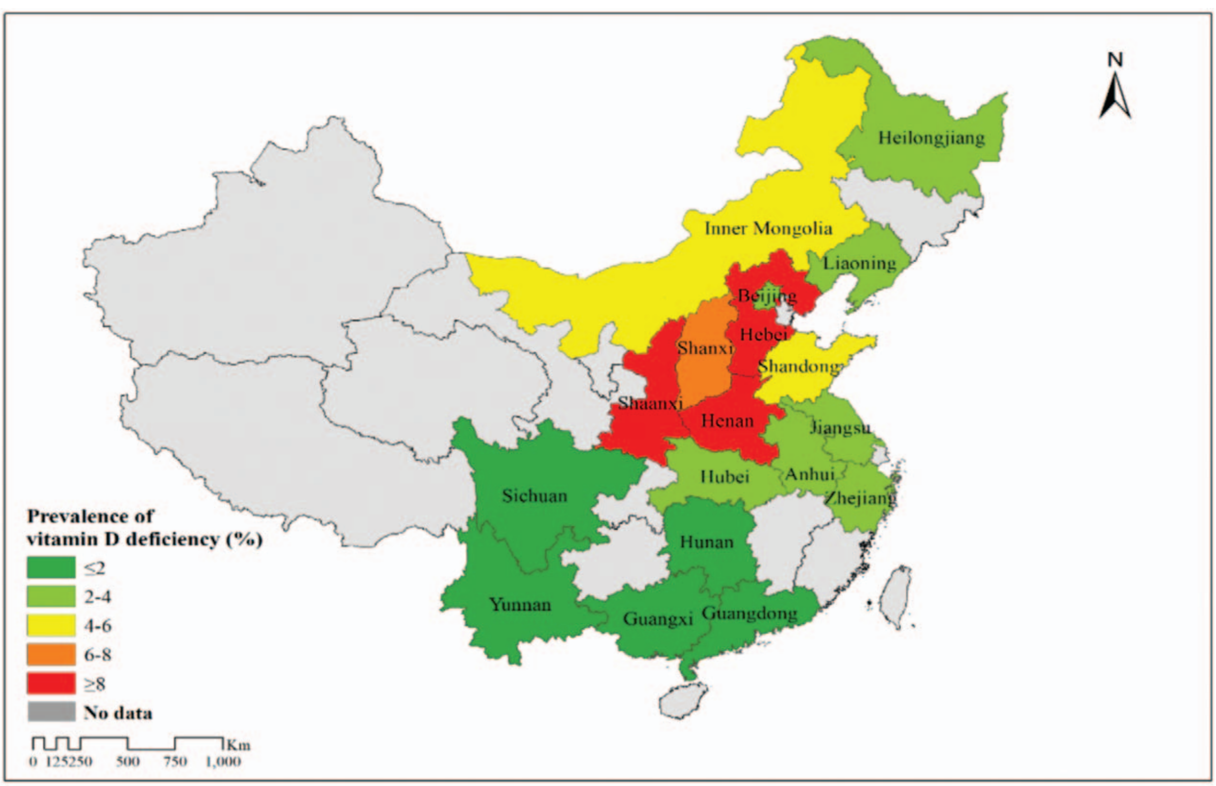

Figure 1. Distribution map of vitamin D deficiency in China.

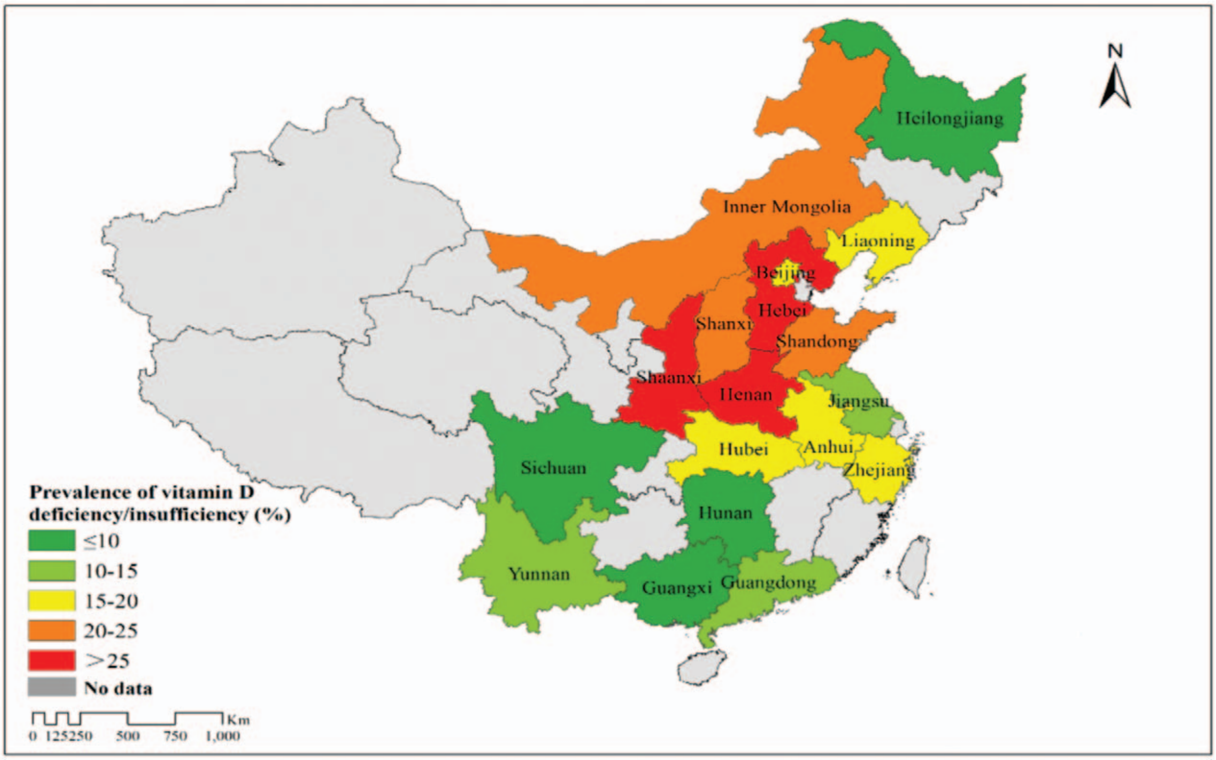

Figure 2. Distribution map of vitamin D deficiency/insufficiency in China.

Table 2

Analysis of influencing factors of vitamin D deficiency in China.

Variables	β	SE	*P*	OR (95% CI)
Sex				
Male	−0.18	0.01	<.001	0.84 (0.82–0.86)
Female	—	—	—	Ref
Age				
Neonatal period	—	—	—	Ref
Infant period	−3.47	0.02	<.001	0.03 (0.03–0.03)
Toddle period	−4.28	0.03	<.001	0.01 (0.01–0.02)
Preschool age	−3.17	0.02	<.001	0.04 (0.04–0.04)
School age	−2.58	0.03	<.001	0.08 (0.07–0.08)
Adolescence	−1.88	0.03	<.001	0.15 (0.14–0.16)
Seasons				
Spring	—	—	—	Ref
Summer	−1.54	0.02	<.001	0.21 (0.2–0.22)
Autumn	−0.77	0.02	<.001	0.46 (0.45–0.48)
Winter	0.61	0.02	<.001	1.84 (1.78–1.9)
Hospital nature				
Non-Maternal and child	—	—	—	Ref
Maternal and child	0.13	0.02	<.001	1.14 (1.11–1.17)
Hospital level				
Tier 1	1	0.08	<.001	2.71 (2.31–3.17)
Tier 2	1.23	0.04	<.001	3.43 (3.15–3.74)
Tier 3	1.2	0.04	<.001	3.32 (3.05–3.63)
Other	—	—	—	Ref
Region				
Eastern	−0.15	0.02	<.001	0.86 (0.83–0.89)
Central	−0.26	0.02	<.001	0.77 (0.74–0.8)
Western	—	—	—	Ref

CI = confidence interval; OR = odds ratio.

Table 3

Analysis of influencing factors of vitamin D deficiency/insufficiency in China.

Variables	β	SE	*P*	OR (95% CI)
Sex				
Male	−0.21	0.01	<.001	0.81 (0.8–0.83)
Female	—	—	—	Ref
Age				
Neonatal period	—	—	—	Ref
Infant period	−4.19	0.03	<.001	0.02 (0.01–0.02)
Toddle period	−4.08	0.03	<.001	0.02 (0.02–0.02)
Preschool age	−2.87	0.03	<.001	0.06 (0.05–0.06)
School age	−2.38	0.03	<.001	0.09 (0.09–0.1)
Adolescence	−1.92	0.03	<.001	0.15 (0.14–0.16)
Seasons				
Spring	—	—	—	Ref
Summer	−1.43	0.01	<.001	0.24 (0.23–0.25)
Autumn	−0.64	0.01	<.001	0.53 (0.52–0.54)
Winter	0.51	0.01	<.001	1.66 (1.62–1.69)
Hospital nature				
Nonmaternal and child	—	—	—	Ref
Maternal and child	0.06	0.01	<.001	1.07 (1.05–1.09)
Hospital level				
Tier 1	0.9	0.04	<.001	2.47 (2.26–2.69)
Tier 2	1.02	0.02	<.001	2.78 (2.67–2.89)
Tier 3	0.92	0.02	<.001	2.5 (2.4–2.61)
other	—	—	—	Ref
Region				
Eastern	0.1	0.01	<.001	1.11 (1.09–1.13)
Central	−0.04	0.01	.002	0.96 (0.94–0.98)
Western	—	—	—	Ref

CI = confidence interval; OR = odds ratio.

for health examination in 825 hospitals from 18 provinces participated in this study. The results showed that Vitamin D deficiency/insufficiency (22.61%) was highly prevalent in children in mainland China. Vitamin D status was worse in girls, newborns, and those visiting the hospital in the winter. 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 and kidneys to 1,25(OH)2D, which plays a direct role in the transcription of genes related to bone-mineral metabolism. A deficiency of 25(OH)D is closely associated with osteomalacia and skeletal deformities in children.[2] Compared with data from other country, the prevalence of vitamin D deficiency/insufficiency in China was similar with that in Mexico, Iran, and worldwide.[5,12] Compared with the study conducted in Guangdong province in China,[10] the prevalence of vitamin D deficiency and insufficiency in our study was lower than that; the possible reasons were as follows. First, there are differences in the age of the included participants; the study included participants aged 0 to 6 years; however, the age of participants in our study ranged from 0 to 18 years, and it is easier for younger children to be vitamin D deficiency. Second, the difference in the proportion of the included participants in different seasons will lead to inconsistent prevalence of vitamin D deficiency; the proportion of participants included in our study in summer (29.5%) was higher than that in Guo' study (22.9%); as we know, the prevalence of vitamin D deficiency was higher in spring, autumn, and winter than in summer due to sufficient sunlight in summer. Third, the study conducted in Guangdong Women and Children Hospital was a single-center study; the source of patients was relatively single, so the results may differ from the results of the multicenter study. The study by Yu et al[9] found that vitamin D deficiency were common in newborns in Shanghai and the prevalence of vitamin D deficiency in newborns was 36.3%, which was lower than that in our study, because vitamin D deficiency was defined as a serum 25(OH)D concentration $<$20 ng/mL, which was different from our study, so it will cause a certain difference in results.

For the factors influencing vitamin D deficiency and insufficiency, we found that a higher prevalence of vitamin D deficiency and insufficiency was observed in newborns and older children, which are similar with those in other studies; the previous studies showed that increasing age was associated with lower levels of 25 (OH)D.[13,14] In addition, we also found vitamin D deficiency and insufficiency was common in spring and winter. As we know, levels of 25 (OH) are determined by many factors; there are several possible reasons for vitamin D deficiency and insufficiency. First, lack of direct exposure to sunlight: newborns and young children have fewer opportunities for outdoor activities due to their limited mobility. Due to the cold weather in winter and spring, parents seldom take their children out for activities, and often close the windows at home, making it difficult to receive sunlight for children, so vitamin D deficiencies are more common in winter and spring. Second, insufficient intake of vitamin D in food: Vitamin D content in human milk, cow milk, and general foods is very low, so it could not meet the growth and development needs of children. If vitamin D could not be synthesized from ultraviolet radiation, and no supplementary foods such as cod liver oil or fortified vitamin D are taken, vitamin D deficiency and insufficiency could easily occur. Third, improper proportion of calcium and phosphorus in food: although milk contains a lot of calcium, which is much higher than the calcium content in human milk, the ratio of calcium and phosphorus is not as suitable as that in human milk, and the proportion of calcium absorbed through the intestine is worse than that of human milk. Therefore, infants fed artificially are more likely to develop rickets than breastfed infants. Fourth, chronic diarrhea and hepatobiliary diseases could affect vitamin D absorption and utilization.

Thus, interventions are needed to improve the vitamin D status in children. First, physicians must routinely test vitamin D levels in China to identify the high-risk populations. Second, education should be considered, as it may raise the awareness of health care professionals and family members about the importance of vitamin D supplementation. Third, China could establish rickets surveillance to evaluate the risk of vitamin D deficiency in early childhood. Last, in order to prevent rickets, it is necessary to increase the children's outdoor activities and sunshine exposure, especially for children born in winter with little outdoor activities, cod liver oil should be taken for prevention.

This study had some limitations. First, the data were collected from hospitals and were not population-based. Second, data from some provinces in China were lacking; therefore, selective bias may exist. Third, some factors that may influence vitamin D status, such as supplementation, obesity status, and sunlight exposure, were unavailable.

5. Conclusion

The prevalence of vitamin D deficiency is high among Chinese children and adolescents. Studies on population estimates, cost-effective screening strategies, and interventions for high-risk cases are needed.

Acknowledgments

We also thank Diane Civic, PhD, from Liwen Bianji, Edanz Group China (www.liwenbianji.cn/ac), for editing the English text of a draft of this manuscript.

Author contributions

Chunsong Yang and Ping Li: designed the review, collected data, carried out analysis and interpretation of the data and wrote the review. Dan Yu and Meng Mao: designed the review, collected data, checked the data, and wrote the review, designed the review, commented on drafts for previous version.
Data curation: Chunsong Yang, Li Ping, Dan Yu, Meng Mao.
Formal analysis: Li Ping, Dan Yu.
Methodology: Chunsong Yang.
Writing – review & editing: Chunsong Yang, Meng Mao.

References

[1] Al-Ishaq RK, Kubatka P, Brozmanova M, et al. Health implication of vitamin D on the cardiovascular and the renal system. Arch Physiol Biochem 2019;10:1–5.
[2] Holick MF. Vitamin D deficiency. N Engl J Med 2007;357:266–81.
[3] Roth DE, Abrams SA, Aloia J, et al. Global prevalence and disease burden of vitamin D deficiency: a roadmap for action in low- and middle-income countries. Ann N Y Acad Sci 2018;1430:44–9.
[4] Antonucci R, Locci C, Clemente MG, et al. Vitamin D deficiency in childhood: old lessons and current challenges. J Pediatr Endocrinol Metab 2018;31:247–60.
[5] Brito A, Cori H, Olivares M, et al. Less than adequate vitamin D status and intake in Latin America and the Caribbean: a problem of unknown magnitude. Food Nutr Bull 2013;34:52–64.

[6] Akkermans MD, van der Horst-Graat JM, Eussen SR, et al. Iron and vitamin D deficiency in healthy young children in western Europe despite current nutritional recommendations. J Pediatr Gastroenterol Nutr 2016;62:635–42.
[7] Fraser DR. Vitamin D-deficiency in Asia. J Steroid Biochem Mol Biol 2004;89-90:491–5.
[8] Yu X, Wang W, Wei Z, et al. Vitamin D status and related factors in newborns in Shanghai, China. Nutrients 2014;6:5600–10.
[9] Liang GY, Qin R, Li J, et al. Optimal level of 25-(OH)D in children in Nanjing (32 degrees N Lat) during winter. Pediatr Int 2011;53:541–5.
[10] Guo Y, Ke HJ, Liu Y, et al. Prevalence of vitamin D insufficiency among children in southern china: a cross-sectional survey. Medicine (Baltimore) 2018;97:e11030.
[11] Munns CF, Shaw N, Kiely M, et al. Global Consensus Recommendations on Prevention and Management of Nutritional Rickets. Horm Res Paediatr 2016;85:83–106.
[12] Jazayeri M, Moradi Y, Rasti A, et al. Prevalence of vitamin D deficiency in healthy Iranian children: a systematic review and meta-analysis. Med J Islam Repub Iran 2018;32:83.
[13] Andiran N, Celik N, Akca H, et al. Vitamin D deficiency in children and adolescents. J Clin Res Pediatr Endocrinol 2012;4:25–9.
[14] Saki F, Dabbaghmanesh MH, Omrani GR, et al. Vitamin D deficiency and its associated risk factors in children and adolescents in southern Iran. Public Health Nutr 2017;20:1851–6.