

Relationship between newborn craniotabes and vitamin D status

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ABSTRACT

OBJECTIVE: In recent studies, vitamin D deficiency during pregnancy and early infancy has been reported to predispose children to many chronic diseases, except those of the skeletal system. The aim of this study was to investigate whether craniotabes in otherwise healthy newborns is physiological, its relationship to vitamin D deficiency and whether or not it requires treatment.

METHODS: A total of 150 healthy newborns with a weight of over 2000 g were included. Newborns were divided into two groups during postnatal discharge (1-3.'s day): those with and without craniotabes. The 25-hydroxy (OH) vitamin D levels of the newborns' mothers were measured, and all infants were re-evaluated for craniotabes, as well as tested to determine levels of serum calcium (Ca), phosphorus (P), alkaline phosphatase (ALP), parathyroid hormone (PTH) and 25(OH) vitamin D, urine calcium and creatinine.

RESULTS: Craniotabes was present in 45 (30%) of newborns enrolled in the study. Craniotabes of the newborns born during the winter months was significantly higher. PTH level was significantly higher in 1-month-old newborns with craniotabes than those without craniotabes. No relationship was observed between diet and craniotabes, but in exclusively breastfed infants, vitamin D level was statistically significantly lower. No statistically significant difference was found in the occurrence of craniotabes in newborns with or without vitamin D support.

CONCLUSION: The relationship between newborn craniotabes and maternal vitamin D deficiency is not clear. However, the present study illustrates that maternal vitamin D deficiency is still a major problem. Therefore, measures to prevent maternal vitamin D deficiency should be strengthened.

Keywords: Craniotabes; newborn; vitamin D deficiency.

Craniotabes is the softening of the bones of the skull and is known to be associated with many diseases such as rickets, hypervitaminosis, osteo-

genesis imperfecta, hydrocephalus and congenital syphilis. Craniotabes in otherwise normal newborns has largely been regarded as a physiological condi-



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tion that does not require treatment. It is found in up to 30% of healthy neonates, and usually heals within 2-3 months [1, 2]. Craniotabes is thought to be due to minor changes in calcium metabolism and the physiological compaction of premature engagement of the head [1].

Unlike classical vitamins, vitamin D is synthesized in the body and termed a hormone. In recent studies, vitamin D deficiency during pregnancy and early infancy has been reported to predispose children to many chronic diseases, except those of skeletal system [3, 4]. For this reason, requiring normal vitamin D values has gained more importance [5, 6]. In studies conducted in Turkey, maternal vitamin D deficiency is reported to be 80% [7].

Intrauterine exposure to temporary vitamin D deficiency during infancy or childhood creates an increased risk for type 1 diabetes mellitus, asthma, lower respiratory tract infections and even schizophrenia [4, 8-10]. If craniotabes in normal neonates reflects vitamin D deficiency in utero, and if the condition persists in infancy, it may lead to a variety of health problems later in life. Accordingly, treatment with vitamin D would be appropriate in those newborns [11]. The aim of this study was to investigate whether craniotabes in otherwise healthy newborns is physiological, its relationship to vitamin D deficiency and whether or not it requires treatment.

MATERIALS AND METHODS

The study consisted of 150 neonates born at term between April 2012 and April 2013 in Bulent Ecevit University Medical Faculty Hospital and was conducted prospectively. It included 150 healthy, term infants with a body weight of more than 2000 g. No sex discrimination was made. Infants whose families declined to sign a written consent agreement, and those with acute illness, major congenital anomalies, abnormal calcium metabolism or liver disease were excluded.

Newborns included in the study were examined by one physician for craniotabes (first and third day) on discharge and divided into two groups: those with craniotabes (study group) and without craniotabes (control group). Presence of soft bones,

inward collapse when pressure was applied to parieto-occipital region with the index and middle fingers of both hands and typically snapping back when pressure was relieved was considered to constitute craniotabes.

Serum 25-hydroxy (OH) vitamin D levels were measured in all mothers of participating infants. The same physician repeated the physical examination of all the newborns when they were 1 month old to evaluate the presence of craniotabes and levels of serum calcium (Ca), phosphorus (P), alkaline phosphatase (ALP), parathyroid hormone (PTH), 25 (OH) vitamin D, urinary calcium and creatinine.

Epidemiological data was gathered, including, date of birth; birth weight; gestational week; gender; maternal age; number of pregnancies; number of children; mother's education level; mother's occupation; mother's clothing style; daily, weekly and monthly average duration of exposure to the sun; cigarette usage; place of residence (rural/urban), calcium and vitamin D supplementation during pregnancy; nutritional status of baby up to 1 month of age; vitamin D supplementation in infancy and if provided, date initiated. Infants who were breast-fed but received more than 40 mL per day formula were considered to be mixed-fed. The information obtained was examined for relationship to craniotabes.

The study was approved by the Ethics Committee of Bulent Ecevit University School of Medicine and written informed consent was obtained from parents.

Data were evaluated using SPSS software (version 13.0; SPSS Inc., Chicago, IL, USA). Numerical variables were presented as mean, standard deviation, median, minimum and maximum values; categorical variables were shown with frequencies and percentages. All comparisons in statistical analysis with p-value of <0.05 were considered statistically significant.

RESULTS

The study included 150 neonates born at term between April 2012 - April 2013 in Bulent Ecevit

TABLE 1. Gestational ages, birth seasons, birth weights of newborns

Craniotabes (n)	Gestational Age (days)	Birth Weight (g)	Season	
			Summer n (%)	Winter n (%)
With (45)	268.87±7.51	3027.44±486.11 (2100-3940)	0 (0)	45 (45,9)
Without (105)	271.43±8.21	3317.38±460.43 (2400-4740)	46 (100)	53 (54,1)
p	0.091	0.002*	<0,001*	

University Medical Faculty Hospital. Of the total, 79 were female (52.6%) and 71 were male (47.4%). Craniotabes was detected in 45 (30%) of the newborns enrolled in the study and the sex ratio of participants with and without craniotabes was similar.

Neonates with and without craniotabes were compared in terms of gestational age and birth weight. No statistically significant relationship was detected between craniotabes and weeks of gestation, but in newborns with low birth weight, the incidence of craniotabes was found to be significantly higher ($p=0.002$). All of the patients with cranio-

tabes were born in the fall and winter months with poor sunlight (Table 1). The incidence of craniotabes was significantly higher in infants born during the winter months ($p<0.001$).

There was no statistically significant relationship between education, profession, the family residence, clothing styles and craniotabes (Table 2). Mothers' use of cigarettes did not increase the incidence of craniotabes statistically, but detection of craniotabes in 50% of infants whose mothers smoke and only in 27.9% of infants of non-smoking mothers suggests that smoking may increase the risk of craniotabes.

TABLE 2. Relationship between craniotabes and some perinatal maternal factors

Mother's		With Craniotabes		Without Craniotabes		Total	p
		n	%	n	%		
Education	Primary school	26	27.1	70	72.9	96	0.539
	High school	13	37.1	22	62.9	35	
	University	6	31.6	13	68.4	19	
Profession	Housewife	35	28.9	86	71.1	121	0.778
	Worker	5	38.5	8	61.5	13	
	Officer	5	31.3	11	68.8	16	
Clothes	Modern	17	30.9	38	69.1	55	0.351
	Traditional	28	29.5	67	70.5	95	
Family residence	Urban	32	30.5	73	69.5	105	0.254
	Rural	13	28.9	32	71.1	45	
Smoking status	Smoker	7	50	7	50	14	0.123
	Non-smoker	38	27.9	98	72.1	136	

TABLE 3. 25-hydroxy (OH) vitamin D level and duration of calcium (Ca)-vitamin D intake of mother

Craniotabes	Duration of Ca-Vit D supplementation of mother (months)	25 (OH) vitamin D level of mother (ng/mL)
With	4.52±2.15 (1-9)	22.7± 6.8 (4.9-36.3)
Without	4.35± 1.8 (1-9)	22± 5.9 (8.2-35.9)
P	0.843	0.410

Mothers were evaluated in terms of receiving calcium and vitamin D supplementation during pregnancy. Groups were defined as receiving either calcium or vitamin D, receiving both, and receiving neither in terms of likelihood of craniotabes; no statistically significant difference was detected between the groups. Additionally, craniotabes incidence and calcium and vitamin D supplementation period of mothers and maternal 25 (OH) vitamin D levels were compared. There was no statistically significant difference (Table 3). However, serum 25 (OH) vitamin D levels <10 ng/mL were detected in 6.6% of mothers of neonates with craniotabes, while serum 25 (OH) vitamin D levels <10 ng/mL were detected in 0.95% of mothers of neonates without craniotabes. Vitamin D deficiency was observed in 96% of mothers while 90% of neonates had normal (>20ng/ml) vitamin D levels. No statistically significant relationship was detected between craniotabes

and daily, weekly and monthly sunshine exposure.

All neonates were examined at the newborn clinic at 1 month of age. Of 45 newborns that initially had craniotabes (68.8%), it was still present in 31 at 1 month of age. No statistically significant relationship was found between gender and persistent craniotabes. Although no significant difference was observed between gestational age and persistent craniotabes, more low birth weight newborns had craniotabes than newborns with normal birth weight. Those with craniotabes had 2899.5±448.3 g average birth weight, while the average birth weight was 3316.6±458.2 g for newborns without craniotabes (p<0.001).

Mothers who received calcium and vitamin D supplementation and those who did not were compared, and there was no statistically significant difference between the two groups in terms of average maternal 25 (OH) vitamin D level and serum Ca,

TABLE 4. Relationship between craniotabes seen soon after birth and Ca, P, ALP, PTH, 25(OH) vitamin D, urine Ca/creatinine levels of newborns

Craniotabes	Newborns at 1 month					
	Serum Ca mg/dL	Serum P mg/dL	ALP U/L	PTH pg/mL	25(OH) vitamin D ng/mL	UrineCa/Cr
With	10.40±0.42 (9.6-11.5)	6.60±0.56 (5-7.4)	312.8±64.5 (156-466)	39.8±21.9 (3-92)	31.7±12.5 (11.6-83)	0.61±0.42 (0.1-1.82)
Without	10.5±0.35 (9.8-11.4)	6.50±0.54 (4.6-7.7)	337.2±109 (140-712)	32.6±17.9 (3-100)	30.2±8.5 (10.5-65.5)	0.58±0.33 (0.04-2.23)
p	0.053	0.176	0.387	0.03*	0.499	0.972

Ca: calcium; P: phosphorus; ALP: alkaline phosphatase; PTH: parathyroid hormone; OH: hydroxy.

P, ALP, PTH, 25 (OH) vitamin D, and urine calcium/creatinine levels of newborns at 1 month of age. Newborns who had craniotabes and were exclusively breastfed had significantly higher serum PTH levels than those without craniotabes ($p=0.03$). Between the two groups, there was no significant correlation in terms of 25 (OH) vitamin D levels of mothers and newborns (Table 4).

Of the 150 newborns in the study, 86 (57.3%) were breastfed, 4 (2.7%) were formula-fed and 60 (40%) were both breastfed and formula-fed. When the relationship between feeding patterns and craniotabes persisting at 1 month of age was evaluated, no statistically significant difference was found.

Infants who were exclusively breastfed had an average of 27.5 ± 7.5 ng/mL 25 (OH) vitamin D level, whereas formula and mixed-fed infants had an average of 34.8 ± 10.9 ng/ml 25 (OH) vitamin D level ($p < 0.0001$, Figure 1). Four newborns (2.7%) had vitamin D deficiency (< 15 ng/mL), 11 (7.3%) had vitamin D insufficiency (15-20 ng/mL), and 135 (90%) of all newborns had vitamin D levels within normal limits (> 20 ng/ml). According to maternal vitamin D levels, 103 of 150 mothers (68.7%) had vitamin D deficiency (< 25 ng/mL), 41 of them (27.3%) had vitamin D insufficiency (25-32 ng/

mL). Only 6 of those (4%) had vitamin D levels within normal limits (> 32 ng/mL). No statistically significant relationship was found between vitamin D levels of mothers and presence of craniotabes at discharge or at 1 month of age. Analysis revealed that 95.3% of the newborns had 400 IU of vitamin D supplementation. No statistically significant relationship was found between the incidence of craniotabes and vitamin D supplementation.

DISCUSSION

Vitamin D is a fat-soluble vitamin; however, it is produced in tissue and released into the bloodstream. It acts on other tissue with "feedback" mechanisms and is considered a steroid hormone rather than a vitamin [12, 13].

Craniotabes is detected in 30% of healthy newborns and usually disappears in 2-3 months [1, 2]. A study in Japan suggested that physiological craniotabes frequency in newborn infants might be a result of in utero exposure to vitamin D deficiency [11]. Craniotabes was detected in 22% of neonates in that study, and 27% still had craniotabes at 1 month of age. In the present study, 30% of newborns had craniotabes, and 68.8% of those had persistent craniotabes at 1 month of age. Although no statistically significant relationship was found in terms of frequency of craniotabes among mothers who smoke cigarettes, 50% of smokers' infants had craniotabes whereas this was true for only 27.9% of non-smokers' infants. Recently, many studies conducted in various countries have found that 25 (OH) vitamin D levels in mothers who give birth in the summer and autumn months were higher than in those who give birth in the winter and spring months [14-17]. In one study, 25 (OH) vitamin D levels were found to be higher in patients diagnosed with nutritional rickets during summer months than those diagnosed during winter months [18]. In the present study, craniotabes was significantly higher in neonates born during the winter months. But no statistically significant difference was found in terms of 25 (OH) vitamin D levels of neonates born in summer or winter months and their mothers.

Recent studies have also found that adminis-

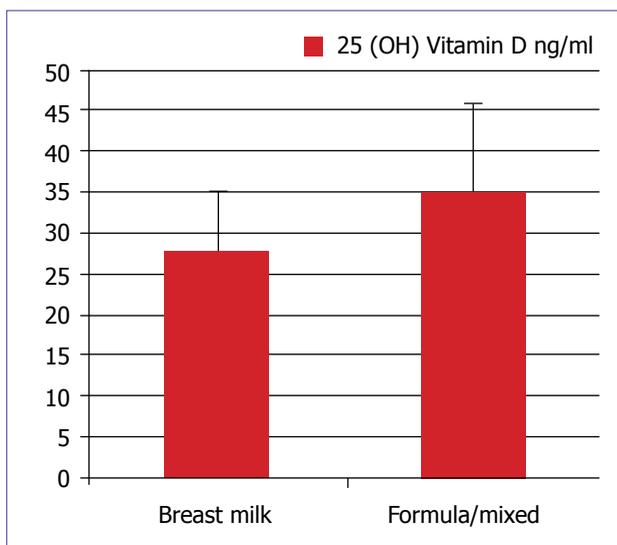


FIGURE 1. Dietary patterns of newborns and Vitamin D levels.

tration of 800-1600 IU/day of vitamin D during pregnancy was insufficient for normal serum 25-OH vitamin D levels [19, 20]. In a study with broad participation, 25 (OH) vitamin D level was found to be higher in mothers given vitamin D supplementation during pregnancy and in their infants at sixth postnatal day [21]. In the present study, only 3 mothers (2%) were given 1200 IU of vitamin D supplementation. Infants with and without cranio-tabes were evaluated according to their mothers' calcium and vitamin D supplement intake during pregnancy and duration of supplementation. There were no statistically significant differences between the two groups. In conclusion, despite a program launched in 2011 in Turkey, pregnant women still do not receive adequate vitamin D supplementation. All physicians dealing with the issue in the country have a big responsibility in this respect. Breast milk is poor in vitamin D, containing about 10 to 60 U/L [22]. A study compared infants fed breast milk and fed vitamin D-fortified formula in addition to breast milk and found, similar to the present study, serum 25-OH vitamin D levels were higher in formula-fed [23] infants. There was no statistically significant difference between infants with or without cranio-tabes in terms of their feeding patterns and vitamin D supplementation status.

In the present study, vitamin D status in children was evaluated according to proposals of American Pediatric Endocrine Association [24]. In only 2.7% of newborns were 25 (OH) vitamin D levels <15ng/mL. All of those were breastfed and 50% did not have vitamin D supplementation. Vitamin D levels (>20 ng/mL) were adequate in 90% of the newborns. This indicates that a free vitamin D support program for newborns started in 2005 by the Ministry of Health in Turkey is being implemented effectively and that 400 IU of vitamin D is sufficient for newborns [25]. In the present study, no statistically significant difference was observed between the two groups in terms of cranio-tabes detected at 1 month of age and serum Ca, P, ALP, 25 (OH) vitamin D, PTH levels and spot urine calcium/creatinine levels. The vitamin D support program has also had a positive effect on incidence of rickets, which has decreased noticeably [18].

Recently, reports in different countries have been published about frequent vitamin D deficiency in women of childbearing age, pregnant and nursing mothers and significant risks of this situation for mothers and babies [26-28]. In studies conducted in Turkey, vitamin D levels of mothers are quite low, as were the levels in the present study [15, 29, 30]. The present analysis indicated median maternal vitamin D levels did not differ significantly between the two groups, but 6.6% of the mothers of infants with cranio-tabes had 25 (OH) vitamin D levels <10 ng/mL; only 0.95% of mothers of infants without cranio-tabes had 25 (OH) vitamin D level <10 ng/mL (8.2 ng/mL). Only 6 of the mothers had vitamin D levels in normal range (>32 ng/mL). This suggests that in Turkey, pregnant women do not get appropriate supplementation of vitamin D.

As a result of this study, although we cannot identify a clear relationship between neonatal cranio-tabes and maternal vitamin D deficiency, we suggest that more extensive studies be conducted focusing on the subject. Maternal vitamin D deficiency is still a major issue in Turkey. The authors suggest that at least 1600-2000 IU of vitamin D supplementation per day should be included in antenatal care for pregnant women.

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