Incidence of maternal vitamin D deficiency in a region of Ankara, Turkey: a preliminary study

Gökçe GÜR[1], Ayhan ABACI[2],*, Adem Yasin KÖKSOY[1], Ahmet ANIK[2], Gönül ÇATLI[2],
Fatih Mehmet KIŞLAL[1], Kadir Okhan AKIN[3], Nesibe ANDIRAN[1]

[1]Department of Pediatric Endocrinology, Keçiören Training and Research Hospital, Ankara, Turkey
[2]Department of Pediatric Endocrinology, Faculty of Medicine, Dokuz Eylül University, İzmir, Turkey
[3]Department of Biochemistry, Keçiören Training and Research Hospital, Ankara, Turkey

Background/aim: To evaluate vitamin D levels and risk factors for vitamin D deficiency in healthy newborns and their mothers.

Materials and methods: Ninety-nine healthy pregnant women (≥37 weeks of gestation) were enrolled in the study. Previous history of pregnancies and births, nutritional status, multivitamin supplementation, educational status, type of clothing, and the economic level of the family were recorded. Blood samples were drawn from the mothers and the umbilical cord of the newborns to measure serum 25(OH)D3, calcium, phosphorus, and parathormone levels.

Results: While vitamin D insufficiency was identified as 62.6% in mothers, it was 58.6% in newborns; on the other hand, the incidence of vitamin D deficiency was 18.2% and 15.2% in mothers and newborns, respectively. Maternal serum 25(OH)D3 concentrations were not significantly related to the number of pregnancies or births, type of clothing, or the nutritional, economical, or educational status of the family (P > 0.05).

Conclusion: These findings suggest that despite a sunny environment, maternal vitamin D deficiency and insufficiency are still important health problems in a developed region of Turkey. Therefore, more effective vitamin D prophylaxis programs are required to prevent vitamin D deficiency in pregnant women and their offspring.

Key words: Vitamin D, pregnancy, newborn

1. Introduction

Maternal vitamin D deficiency begins to have an impact during the intrauterine period. Congenital rickets and neonatal hypocalcemic seizures are the early neonatal findings of maternal vitamin D deficiency (1,2). In mothers with low vitamin D levels, in addition to the classical findings of vitamin D deficiency, the risks of preeclampsia, gestational diabetes, prematurity, and infants small for gestational age have been found to be high (3–5). Besides the early neonatal effects of maternal vitamin D deficiency, long-term effects have also been reported. Irrespective of their own vitamin D intake, children with maternal vitamin D deficiency (especially those younger than 5 years old) have been found to exhibit asthma symptoms at a certain time during their lives (6). Furthermore, the mental and psychomotor development scores of children with a maternal vitamin D level of above 30 ng/mL during pregnancy were higher compared to children with a maternal vitamin D level below 20 ng/mL (7). Maternal

vitamin D deficiency has been demonstrated to have unfavorable metabolic effects on skeletal development during childhood (8,9). Maternal vitamin D deficiency has been highlighted for its negative effects on the development of long bones in the intrauterine period and its association with premature birth (10). To prevent these undesirable effects of vitamin D deficiency, vitamin D prophylaxis of 400 IU/day for infants and 600–2000 IU/day for pregnant women (recommendation of the International Association of Endocrinology) is recommended (11,12).

In Turkey, until May 2011, a health policy on vitamin D prophylaxis for pregnant women did not exist; thus, under the best circumstances, the vitamin D supplements prescribed for pregnant women were limited to low doses (200–400 IU), amounts generally included in commercial multivitamin preparations. Due to the current ineffectiveness of preventive health services, newborn babies are brought to clinics with early and late neonatal hypocalcemic seizures due to maternal vitamin

* Correspondence: ayhanabaci@gmail.com

D deficiency. The aim of this study was to identify the prevalence and risk factors of vitamin D deficiency in mothers and their offspring.

2. Materials and methods

Included in the study were 99 healthy pregnant women who presented to the Obstetrics and Gynecology Services of the Ankara Keçiören Training and Research Hospital with their babies, born to term with a birth weight of >2500 g, between November 2009 and February 2010. Information about the mothers was obtained through a survey including questions about age, number of pregnancies, level of education, type of clothing, type of home in which the family resides (apartment, slum), and socioeconomic status of the mothers. The number of pregnancies and the duration between the pregnancies, nutrition during the pregnancy (daily consumption of milk, milk products, and sea food), and intake of calcium and vitamin D supplements were recorded. Mothers who wore headscarves or long clothing covering their arms and legs completely were classified as veiled, and others were classified as not veiled. Mothers were grouped according to their skin color as white, olive, or dark.

All mothers were informed about the study in detail and informed consent was obtained. Venous blood samples were drawn from the mothers just before giving birth. Umbilical cord blood was obtained immediately after birth with double clamping of the umbilical cord. Laboratory studies were performed on the same day and in the same series after all samples were collected to prevent variations within and between days. Serum calcium (Ca), phosphorus (P), alkaline phosphatase (ALP), and $25(OH)D_3$ levels were measured in the blood samples. Serum $25(OH)D_3$ levels were measured using the RIA method. A 25OH-VIT.D_3-RIA-CT kit was used (Catalog No. KIP1961, Biosource, Nivelles, Belgium). The intraassay coefficient of variation (CV) was 5.2%–5.3% (n = 12) and interassay CV was 3.3%–4.7% (n = 12), the measurement range was 2.1–154 ng/mL, and the detection limit was 0.6 ng/mL for $25(OH)D_3$. For mothers, a serum $25(OH)D_3$ level of ≤20 ng/mL was considered vitamin D deficient (group I), 21–29 ng/mL was considered vitamin D insufficient (group II), and ≥30 ng/mL was considered normal vitamin D status (group III) (11). For newborns, a serum $25(OH)D_3$ level of <15 ng/mL was considered vitamin D deficient (group 1), 15–20 ng/mL vitamin D insufficient (group II), and >20 ng/mL normal vitamin D status (group III) (13).

Serum calcium (mg/dL), phosphorus (mg/dL), and alkaline phosphatase (IU/L) levels were analyzed with an Olympus AU 5200 autoanalyzer using Diasis Diagnostic System (DDS) kits. Normal levels were accepted as 9–11.5 mg/dL and 8.4–10.2 mg/dL for serum total Ca in umbilical

cord blood and in adults, respectively [the intraassay CV was 1.61%–4.59% (for concentrations of 0.94–0.96), interassay CV was 0.48%–0.65% (for concentrations of 21–856), and detection limit was 4 mg/dL]; as 4.0–7 mg/dL and 2.5–5 mg/dL for serum P in newborns and adults, respectively (the intraassay CV was 0.9%–2.1%, interassay CV was 0.6%–1.9%, and detection limit was 0.5 mg/dL); as 145–420 U/L and 65–260 U/L for serum ALP in newborns and adults, respectively [the intraassay CV was 0.93%–11.09% (for concentrations of 21–856), interassay CV was 0.4%–7.67% (for concentrations of 21–856), and detection limit was 5 U/L]; and as 10–65 pg/mL for parathormone [PTH; CLSI EP17, LIAISON N-TACT PTH II Assay; intraassay CV was 2.3%–8% (for concentrations of 7.8–797.4), interassay CV was 5.6%–13.7% (for concentrations of 21–260), and detection limit was <4 pg/mL for PTH].

Body weight and height of the mothers before birth were recorded. Body mass index (BMI) was calculated by dividing the body weight in kilograms by the square of the height in meters.

Statistical analysis was performed using SPSS 21.0 for Windows. The normal distribution of continuous variables was analyzed using the Kolmogorov–Smirnov test, while group means were compared using the Kruskal–Wallis test. When the test statistics were found to be significant, a nonparametric multiple comparison test (Mann–Whitney U test) was performed to identify which group caused the significance. Nominal variables were evaluated using Pearson's chi-square or Fisher's exact test. The correlation between the independent parameters was investigated with Spearman correlation analysis. Data were presented as median (minimum–maximum) and P < 0.05 was accepted as significant.

3. Results

Among the 99 mothers included in the study, 62.6% and 18.2% were identified as having vitamin D deficiency (group I) and vitamin D insufficiency (group II), respectively, and 19.2% were found to have normal vitamin D levels (group III). Among the newborns, 58.6% and 15.2% were identified as having vitamin D deficiency and vitamin D insufficiency, respectively, and 26.3% were found to have normal vitamin D levels. The mean vitamin D level of the mothers was 15.1 ± 4.4 ng/mL, while it was 15.0 ± 10.3 ng/mL in the umbilical cord blood of the newborns (P = 0.988). Laboratory parameters of the mothers and the newborns are summarized in Tables 1 and 2. Six mothers (9.5%) in group I who had vitamin D deficiency had high PTH levels, while 1 mother (5.8%) in group II who had vitamin D insufficiency had a high PTH level. No mothers in group III had high PTH levels. The calcium levels of 3 mothers in group I who had high PTH levels were lower than normal. Additionally, a significant

Table 1. Laboratory results of the pregnant women according to the groups.

	Group I (n = 64)	Group II (n = 17)	Group III (n = 18)	P*
Ca (mg/dL)	8.8[a] (8.1–10)	8.7 (8.2–9.3)	8.9[a] (8.4–9.5)	0.016
P (mg/dL)	3.9 (1.83–5.9)	4.2 (4.0–4.5)	2.7 (2.4–2.9)	0.256
ALP (IU/L)	188 (70–353)	155 (124–186)	236 (93–379)	0.623
PTH (pg/mL)	43 (11–162)	54.2 (11.5–84.4)	47.9 (48.5–60)	0.840
Vitamin D (ng/mL)	6.0[a,b] (4–13.8)	20.6[b,c] (17.7–23.5)	31.5[a,c] (28.9–34.2)	0.001

*: Kruskal–Wallis Test, [a,b,c]: Mann–Whitney U test (P < 0.05), data are given as median (minimum–maximum), Ca: calcium, P: phosphorus, ALP: alkaline phosphatase, PTH: parathormone.

Table 2. Laboratory results of newborn umbilical cord blood according to the groups.

	Group I (n = 58)	Group II (n = 15)	Group III (n = 26)	P*
Ca (mg/dL)	9.6 (7.7–11.3)	9.5 (8.3–11.2)	9.3 (8.6–11.3)	0.998
P (mg/dL)	3.9 (2.6–6.6)	4.0 (3.1–5.2)	3.7 (3.2–5.4)	0.866
ALP (IU/L)	246.5 (34–740)	264 (107–537)	197.5 (67–380)	0.139
PTH (pg/mL)	43 (16–168)	48.5 (12–103)	34 (11–67)	0.174
Vitamin D (ng/mL)	8.5[a,c] (4–14.8)	16.3[b,c] (15–20)	28.3[a,b] (21.3–39.7)	0.001

*: Kruskal–Wallis Test, [a,b,c]: Mann–Whitney U test (P < 0.05), data are given as median (minimum–maximum), Ca: calcium, P: phosphorus, ALP: alkaline phosphatase, PTH: parathormone.

positive correlation between the vitamin D levels of the mothers and the umbilical cord blood of the newborns was detected (Spearman's rho = 0.850, P = 0.001) (Figure).

Among the groups of different maternal vitamin D levels (groups I, II, and III), no differences were found in maternal age, BMI, number of pregnancies and births, duration between the last 2 pregnancies (in years), maternal skin color, status of veiling, education, level of income, and type of housing (P > 0.05) (Tables 3 and 4).

On the other hand, in the group with vitamin D deficiency (group I), the rate of using vitamin D supplements was statistically low compared to the other groups (groups II and III) (P = 0.037). Although there were no statistically significant differences in the socioeconomic status or level of education between the groups, the level of education and income were lower in group I, and mothers in this group were found to be veiled and to live in slum houses at higher rates compared to the other groups (Table 4).
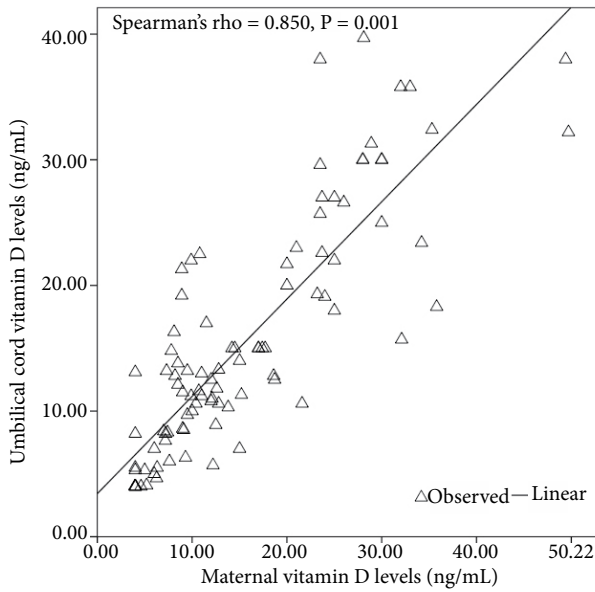
Figure. Correlation of vitamin D levels in mothers and umbilical cord blood of newborns.

4. Discussion

Vitamin D deficiency in mothers and their offspring is still an important health problem in developing countries. The primary source of vitamin D for a newborn baby is the vitamin D that passes transplacentally to the baby from the mother in the intrauterine period (14). In a baby with maternal vitamin D deficiency, findings of vitamin D deficiency (neonatal hypocalcemia and congenital rickets) may appear immediately after birth since the breast milk is also a poor source of vitamin D (15). Therefore, maternal vitamin D levels are important for both the mother and the baby.

Currently, vitamin D intake during pregnancy and breast-feeding has been reported to be insufficient throughout the world. In an Irish study, 14.3%–23.7% and 34.3%–52.6% of pregnant women were found to have vitamin D deficiency and vitamin D insufficiency, respectively (10). Although many reports of vitamin D deficiency in pregnant women have been published to date, it is still a public health problem in Turkey due to the lack of an effective prophylaxis program directed towards pregnant women and breast-feeding mothers. This study aimed to perform a screening of vitamin D levels in 99 mothers and their healthy babies in Ankara, considered to be a developed city in Turkey, to compare the results with prior data and to reemphasize the importance of preventive medicine services in terms of vitamin D prophylaxis in pregnant women.

Although there is no clear consensus on the level of maternal vitamin D deficiency, the International Association of Endocrinology suggests a vitamin D level of 21–29 ng/mL for vitamin D insufficiency and <20 ng/mL as a lower limit for vitamin D deficiency (11). These criteria were used in this study. The incidence of maternal vitamin D deficiency was reported to be between 18% and

Table 3. Demographics of the mothers according to groups.

	Group I (n = 62)	Group II (n = 18)	Group III (n = 19)	P*
Mother's age (years)	28 (19–37)	29.1 (22–42)	29 (23–37)	0.076
BMI (kg/m^2)	28.3 (22.9–38.1)	28.0 (23.1–37.3)	30.0 (23.6–33.9)	0.810
Number of pregnancies	2 (1–7)	2 (2–7)	2 (2–3)	0.545
Number of births	2 (1–7)	2 (1–5)	2 (1–3)	0.572
Period of time between last 2 pregnancies (years)	3.5 (0.5–15)	4.5 (0.5–15)	5 (1–15)	0.718[a]
Multivitamin use (%)	58.1[a,b]	83.3[a]	83.3[b]	0.037

*: Mann–Whitney U Test, [a,b]: chi-square test (P < 0.05), data are given as median (minimum–maximum), BMI: body mass index.

Table 4. Maternal vitamin D levels according to socioeconomic level and educational status.

Variables	Group I (n = 62)	Group II (n = 18)	Group III (n = 19)	P
Mother's educational status				
Uneducated (%)	2 (3.2)	0 (0)	0 (0)	
Primary school (%)	15 (24.2)	5 (27.8)	4 (27.2)	0.111
Middle school (%)	34(54.8)	7 (38.9)	7 (38.9)	
High school (%)	8 (12.9)	3 (16.7)	1 (5.6)	
University (%)	3 (4.8)	3 (16.7)	6 (33.3)	
Skin color				
White (%)	58.1	44.4	52	0.160[a]
Olive (%)	41.9	55.6	46.9	
Dark (%)	0	0	1	
Mother's headscarf status (%)				
Covered (%)	43 (69.4)	9 (50)	8 (44.4)	0.09
Family income level (monthly)				
<500 TL (%)	9 (14.5)	1 (15.6)	1 (5.6)	
500–1000 TL (%)	35 (56.5)	7 (38.9)	5 (27.8)	0.05
1000–1500 TL (%)	12 (19.4)	4 (22.2)	7 (38.9)	
>1500 TL (%)	6 (9.7)	6 (33.3)	5 (27.8)	
Type of family residence				
Apartment (%)	19 (30.6)	5 (27.8)	6 (33.3)	0.937
Slum (%)	43 (69.4)	13 (72.2)	12 (66.7)	

No statistically significant differences were found in the amounts of milk, yogurt, and fish consumed among the groups (P > 0.05). [a]: Chi-square test (P < 0.05).

84% in studies from different countries that accepted a level of 25(OH)D of <10 ng/mL as vitamin D deficiency (16–19). In the study by Andiran et al. performed in 2002 in Ankara, the rate of vitamin D deficiency (<10 ng/mL) was found to be 46% and 80% in mothers and their babies, respectively (20). In another study from Ankara in 2009, vitamin D deficiency was classified as severe and intermediate; cases with a vitamin D level of less than 11 ng/mL were defined as severe and levels between 11 and 25 ng/mL were defined as intermediate vitamin D deficiency (14). Vitamin D deficiency was seen in 81.4% of mothers, with 27% and 54.3% of them having severe and intermediate types of deficiency, respectively; 64.3% of newborns had severe vitamin D deficiency and 32.9% had intermediate vitamin D deficiency, with a total incidence of 97.2% (14). In a study by Pehlivan et al. performed in

Kocaeli in 2003, vitamin D levels were found to be <16 ng/mL in 95% of the mothers and <10 ng/mL in 80% of the mothers (12). In a recent study from İzmir performed on 258 mothers and newborns, the incidence of vitamin D deficiency (≤20 ng/mL) was detected to be 90.3% (21).

In the present study, 62.6% and 18.2% of the pregnant women residing in Ankara in the district of Keçiören (2009–2010) were found to have vitamin D deficiency and vitamin D insufficiency, respectively, while the newborn babies of those mothers were found to have vitamin D deficiency and insufficiency in 58.6% and 15.2% of the cases, respectively. The strong positive correlation between the maternal serum and newborn umbilical cord blood vitamin D levels was compatible with the literature knowledge and suggested that the most important cause of vitamin D deficiency in newborn babies was maternal

vitamin D deficiency. Although 8 years have passed since the study of Andiran et al. in the Ankara region, it is obvious that up to now no change has arisen in the maternal and newborn incidences of vitamin D deficiency. These results suggest that pregnant and breast-feeding women are at risk for vitamin D deficiency and that vitamin D prophylaxis is quite important and necessary in these groups of women. Therefore, it is imperative that the vitamin D supplementation program in our country for pregnant women that was implemented in May 2011 by legislation of the Turkish Ministry of Health be supported.

The strong positive correlation between the vitamin D levels of pregnant women and the level of vitamin D in the umbilical cord blood has been demonstrated in many studies, and the most important indicator of the vitamin D levels of the newborn have been emphasized to be maternal vitamin D levels (20–22). $25(OH)D_3$ transfers to the baby during pregnancy through the placenta and, thus, the vitamin D level of the umbilical cord blood of the baby indicates 80%–100% of the maternal vitamin D level (22). Similarly, Ergür et al. suggested that $25(OH)D_3$ levels in the umbilical cord blood were a good predictor of the vitamin D level in the newborn, and hence it could be a feasible method to use in newborns that are thought to be in the risk group for vitamin D deficiency, as it is a noninvasive test (14). Similarly, the identification of a strong positive correlation between maternal and umbilical cord blood vitamin D levels was found to be compatible with the literature findings.

The administration of vitamin D to pregnant women is quite important for the health of both the mother and the baby when the high prevalence of nutritional rickets in Turkey and the immunomodulation and infection-preventing effects of vitamin D are considered (23). There is no consensus on how long and at what dose vitamin D should be administered to pregnant women. The United States Association of Endocrinology emphasizes that the target vitamin D level should be >30 ng/mL and 1500–2000 IU of vitamin D should be administered daily to reach this target level (11). In a randomized, double-blind study, pregnant women were divided into 3 groups and were given vitamin D in 3 different doses (400 IU, 2000 IU, and 4000 IU daily) to be started in the 12th–16th weeks of pregnancy and to be used until delivery. As a result of that study, vitamin D at a dose of 4000 IU was found to be safe and to provide the required vitamin D levels, and hence the recommendation of previous groups was found to be inadequate (24). In Turkey, although the Ministry of Health recommends vitamin D at a dose of 1200 IU/day for pregnant women to be taken in the last trimester, it has been demonstrated by many studies that this recommendation was not implemented in the majority of pregnancies (21). Prenatal vitamin D administration is limited to 200 IU/

day, which is generally included in multivitamins; however, even 400 IU/day is not sufficient to provide an adequate serum level of $25(OH)D_3$ during pregnancy and lactation (24–26). Due to the lack of a national health policy on vitamin D prophylaxis, the previous level was limited to 200–400 IU/day, which was included in the multivitamin preparations until recently, when the Turkish Ministry of Health provided updated recommendations in 2011. In this study, it was accepted that the daily intake of vitamin D was limited to 200–400 IU in patients that were taking multivitamin supplements. In addition, the development of deficiency in spite of multivitamin use in 58.1% of pregnant women who had vitamin D deficiency (group I) demonstrated that the replacement dose was inadequate and suggested that higher doses of vitamin D prophylaxis should be administered to pregnant women.

In this study, mothers with vitamin D deficiency were found to have a low income and education levels, though not statistically significant, and they were found to be more veiled and had a higher rate of living in a slum. Pehlivan et al. reported the risk factors for maternal vitamin D deficiency as low socioeconomic status, inadequate intake of vitamin D in the diet, and a covered style of dress (12), while Andiran et al. similarly reported that low socioeconomic status, a covered style of dress, and a lower level of education were the risk factors for maternal vitamin D deficiency (20). Halicioglu et al., on the other hand, found statistically significant associations between a covered style of dress, daily consumption of milk and milk products, and multivitamin use in pregnancy and maternal vitamin D levels (27). In previous studies, insufficient exposure to sunlight during the winter months has been reported to be an important factor contributing to maternal vitamin D deficiency (10,14). Therefore, the high rate of maternal vitamin D deficiency in our study could also be related to time of blood sampling, which was done during the winter months.

Vitamin D levels were reported to be statistically significantly lower in the newborns of mothers who were obese during pregnancy and in children with a high obesity index in the neonatal period (27). In the present study, no statistically significant differences were found between vitamin D levels and the age of the mother, BMI, mean number of pregnancies, number of births, duration between the last 2 pregnancies, and rate of olive skin color in mothers among the different groups (groups I, II, and III). Similarly, Andiran et al. found no relation between vitamin D levels and BMI (20).

Hypocalcemia in a newborn is the most important and earliest sign of maternal vitamin D deficiency. Vitamin D deficiency may result in neonatal hypocalcemia, especially if it caused secondary hyperparathyroidism and osteomalacia in the mother (28). It has been suggested that

even in intermediate and severe vitamin D deficiencies, the expected PTH increase may not occur, and the clinical and laboratory findings of vitamin D deficiency are related not only with the severity of the deficiency but also with the duration of it (29). In this study, increased PTH was identified in 6 mothers (9.5%) and in 1 mother (5.8%) among vitamin D deficient and insufficient mothers, respectively, and it was not observed in any of the babies. One of the reasons for the absence of any symptomatic cases in spite of the high prevalence of vitamin D deficiency in mothers and their newborn babies might be due to the short duration of the deficiency.

In conclusion, vitamin D deficiency, which was found at high rates in mothers and their babies in this study, impacts the health of both the mothers and babies in the short and long terms and it continues to be a frequently seen public health problem. The results of this study are important in demonstrating the necessity of vitamin D prophylaxis in pregnant women. Therefore, we suggest that physicians inform all pregnant women about the importance of maintaining adequate vitamin D stores during pregnancy and breastfeeding and implement vitamin D prophylaxis programs for risk groups for the health of both mothers and infants.

References

1. Ahmed I, Atiq M, Iqbal J, Khurshid M, Whittaker P. Vitamin D deficiency rickets in breast-fed infants presenting with hypocalcaemic seizures. Acta Paediatr 1995; 84: 941–942.

2. Camadoo L, Tibbott R, Isaza F. Maternal vitamin D deficiency associated with neonatal hypocalcaemic convulsions. Nutr J 2007; 6: 23.

3. Wei SQ, Audibert F, Hidiroglou N, Sarafin K, Julien P, Wu Y, Luo ZC, Fraser WD. Longitudinal vitamin D status in pregnancy and the risk of pre-eclampsia. BJOG 2012; 119: 832–839.

4. Wei SQ, Qi HP, Luo ZC, Fraser WD. Maternal vitamin D status and adverse pregnancy outcomes: a systematic review and meta-analysis. J Matern Fetal Neonatal Med 2013: 26; 889–899.

5. Zhang C, Qiu C, Hu FB, David RM, van Dam RM, Bralley A, Williams MA. Maternal plasma 25-hydroxyvitamin D concentrations and the risk for gestational diabetes mellitus. PLoS One 2008; 3: e3753.

6. Litonjua AA, Weiss ST. Is vitamin D deficiency to blame for the asthma epidemic? J Allergy Clin Immunol 2007; 120: 1031–1035.

7. Morales E, Guxens M, Llop S, Rodriguez-Bernal CL, Tardon A, Riaño I, Ibarluzea J, Lertxundi N, Espada M, Rodriguez A et al. Circulating 25-hydroxyvitamin D3 in pregnancy and infant neuropsychological development. Pediatrics 2012; 130: e913–e920.

8. Gale CR, Robinson SM, Harvey NC, Javaid MK, Jiang B, Martyn CN, Godfrey KM, Cooper C; Princess Anne Hospital Study Group. Maternal vitamin D status during pregnancy and child outcomes. Eur J Clin Nutr 2008; 62: 68–77.

9. Orbak Z, Karacan M, Doneray H, Karakelleoglu C. Congenital rickets presenting with hypocalcaemic seizures. West Indian Med J 2007; 56: 364–367.

10. O'Riordan MN, Kiely M, Higgins JR, Cashman KD. Prevalence of suboptimal vitamin D status during pregnancy. Ir Med J 2008; 101: 242–243.

11. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH, Weaver CM. Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2011; 96: 1911–1930.

12. Pehlivan İ, Hatun Ş, Aydoğan M, Babaoğlu K, Gökalp AS. Maternal vitamin D deficiency and vitamin D supplementation in healthy infants. Turk J Pediatr 2003; 45: 315–320.

13. Misra M, Pacaud D, Petryk A, Collett-Solberg PF, Kappy M. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. Pediatrics 2008; 122: 398–417.

14. Ergür AT, Berberoğlu M, Atasay B, Şıklar Z, Bilir P, Arsan S, Söylemez F, Öcal G. Vitamin D deficiency in Turkish mothers and their neonates and in women of reproductive age. J Clin Res Pediatr Endocrinol 2009; 1: 266–269.

15. Kovacs CS. Maternal vitamin D deficiency: fetal and neonatal implications. Semin Fetal Neonatal Med 2013; doi: 10.1016/j.siny.2013.01.005 (Epub ahead of print).

16. Bassir M, Laborie S, Lapillonne A, Claris O, Chappuis MC, Salle BL. Vitamin D deficiency in Iranian mothers and their neonates: a pilot study. Acta Paediatr 2001; 90: 577–579.

17. Dawodu A, Wagner CL. Mother-child vitamin D deficiency: an international perspective. Arch Dis Child 2007; 92: 737–740.

18. Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. Am J Clin Nutr 2005; 81: 1060–1064.

19. van der Meer IM, Karamali NS, Boeke AJ, Lips P, Middelkoop BJ, Verhoeven I, Wuister JD. High prevalence of vitamin D deficiency in pregnant non-Western women in The Hague, Netherlands. Am J Clin Nutr 2006; 84: 350–353.

20. Andiran N, Yordam N, Ozon A. Risk factors for vitamin D deficiency in breast-fed newborns and their mothers. Nutrition 2002; 18: 47–50.

21. Halicioglu O, Aksit S, Koc F, Akman SA, Albudak E, Yaprak I, Coker I, Colak A, Ozturk C, Gulec ES. Vitamin D deficiency in pregnant women and their neonates in spring time in western Turkey. Paediatr Perinat Epidemiol 2012; 26: 53–60.

22. Thandrayen K, Pettifor JM. Maternal vitamin D status: implications for the development of infantile nutritional rickets. Endocrinol Metab Clin North Am 2010; 39: 303–320.

23. Hewison M. Antibacterial effects of vitamin D. Nat Rev Endocrinol 2011; 7: 337–345.

24. Hollis BW, Johnson D, Hulsey TC, Ebeling M, Wagner CL. Vitamin D supplementation during pregnancy: double-blind, randomized clinical trial of safety and effectiveness. J Bone Miner Res 2011; 26: 2341–2357.

25. Abrams SA. In utero physiology: role in nutrient delivery and fetal development for calcium, phosphorus, and vitamin D. Am J Clin Nutr 2007; 85: 604S–607S.

26. McCullough ML. Vitamin D deficiency in pregnancy: bringing the issues to light. J Nutr 2007; 137: 305–306.

27. Josefson JL, Feinglass J, Rademaker AW, Metzger BE, Zeiss DM, Price HE, Langman CB. Maternal obesity and vitamin D sufficiency are associated with cord blood vitamin D insufficiency. J Clin Endocrinol Metab 2013; 98: 114–119.

28. Specker BL. Does vitamin D during pregnancy impact offspring growth and bone? Proc Nutr Soc 2012; 71: 38–45.

29. Cianferotti L, Marcocci C. Subclinical vitamin D deficiency. Best Pract Res Clin Endocrinol Metab 2012; 26: 523–537.