Overview article

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Vitamin D supplementation in infants: a narrative review of guidelines in Asia

Ha Vo Van Anh[1], Zhao Yun[2], Binns W. Colin[2]
[1]Faculty of Public Health, Pham Ngoc Thach University of Medicine, Ho Chi Minh City 700000, Vietnam
[2]Faculty of Health Sciences, School of Public Health, Curtin University, Perth, WA 6102, Australia

Abstract

Vitamin D supplementation is recommended in two main contexts: for the treatment of rickets, for persons with potential vitamin D deficiency, defined as serum 25(OH) D below a defined threshold (i.e., 25 nmol/L) or in populations in locations where endogenous production may be insufficient. Longitudinal studies have indicated a significant association of the low vitamin D status in pregnant mothers and their offspring. Breastfeeding is shown as a risk factor determining a low serum 25(OH)D in infants, even in locations with an abundance of sunlight resulting in recommendations for the supplementation of infants, particularly breastfed infants. Ten micrograms of vitamin D are commonly recommended as a safe level of supplementation. In Asia there have been few, large - scale studies on plasma vitamin D concentration in infants. A review of recommendations for infant supplementation in Asia with vitamin D reveals inconsistent practices, showing the need for further research.

Keywords: Asia Pacific, 25 - hydroxyvitamin D, pregnancy, vitamin D deficiency, infancy, dietary supplements, cholecalciferol, lactation

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Author contact:
Ha Vo Van Anh
Email:
anhhvv@pnt.edu.vn
Phone: +84 908495351

1. INTRODUCTION

Vitamin D is a group of related chemicals produced endogenously in response to ultra violet radiation and obtained from food. Many functions are now ascribed to vitamin D, but it primarily affects bone and muscle health in children [1]. Nutritional rickets is the classical sign of vitamin D deficiency and is most often observed when the infant begins to walk or when her legs are under pressure of bodyweight [1]. Infants obtain vitamin D from breastmilk (a relatively poor source), transferred in cord blood, sunlight, and vitamin D supplements. Infant formula is always fortified with vitamin D. Recent literature reported that serum 25(OH) D concentrations < 25 nmol/L increased risk of nutritional rickets in infants [2]. To protect against vitamin D deficiency - related nutritional rickets, the American Academy of Pediatrics (AAP) and the European Society for Clinical Nutrition and Metabolism recommend daily vitamin D supplementation for infants starting from the first few days of life until twelve months old [3 4]. World Health Organization also recommends vitamin D supplementation in breastfed, term infants in 2022 [5]. However, authors of several studies have reported vitamin D deficiency (25(OH)D < 25 nmol/L) has been prevalent in newborns in most World Health Organization (WHO) regions [6]. The prevalence of vitamin D deficiency (25(OH) D less than 25 nmol/L) was reported as 66% among Danish newborns [6].

In many parts of Asia, nutritional rickets, symptomatic of vitamin D deficiency, can still be found in Japan, Korea, Taiwan, Mongolia, and China [2 7-10]. Although many of Asian countries are exposed to full sunlight all year

round, vitamin D insufficiency and deficiency have been found to be prevalent in several studies of pregnant women and infants; for example, in Thailand, Vietnam, Sri Lanka, and Malaysia [11-14]. Exclusive breastfeeding, a poor diet, and sun avoidance habits are major risk factors of vitamin D deficiency in infants and mothers in Asia [7 15 16]. In Asian populations, an inverse association between low vitamin D status in mothers and infant growth and development has been described [17 18]. Aside from the prevention of rickets and skeletal health problems in infants, achieving vitamin D adequacy in pregnancy and early days of life potentially support immune responses against infections (e.g., acute respiratory infection), dental caries, and neuropsychological functioning [19 - 21]. Despite evidence of deficiencies in infants' recommendation on vitamin D supplementation in infants are inconsistent in Asian populations, there have been limited recent reviews of vitamin D status in Asian infants.

The aim of this study was to identify and retrieve vitamin D supplementation recommendations in infants in the Asia Pacific region from fifteen Asian countries: Korea, Japan, China, Sri Lanka, Mongolia, Vietnam, Laos, Cambodia, Taiwan, Singapore, Malaysia, Indonesia, Thailand, Myanmar, and Philippines.

2. REVIEWS

2.1. Eligibility Criteria

All recommendations were included when their years of dissemination are within 2000 - 2023 and English or Vietnamese. Recommendations which were written in both published manuscripts and websites of professional associations and governmental agencies are eligible for inclusion. When the guideline or recommendation on vitamin D supplementation of a location or country of interest is unable to retrieve, it is not listed on the study finding.

2.2. Search Strategy

The search strategy involves infants (0 - 12 months of age) and relevant terms (vitamin D) with Medical Subject Headings (MeSH) and text words: vitamin D deficiency [MeSH], infant [MeSH], pregnancy [MeSH], breast feeding [MeSH] ("asia"[MeSH Terms] OR Asia[Text Word]) for PubMed. For Scopus, the search terms include "vitamin D", "25 - hydrioxyvitamin D", infant*, asia*, keywords ("humans", "vitamin D deficiency", "vitamin blood level", "vitamin supplementation, "newborn", "dietary supplements", "diet supplementation", "dietary intake", "umbilical cord blood, and "rickets", and the search was limited to included countries, and time range.

2.3. Information Sources

The review retrieved records of interest by searching for databases and other sources. The following databases were searched: PubMed (conducted between 30 April and 14 June 2023) and Scopus (conducted between 13 May and 14 June 2023).

Websites of professional associations, governmental agencies and scholarly platforms in countries of interest were browsed and searched: the Vietnam Institute of Nutrition, the National Nutrition Council Philippines, Ho Chi Minh City Journal of Medicine, Vietnam Journal of Nutrition and Food, the Indonesian Journal of Public Health Nutrition, the Malaysian Journal of Nutrition, the Singapore Medical Journal, the Singapore Ministry of Health, Singapore Health Promotion Board, the Chinese Nutrition Society, World Health Organization (Institutional Repository for Information Sharing IRIS, Global database on the Implementation of Nutrition Action (GINA), the Philippines' Knowledge Center on Food and Nutrition, Ministry of Health in Cambodia, Laos, Indonesia, Vietnam, Sri Lanka, and Malaysia, Myanmar Ministry of Health and Sports, Japan Ministry of Health and Welfare, the UNICEF (the United Nations Children's Fund), and the Southeast Asia Public Health Nutrition Network (SEA-PHN). References cited in study and professional association reports on vitamin D in infants, pregnant and lactating women were also examined.

2.4. Selection of Recommendations and Studies of vitamin D status

The review included the publications recording recommendations on vitamin D supplementation, vitamin D status/deficiency with the following criteria: (1) for newborns and infants, and pregnant and lactating women, (2) for Asian countries: Korea, Japan, China, Sri Lanka, Mongolia, Vietnam, Laos, Cambodia, Taiwan, Singapore, Malaysia, Indonesia, Thailand, Myanmar, and Philippines. Full text was obtained for further screening in studies on vitamin D in children in Asian countries of interest.

2.5. Data extraction

All recommendations were searched and reported in detail: country/location, professional associations/agencies, year of recommendation released, type of document, content of recommendation, and reference. Information on multiple micronutrient powder distribution was also retrieved if the powder was noted to contain vitamin D in the literature.

2.6. Results and Discussion

This narrative review was to retrieve recommendations on vitamin D supplementation in infants (plasma 25(OH)D levels) in infants in Korea, Japan, China, Sri Lanka, Mongolia, Vietnam, Laos, Cambodia, Taiwan, Singapore, Malaysia, Indonesia, Thailand, Myanmar, and Philippines. We searched nutrition policies from WHO-GINA, professional bodies at national levels and local professional journals which websites are available, PubMed, and Scopus.

All papers related to vitamin D status in infants, and recommendations on vitamin D supplementation in infants were included and presented in Table 1. Figure 1 describes the flow chart of search strategy and study selection. Overall, 8 results were included for searching available recommendations in the study populations of interest.

We retrieved the recommendations on vitamin D supplementation in infants from four Asian countries, including China, Korea, Mongolia, and Taiwan (Table 1). Four countries included recommendations on vitamin D supplementation for infants, but only one document was released by the government as a national strategy (Mongolia). Two recommendation documents were efforts from national nutrition societies (China and Korea) and the last retrieved document reflect the interest of a national pediatric association (Taiwan).

Of five countries distributing multiple micronutrient powders (MNPs) to infants (i.e., Cambodia, Philippines, Laos, Myanmar, and Philippines), Cambodia is the only country noting the inclusion of vitamin D in MNPs (5 µg vitamin D/sachet), which every child aged 6 to 23 months receives 15 sachets per month [22]. In Dietary Reference for Japanese, it is not recommended the supplementation of vitamin D for infants. However, accordingly, the adequate intake of vitamin D for infants under 5 months is 5µg/day with the assumed intake of 10µg from supplements and 2.38µg from breastmilk per day [23].

The literature retrieved from Ministry of Health in Malaysia has not shown available recommendations on vitamin D supplementation for infants but their recent concern in vitamin D status in children under five years old was shown in their national nutrition plan during 2016 - 2025. Most guidelines across Asian countries surveyed have not taken considerations of levels of sunlight exposure, except Mongolia. Breastfeeding was included in the Taiwanese recommendation only. Vitamin D supplementation, therefore, is limited to specific groups of infants in Taiwan and Mongolia, while all infants in China and Korea have been recommended vitamin D supplementation.

Mongolian government recommends a higher dosage (i.e., 50,000 IU (=1,250 µg) than that in China and Taiwan (10 µg). Korean recommendation suggests the lowest dosage: 5 µg per day. Notably, while cholecalciferol (vitamin D3) is recommended in China, infants in Mongolia have been recommended to supplement with vitamin D2 (ergocalciferol). Despite of different daily dosages recommended

(5 µg in South Korea versus 10 µg in China), all infants are recommended to supplement vitamin D by the Chinese Nutrition Society and the Korean Nutrition Society. These recommendations are likely consistent with the recommendations released by Alberta Health Service in Canada (10 µg per day for all healthy term infants, including those with breastfeeding and formula feeding) and the European Society for Clinical Nutrition and Metabolism [3 24].

Most children with nutritional rickets were reported to be breastfed [25 26]. Breastfed infants are also observed with a higher prevalence of vitamin D deficiency, compared to formula-fed infants [27 28]. As a result, vitamin D supplementation is recommended for infants, taking consideration of breastfeeding by many professional bodies from the WHO, the U.S., Australia, and Europe. The American Academy of Pediatrics (AAP), the Health Council of the Netherlands, the joint statement of Health Canada, Canadian Paediatric Society, Dietitians of Canada, and Breastfeeding Committee for Canada, and the RANZCOG (the Royal Australian and New Zealand College of Obstetricians and Gynaecologists) recommend 10 µg daily vitamin D supplementation for breastfed infants [5 29 30]. Notably, for vitamin D-fortified formula milk, Dutch infants with more than 0.5 liter/day of infant formula and American infants with more than one liter per day are excluded [4 31]. Of 15 Asian countries surveyed in this study, only the Taiwan Pediatric Association has a moderately similar recommendation with the recommendations of WHO and in the US, Netherlands, and Australia. However, the review was unable to document if there are any recommendations for infants with a limited consumption of formula milk.

Vitamin D3 for supplements and food enrichment is prepared from sheep wool and considered to be more effective than vitamin D2 in raising serum 25(OH)D concentrations [32]. Therefore, the WHO and many countries, including the USA, Canada, and China give preference to cholecalciferol (vitamin D3) for infants [5 30 33]. Mongolia has recommended ergocalciferol (vitamin D2) for infants with a high dose. Vitamin D2 with doses of 50,000 IU is also practiced in the USA as a prescription medication. The distribution of a high dose of vitamin D2 in Mongolia might be used as a treatment rather than a public health prevention. Besides, vitamin D2 are also preferred for vegans because it is derived from a fat extract of yeast. Except China and Mongolia, Taiwan and South Korea have not mentioned the specific form of vitamin D recommended for infants.

A lack of consideration for climate and weather was shown in the recommendations on vitamin D supplementation for infants 0 - 12 months of age. One recommendation document made exceptions for infants in cold seasons (Mongolia). The geographical location of northern Asia (eg. Mongolia) may expect a priority of recommending vitamin D supplementation during cold seasons, compared to countries in tropical regions having a higher UV index (e.g., Indonesia, Thailand, Singapore, Hong Kong, Shanghai, Vietnam, Cambodia, and Malaysia). In the meantime, some sociocultural and behavioral risk factors (i.e., use of sunscreen cream, the preference of indoor activities and white skin) in tropical countries of Asia due to the avoidance of sunlight may affect vitamin D status in infants in this area [34].

3. CONCLUSIONS

Greater awareness of the role of vitamin D deficiency in infants on nutritional rickets in Asian countries results in a considerable number of recommendations on vitamin D supplementation in Asian infants. Nevertheless, the recommendations for infants were variable in terms of dosage, breastfeeding status, vitamin forms, and geographical locations in Asian countries. Countries, including Cambodia, Malaysia, Singapore, Sri Lanka, Vietnam, Laos, Singapore, Indonesia, Myanmar, Philippines, are expected to have more exposure to sunlight compared to countries having published recommendations

on vitamin D supplementation. We recommend systematic reviews to generate evidence on the impacts of these recommendations of vitamin D supplementation on vitamin D concentration in infants in these Asian countries, in comparison with their counterparts.

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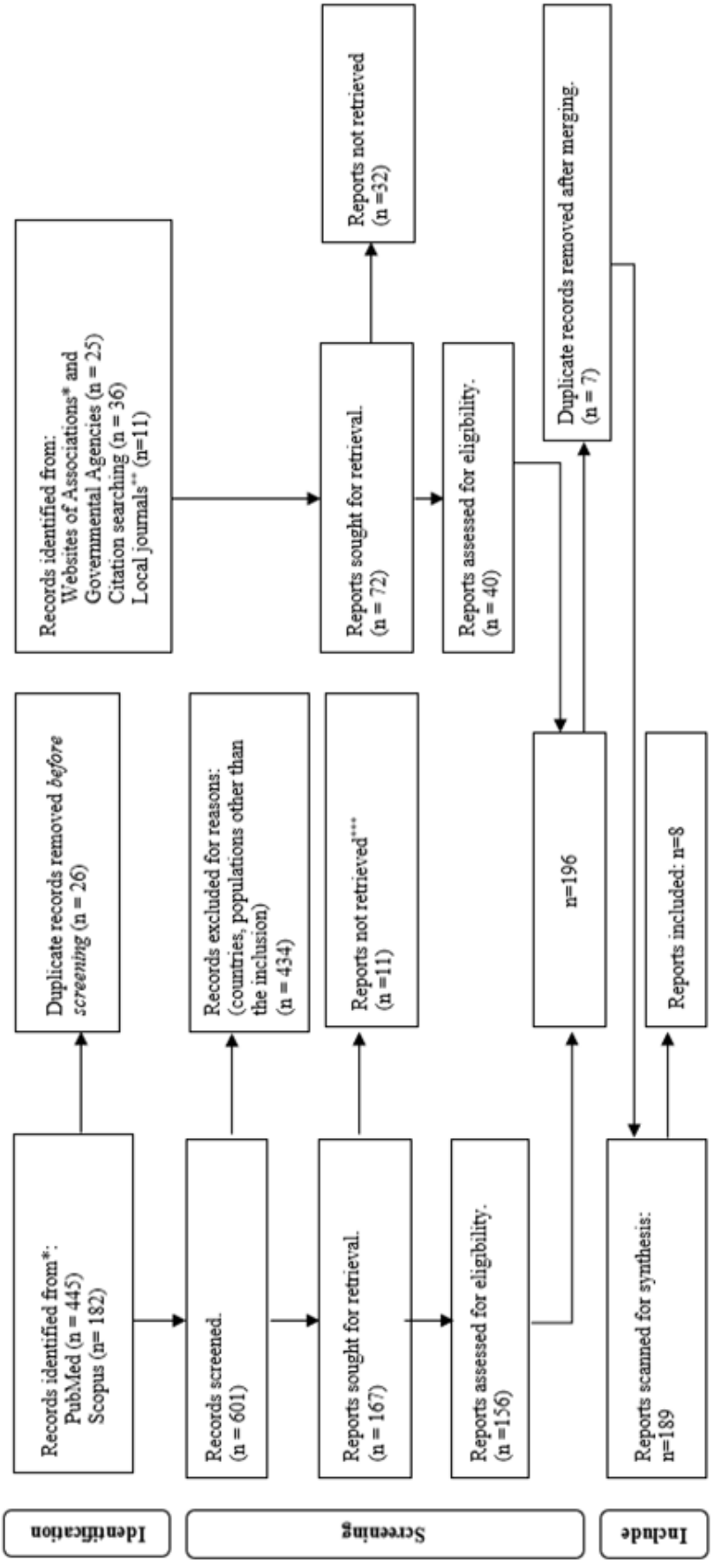

Figure 1. Prisma flow of record/document selection process

*The Vietnam Institute of Nutrition, the National Nutrition Council Philippines, the Chinese Nutrition Society, the World Health Organization, the Philippines' Knowledge Center on Food and Nutrition, the United Nations Children's Fund (UNICEF), the Southeast Asia Public Health Nutrition Network (SEA-PHN).

**Journal of Medical Association of Thailand, Indonesian Journal of Public Health Nutrition, Ho Chi Minh City Journal of Medicine, Vietnam Journal of Nutrition and Food, Malaysian Journal of Nutrition, and Singapore Medical Journal.

***Due to unavailable full-text or duplication or out of scope.

Tables

Table 1. Vitamin D guidelines for infancy across Asia

Geographical Location/ Country	**Government/ Organisation**	**Status**	**Year of recommendation release**	Type of Document	Recommendation	Reference
Cambodia	Ministry of Health	Micronutrient containing vitamin D	2012	The National Policy and Guidelines for Micronutrient Supplement to Prevent and Control Deficiencies in Cambodia	Multiple Micronutrient Powder for children aged 6-23 months. MNPs are distributed to caregivers monthly by village health support groups (15 sachets per child per month starting at 6 months of age). MNPs' formula contains 5 mcg vitamin D per sachet.	[22]
China	Chinese Nutrition Society	available	2016 and revised in 2019	Chinese Dietary Guidelines	"Vitamin D3 10 mcg (400 IU) supplementation should be given within the first few days after birth".	[35]
Japan	Ministry of Health, Labour and Welfare	No information on vitamin D supplementation recommendations	available between 2015-2019	Dietary Reference for Japanese	0–5-month infants: Adequate Intake (AI) and UL (tolerable upper intake level) of vitamin D is 5 and 25 mcg/ day, respectively. The AI was based on the previous finding which assumes that children are supplemented with 10 mcg vitamin D for 6 months and received a 2.38 mcg vitamin D per day from breast milk. The AI of vitamin D is 5 mcg/day for infants aged 6-11 months with adequate sun exposure.	[23]

Geographical Location/ Country	**Government/ Organisation**	**Status**	**Year of recommendation release**	Type of Document	Recommendation	Reference
South Korea	The Korean Nutrition Society	available	Since 2015	Paper	"For South Korean infants and children, 5mcg/day of vitamin D is recommended"	[36]
Malaysia	Ministry of Health Malaysia	Interest of vitamin D in infants was expressed via the plan.	2016 - 2025	National Plan of Action for Nutrition of Malaysia III 2016-2025	One of national planned activity is "to conduct national survey for micronutrient status for vitamin D using biochemical parameters among children under 5 years old by 2025". No recommendations on vitamin D supplementation have been found in the national plan.	[37]
Mongolia	Government of Mongolia	available	Since 2009	National Strategy	"Vitamin D supplementation (D2, 50,000 IU) has only been distributed to children from birth to 2 years of age once per month in cold seasons. The Government of Mongolia has been expanding National vitamin D supplementation of children since 2009".	[9]
	Government of Mongolia	Micronutrient containing vitamin D	Since 2000	National Program	"Provision of multiple micronutrient powders (MNPs) to young children was previously a national programme in Mongolia, though coverage has diminished due to a lack of funding in recent years with MNPs provided in 2016 as part of emergency response services. MNPs provide iron, vitamin A, zinc, vitamin D, iodine, and other essential nutrients for all children 6-23 months of age".	[38]
Taiwan	Taiwan Pediatric Association	available	Since 2016	unknown	"Exclusively breastfed infants or partially breastfed infants should be provided 400 IU of vitamin D oral supplements daily"	[39]