Editorial
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Comparison of the serum vitamin D level between breastfed and formula-fed infants: several factors which can affect serum vitamin D concentration

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It is common knowledge among pediatricians that exclusively breastfed infants should be supplemented with vitamin D (400 IU/day) because human breast milk contains an inadequate amount of vitamin D. Accordingly, Choi et al.[1)] reported a vitamin deficiency in early infants in a comparative study between breastfed and formula-fed infants in this issue. Although the authors stated some exclusion criteria, the study lacks some guidelines for considerations in the evaluation of vitamin D deficiency, especially those pertaining to factors that can affect the vitamin concentration in the body. Many genetic, dietary, and environmental factors affect the body concentration of vitamin D, calcium, phosphorus, and bone metabolism. Therefore, it is recommended that the authors further consider the variable effects of the following conditions.

In human skin, 7-dehydrocholesterol is converted into previtamin D3 under ultraviolet (UV)-B radiation (290–315 nm). Previtamin D3 is transformed into vitamin D3 through the heat of the skin. Previtamin D3 then binds to the vitamin D-binding protein and is transported to the liver, where it is converted to 25-hydroxyvitamin D (25[OH]D) by 25-hydroxylase. In the kidney, 25(OH)D, the nutritional indicator of vitamin D, is hydroxylated into 1,25-dihydroxyvitamin D (1,25-OH_2-D). Vitamin D is an important prehormone involved in many metabolic processes beyond bone integrity and calcium homeostasis[2)]. Most physicians consider 1,25-OH_2-D as a key substance to the assessment of vitamin D status. However, measuring 1,25-OH_2-D levels as a predictor of vitamin D status can lead to erroneous conclusions because, compared with 25(OH)D levels, 1,25-OH_2-D levels can be normal or even elevated despite vitamin D deficiency due to secondary hyperparathyroidism.

In exclusively breastfed infants, 25(OH)D serum levels were low during the winter despite supplementation[3)], whereas serum levels of 1,25-OH_2-D and vitamin D-binding protein were higher in the winter than in the summer[4)]. A study performed among pregnant women demonstrated that fetal growth, expressed as femur length, was reduced when the mother had low vitamin D levels during the winter in a high-latitude area[5)]. Breastfed infants are at increased risk of hypovitaminosis D, especially if their mothers are multiparous, have dark skin color, live in high-latitude areas, and are vegetarian[6)].

At high-latitude areas, conditions of low UV-B radiation effectively facilitate vitamin D production in humans with light skin color, thereby preventing vitamin D deficiency[7)]. A light skin color may be required in women to produce relatively high amounts of vitamin D necessary for pregnancy and lactation[8)].

Vitamin D-sufficient foods are limited. Human can take vitamin D through fatty fish,

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certain fish oils, animal liver, aquatic mammal fat and egg yolks of vitamin D-fed chickens.

Human breast milk contains little vitamin D. The water-soluble fraction of cow's milk and human milk did not possess significant antirachitic activity. Whole human milk contains a vitamin D concentration of 15–26 IU/L, of which 12 IU is derived from the lipid fraction. This value is much lower than that in cow milk (204–400 IU/L)[9-11]. Although an infant is formula fed, it cannot be automatically assumed that the infant is adequately supplied with vitamin D. The daily amount of formula feeding should be taken into consideration. In the study of Choi et al.[1], 17.5% of the formula-fed infants were vitamin D deficient. The authors overlooked the feeding amount of the formula. All the infant formulas in Korea contain the minimum required vitamin D concentration of 40 IU/100 kcal (258 IU/L in a 20-kcal/oz formula). Formula-fed infants should ingest nearly 1,000 mL of formula for a vitamin D intake of 400 IU/day. However, very young infants cannot take 1,000 mL of formula a day. Therefore, it is possible that even formula-fed young infants are vitamin D deficient.

Breast milk alone can meet the nutrient requirement during the first 6 months of life, with the possible exception of vitamin D. The vitamin A and vitamin E contents of the breast milk are correlated with the amount of the vitamins in the dietary intake of lactating mothers. On the contrary, vitamin D content of the breast milk does not meet the required daily amount for the infants despite adequate dietary supplementation of vitamin D[12], because this supplementing does not substantially increase the vitamin D concentration in human milk[13]. Although nursing mothers were supplemented with 1,000 to 2,000 IU of vitamin D daily, the supplementation had little effect on the vitamin D concentration status of breastfed infants[14].

The American Academy of Pediatrics (AAP) previously recommended a daily vitamin D intake of 200 IU for exclusively breast-fed infants. However, this amount is inadequate for maintaining a 25(OH)D concentration of 50 nmol/L in infants. Recently, AAP recommendation of 400 IU/day for vitamin D supplementation was documented to maintain a 25(OH)D serum concentration higher than 50 nmol/L in exclusively breast-fed infants[15].

In their study, Choi et al.[1] made no mention of whether the mothers took vitamin D supplements or ate vitamin-rich food during their pregnancy. When large amounts of vitamin D (1,000 IU/day) are supplemented during the last trimester to achieve 25(OH)D concentrations of 50 nmol/L in pregnant woman, the vitamin D concentration in the cord blood is consequently increased. These findings suggest that a neonate born to a mother with vitamin D deficiency can be expected to be also deficient of the vitamin[16]. In addition, women with increased skin pigmentation or those with little sunlight exposure are at risk of vitamin D deficiency and may need additional vitamin D supplementation, especially during pregnancy and lactation. Therefore, those who provide care for pregnant women and the pediatric population should take these factors into consideration

Despite severe maternal vitamin D deficiency, fetal rickets may rarely develop. However, rickets may manifest at birth. Therefore, daily supplementation with 400 IU of vitamin D during the last trimester of pregnancy has been practiced, albeit with minimal effect on circulating 25(OH)D concentrations in the mother and infant at term. Nevertheless, it is noteworthy that infants born to unsupplemented vitamin D-deficient mothers were likely to have early vitamin D deficiency compared with those whose mothers were supplemented with vitamin D during pregnancy.

A Canadian study that evaluated serum vitamin D and mineral levels among infants reported that newborns whose mothers had adequate intakes of milk and vitamin D during pregnancy showed increased birth weight but not head circumference or length at birth[17].

The differences in body weight percentile between the breastfed and formula-fed groups indicated no statistical significance. The authors did not take into consideration the height profiles of the newborns even if minerals and vitamin D are key factors of bony growth. If the height percentile differences between the 2 groups had been compared, the results would have been different.

Moreover, the authors included in the study preterm or small-for-gestational age infants, which comprised 11% of the whole study group. It would have been better if this group was excluded in the study. Given that the uterus allows transfer of sufficient amount of 25(OH)D during the prenatal period, especially during the final 3 months of pregnancy, infants born near or at term have higher levels of circulating 25(OH)D than preterm infants. With respect to prenatal supplementation, the generally prescribed daily intake of 400 IU of vitamin D is not sufficient to achieve the optimal vitamin D status in newborns[18].

Many research reports on vitamin D, which is important for bony metabolism and immunity, and has beneficial effects on diverse organs, have been published recently. Vitamin D concentration is affected by many genetic, dietary, and environmental factors; therefore, it is recommended that researchers consider the relative and effective factors when performing studies concerning vitamin D concentrations.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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