Vitamin D deficiency in Mexican mothers and their newborns

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Abstract

Objective: *The purpose of this study is to establish the prevalence of vitamin D deficiency and their newborns and analyze the risk factors related to this deficiency.* **Methods:** *This is an observational, transversal, and prospective study. It included 191 puerperal women and their full-term newborns. Serum 25 hydroxyvitamin D values were analyzes by enzyme immunoassay.* **Results:** *61% of the puerperal presented deficiency and 26% insufficiency of vitamin D. In the newborn group 98% showed deficiency and 66% of them presented severe deficiency. There is a positive correlation between the values of vitamin D in mothers and their newborns (r2 = 0.173 ng/ml; p = 0.017). The lowest levels were in autumn. (15.75 ng/mL mothers, 6 ng/mL newborns). There was no correlation between vitamin D levels in mothers and their dietary intake, maternal skin type, sun time exposure and prenatal body mass index.* **Conclusions:** *This is the first study that shows the existence of a high deficiency of vitamin D in Mexican mothers and their newborns.*

KEY WORDS: *Vitamin D deficiency. Newborns. Pregnancy. Vitamin D.*

Introduction

Vitamin D deficiency is considered a public health problem world-wide. The relevance of this condition lies in that, in addition to its classical function in bone homeostasis, vitamin D also intervenes in different biological processes that are important for growth and development both in prenatal and postnatal life[1-4]. There are risk factors that have been associated with this deficiency, such as residing in northern latitudes, limited sun exposure, regular use of sun blockers, dark skin, obesity and malabsorption syndromes[1]. In pregnancy, vitamin D deficiency is associated with complications such as preeclampsia; in neonates, with low weight and hypocalcemia, as well as poor postnatal growth, bone fragility and increased incidence of autoimmune conditions[1,3,4].

There are reports on vitamin D deficiency in mothers and their newborns in different populations, which is quite variable, even in the same country. In the USA, Mulligan et al.[1] report a prevalence of this deficiency of 5-50% in mothers and 54% in neonates; in turn, Johnson et al.[5] mention that 30% of Hispanic pregnant women had vitamin D deficiency. In India, Jain et al.[6] found vitamin D deficiency in 81% of women at pregnancy and in 66.7% of neonates. On the other hand, in countries such as Greece, Belgium and the Netherlands, 10-30% of women have vitamin D deficiency at pregnancy[1,5].

Owing to the risk for developing both maternal and fetal problems in the face of a condition of vitamin D deficiency, several countries have implemented supplementation programs during pregnancy and the neonatal period[7-9]. To date, there are no reports in

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Date of reception: 17-01-2017
Date of acceptance: 28-04-2017
DOI://dx.doi.org/10.24875/GMM.M18000043

Gac Med Mex. 2017;153:508-514
Contents available at PubMed
www.gacetamedicademexico.com

Mexico about 25-hydroxy-vitamin D (25OHD) serum concentrations in neonates and their mothers that might lend support to a supplementation policy. The purpose of this investigation is to find out vitamin D values in this population and correlate them with different risk factors that can drive to its deficit.

Methods

A cross-sectional, prospective observational study was carried out in puerperal women and their neonates at the Hospital Universitario Dr. José Eleuterio González of Monterrey, NL, Mexico. The study population is resident of Monterrey, a city located at 25° 40' 11"N latitude, within the period of May 20, 2013 to September 30, 2014. The protocol was authorized by the institution's Research and Ethics Committees (PE13-013). The minors' informed consent was signed by both parents.

The inclusion criteria were: Mexican mothers, of any age, with full-term pregnancy; and full-term (37-41 weeks of gestation) and healthy (no complications at birth) neonates. Exclusion criteria were multiple gestation and neonates with major malformations. Censoring criteria were incomplete data or insufficient sample of the mother-child dyad.

In addition to a complete and documented history obtained fom the medical record, all mothers were applied a questionnaire to obtain anthropometric data (prenatal weight and weight at admission for delivery), use of medications and comorbidities. A questionnaire was applied on frequency of vitamin D-containing foods[10] and consumption of vitamin D supplements, cholecalciferol and ergocalciferol (daily and weekly).

Maternal skin color was evaluated by classifying the phototype according to Fitzpatrick[11], as well as the time of sun exposure in minutes/day.

The date of birth registry was obtained in the neonates in order to determine the season of the year prevailing at the moment of birth, taking into account the following: spring, from March to May, summer, from June to August, autumn, from September to November, and winter, from December to February; gestational age, which was established using Capurro's method; 1- and 5-minute Apgar; weight in grams; height and head circumference, which was carried out using a measuring rod (SECA 210, Germany), a measuring tape (SECA 201, Germany) and a digital scale (SECA 354, Germany). Anthropometric variables were analyzed with the z-score and percentiles by means of the Fenton chart.

For vitamin D3 quantification, 5-7 ml of peripheral venous blood were obtained from the mothers' antecubital region within a period of 24 to 48 hours after the obstetric event. In the newborns, a 1-2 ml capillary blood sample was obtained by puncture (at the moment of the metabolic neonatal screen) at 24-48 hours of extrauterine life. Once the samples were collected, the serum was centrifuged for 20 minutes and stored in aliquots at -20 °C. All samples were processed at the same time by the enzyme-linked immunosorbent assay (ELISA) method, using a Cobas 6000 Hitachi equipment (Roche, Switzerland). For that purpose, the vitamin D3 ELISA kit Test CEA920Ge 96 (Cloud-Clone Corp.©, Houston, Tx, USA), the detection range of which is 4.94-400 ng/mL, was used following the provider's specifications. This instrument has a minimum measuring sensitivity of 2.15 ng/mL, high specificity for vitamin D3 detection and an intra-assay precision CV < 10% and inter-assay precision CV < 12%.

25OHD serum concentrations for the mother-child dyad were divided using the Society of Clinical Endocrinology[12] classification, with normal being between 30 and 100 ng/mL, insufficiency with a range of 20 to 29 ng/mL, deficiency between 12 and 19 nh/mL and serious deficiency < 11 ng/mL.

For statistical analysis, the SPSS 20 pack (IBM, Armonk, NY, USA) was used, with central tendency and dispersion measures being obtained. A p-value < 0.05 was considered to be statistically significant, and Student's t-test was used for independent samples. The Kolmogorov-Smirnov test was used to confirm normal distribution, and the chi-square test was used for categorical variables.

In addition, a univariate Pearson linear correlation test was made between maternal and neonatal vitamin D values and the neonatal weight variable. Finally, a linear regression multivariate model was used, with 25OHD maternal values as dependent variable and vitamin D consumption in the maternal diet, skin phototype, time of sun exposure and body mass index (BMI) at the start of gestation as covariates.

Results

A total of 194 mother-child dyads were recruited, out of which three were excluded due to insufficient neonate blood sample, with a total of 191 dyads being left.

Of the mothers, 64% were adults and 36% were adolescents; most were homemakers, had basic

Table 1. Mothers' demographic variables and somatometry, where weight recorded at admission was taken into account for end-of-gestation BMI

	Total (n = 191) (%)
Age	
Adolescents (≤ 19 years)	69 (36)
Adults (≥ 20 years)	122 (64)
Occupation	
Homemaker	169 (88)
Student	9 (5)
Employee	13 (7)
Marital status	
Single	32 (17)
Married	48 (25)
Cohabitating	104 (55)
Divorced	2 (1)
Education	
Illiterate	2 (1)
Primary school	34 (18)
Secondary school	87 (46)
High school	61 (32)
College degree	4 (2)
Weight at pregnancy initiation (kg)	60,39 ± 13,44
Prenatal BMI	24,31 ± 5,08
Normal (< 25)	122 (64)
Overweight (25-29.99)	40 (21)
Obesity (> 30)	29 (15)
Weight at pregnancy conclusion (kg)	72,84 ± 13,87
BMI at pregnancy conclusion	29,35 ± 5,34
Normal (< 25)	42 (22)
Overweight (25-29.99)	76 (40)
Obesity (> 30)	73 (38)
Previous gestations	74 (39)
0	59 (31)
1	33 (17)
2	25 (13)
3+	

BMI: body mass index

education and a stable partner. When maternal anthropometric variables were measured, one third of participants were observed to have initiated pregnancy with overweight or obesity, and at the end of it, this figure increased to 78% (Table 1). In turn, neonatal anthropometric measures were within normal percentiles (Table 2).

Mean 25OHG was 19.74 ± 10.21 ng/mL in the mothers and 9.42 ± 3.53 ng/mL in the neonates. This reveals that only 13% of mothers had normal values (> 32 ng/mL), whereas 26% showed insufficiency (20-31 ng/mL) and 61% had deficiency (< 20 ng/mL). More relevant yet is the fact that all neonates had abnormally low 25OHD values: 2% had insufficiency and

Table 2. Neonatal variables

	Total (n = 191) (%)
Type of delivery	
Vaginal delivery	113 (59)
Cesarean section	78 (41)
Gender	
Male	95 (49)
Female	96 (51)
Apgar	Mean (SD)
1-minute	8 (± 0,60)
5-minute	9 (± 0,80)
Gestational age	39,1 (± 1,19)
Weight (g)	3254,71 (± 411,32)
Z-score	–0,15 (± 0,85)
Height (cm)	50,33 (± 1,81)
Head circumference (cm)	34,30 (± 1,50)

SD: standard deviation

98% had deficiency. Of the latter, 66% had severe deficiency, defined by values < 11 ng/mL.

On the other hand, there is a weak positive correlation between 25OHD values of the mother and neonates 25OHD serum concentrations (r^2 = 0.173; p = 0.017). In addition, maternal 25OHD serum concentrations predict neonatal 25OHD values (r^2 = 0.030; p = 0.017).

Following the previously-used classification, where the sample was divided into groups of adolescent mothers and adult mothers, no statistically significant differences were found in 25OHD serum values between both groups, as well as neither were found in the neonates (Table 3).

Mothers' daily average time of sun exposure during pregnancy was 85 ± 91.06 minutes (range: 5-600). Vitamin D daily consumption through the diet was 172 ± 76.31 IU on average (range: 14-341). Only 52 mothers (27.22%) received vitamin D supplementation, with a mean of 291 ± 76.44 IU/day (range: 171-500) (Table 4); however, no differences were found between the mothers who consumed supplements and those who didn't.

The predominant maternal skin phototype was 3 (40.31%), followed by phototypes 4, 5 and 2. There were no phototypes 1 and 6. When 25OHD means were compared according to the phototype, no statistically significant difference was found (p = 0.62).

Figure 1 shows mothers and newborns mean 25OHD serum values by season of the year at the

Table 3. Comparison of maternal and neonatal serum 25-hydroxyvitamin D according to maternal age

Classification	Total (n = 191) (%)	Adolescent mothers (n = 69) (%)	Adult mothers (n = 122) (%)	p
Maternal				
Normal (32-100 ng/mL)	26 (13)	9 (13)	17 (14)	0.98
Insufficiency (20-31 ng/mL)	49 (26)	18 (26)	31 (25)	
Deficiency (12-19 ng/mL)	95 (50)	35 (51)	60 (49)	
Severe deficiency(< 11 ng/mL)	21 (11)	7 (10)	14 (12)	
Neonatal				
Normal (32-100 ng/mL)	0	0	0	0.3
Insufficiency (20-31 ng/mL)	3 (2)	1 (1)	2 (2)	
Deficiency (12-19 ng/mL)	62 (32)	23 (33)	39 (32)	
Severe deficiency (< 11 ng/mL)	126 (66)	45 (65)	81 (66)	

Table 4. Dietary and supplementary vitamin D consumption

Oral consumption	Total n = 191	Mean ± SD	Range
Diet (IU/day)	191	172 ± 76,31	14-341
Supplement (IU/day)	52	291 ± 76,44	171-500
Diet+supplement (IU/day)	52	462 ± 105,49	239-676

SD: standard deviation.

moment of birth. The lowest values were found in autumn.

In the multivariate correlation, no association was found of maternal 25OHD values with vitamin D dietary consumption (r^2 = -0.10; p = 0.79) or with maternal skin phototype (r^2 = -0.019; p = 0.79), time of sun exposure (r^2 = -0.44; p = 0.54), BMI at the end of pregnancy (r^2 = -0.124; p = 0.08) or season of year (r^2 = 0.033; p = 0.65).

Discussion

Vitamin D is the main hormone in phosphocalcic metabolism regulation. Its deficiency is a health problem all over the world[1-3,7,13] and there are diseases at pediatric age that involve alterations in vitamin D metabolism, such as rickets, chronic renal failure, allergic conditions, cancer, pathologies associated with fat malabsorption (cystic fibrosis, celiac disease), obesity and overweight[7,12,14]. Currently, populations with high deficiency of this vitamin have been described in all continents, including Spanish-speaking countries such as Spain and Argentina[15,16].

Specifically in newborns, the vitamin D reserve depends on maternal transference via the placenta. After birth, this supply depends on the newborn's own production and exogenous supply[1]. In pregnancy, vitamin D deficiency is associated with severe preeclampsia and in the neonate with hypocalcemia, rickets (especially in premature children)[14] and low weight for gestational age[1]. Vitamin D optimal values during pregnancy and at neonatal stage still remain controversial. There are the Institute of Medicine and the Society of Clinical Endocrinology classifications[12], with the latter being the one that was used in the present work, which establishes normality values ranging from 32 to 100 ng/mL, insufficiency ranging from 20 to 31 ng/mL, deficiency ranging from 12 to 19 ng/mL and severe deficiency at < 11 ng/mL. This classification is currently the most widely used and it has shown that insufficiency values are associated with extra-skeletal alterations.

This report revealed that 61% of mothers and 98% of neonates had values indicating 25OHD deficiency. These results are consistent with international investigations that confirm that vitamin D deficiency is highly prevalent among pregnant women and their newborns[16-20]. On the other hand, there was a weakly positive correlation observed between maternal and neonatal 25OHD values (r^2 = 0.173; p = 0.017). This correlation was similar to that reported by Abbasian et al.[13] for maternal serum and umbilical cord 25OHD values in an Iranian population (r^2 = 0.12; p = 0.053).

In our country, there are reports with regard to vitamin D blood values in different age groups. In the National Health Survey[21], 9.8% of adults were reported to have 25OHD deficiency, 20% had insufficiency, and approximately 70% had sufficiency, whereas Elizondo et al.[22] analyzed 6-12-year obese pediatric patients from the same region of our study, and found that they had deficiency at a similar proportion to that found in mothers in the present work. No reports analyzing vitamin D values in the mother-child dyad were found, in addition to this being the first study in Mexican newborns.

In the present investigation, no differences were found between adolescent mothers and adult mothers blood values. This differs from reports in the literature

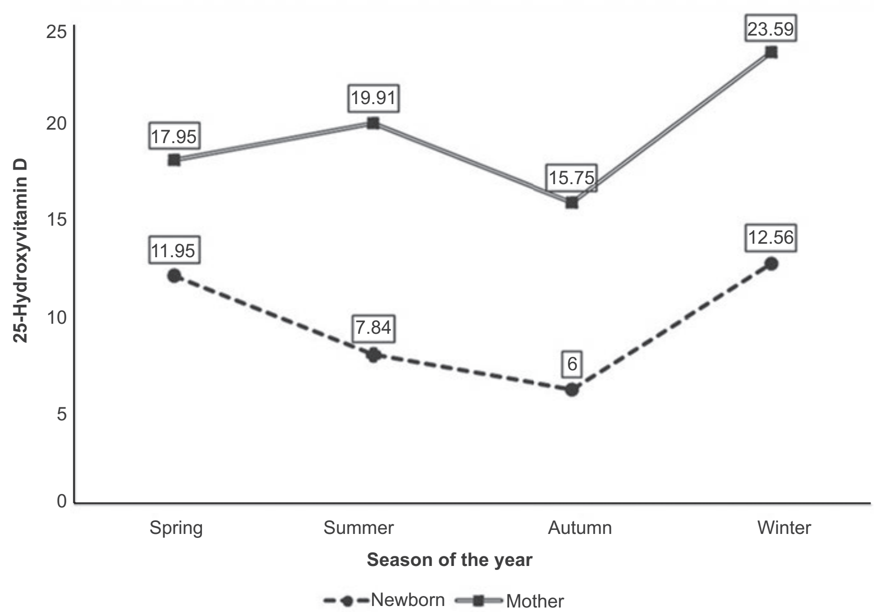

Figure 1. *25-hydroxyvitamin D average values in mothers and newborns according to the season of the year. Seasonal variability is evidenced, with the lowest values being found in autumn.*

on other population groups, where adolescent mothers have higher bone mass loss since the beginning of pregnancy until the sixth week postpartum, indicating that the prevalence of vitamin D deficiency in them is higher[13,23-25].

Our study documented that one third of the mothers had overweight or obesity at the beginning of pregnancy, which was significantly increased at its conclusion. Although no correlation was found between maternal BMI at the end of pregnancy and 25OHD values, vitamin D deficiency has been reported to likely be associated with obesity, and two mechanisms have therefore been proposed: 1) excessive body fat sequesters circulating vitamin D, 2) vitamin D deficiency increases fat accumulation in the body[26-29], 3) the overweight/obesity and insulin resistance association[29]. Elizondo et al.[22] demonstrated that there was higher prevalence of 25OHD deficiency in a group of obese subjects in comparison with a control group of non-obese subjects, but no significant correlation was found between 25OHD levels and maternal BMI at the end of pregnancy in their study. One weakness of the present study is that 25OHD values were not analyzed at the beginning of pregnancy, and their correlation with BMI at the beginning of pregnancy could therefore not be analyzed.

It is important for the skin phototype to be considered, since the concentration of melanin regulates the amount of UVB radiation that penetrates until reaching epidermal layers with maximum 7-dehydrocholesterol concentration[30,31]. Skin phototype, defined as the sun adaptation capability each person has, is classified in six categories according to Fitzpatrick, which range from phototype 1, corresponding to individuals with white skin and red hair, to phototype 6 for people with dark skin and black hair[11,32].

The predominating maternal skin phototype was 3. When the means were compared by phototype, no statistically significant difference was observed. These results are different to reports in the international literature, where vitamin D values are claimed to be inversely associated with the maternal skin phototype, in such a way that the higher it is, the higner the risk for avitaminosis can be[11,32-34].

Another aspect to be highlighted is that, in spite of the fact that the latitude the city of Monterrey is located in (25° 40’ 11” N) has abundant solar radiation, no statistically significant difference was detected in the comparison of 25OHD mean values by time solar of exposure, although we did find a highly important variation between participants. These findings are consistent with those in other populations with high solar exposure, at latitudes that are similar to ours. Such is the case of the Mediterranean region, India and Tunisia[6,35,36].

When the 25OHD values and the season of the year at the moment of the obstetric event were analyzed, no correlation was found; furthermore, the lowest values were in autumn, which is different to observations reported in the literature, where vitamin D lowest values occur in the winter season and early spring[6,33]. A hypothesis would be that the geographic region where the study took place, although with a predominantly dry and semi-dry climate, has a mean yearly precipitation of 650 mm, and rains occur in the months of August and September[37]; therefore, solar exposure is decreased in these months, and since vitamin D synthesis develops in approximately 3 weeks, this might explain the detection of the lowest 25OHD values at the beginning of this season of the year.

The main vitamin D exogenous input is provided by ergocalciferol (D_2) through the diet and cholecalciferol (D_3)[38]. Dietary vitamin D daily consumption was considered in the study participants. It was low, similar to what Ortigosa et al.[39] reported in a sample that included South American women living in Barcelona, Spain. This result may be secondary to the fact that they are native to South America and they continue with alimentary habits and costumes that are similar to those of their place of origin.

Finally, it was demonstrated that only 27% of mothers consumed vitamin D supplements during gestation. This was at doses ranging from 171 to 500 IU/day, which are much lower amounts than those internationally recommended of 600-4000 IU/day[40]. This is due to the fact that in Mexico there is no policy for vitamin D supplementation during pregnancy and, therefore, the amount of it multivitamin supplements prescribed during pregnancy should contain is not regulated. In Mexico, vitamin D deficiency is regarded as a rare pathology[14], especially owing to the lack of scientific evidence, since there are very few prevalence studies and, currently, none has included both puerperal women and their newborns. The results obtained in the present investigation document that there is a high prevalence of vitamin D deficiency at birth, although immediate complications in newborns could not be evinced. However, this does not exclude the possibility of long-term hypovitaminosis D-related complications. Maternal milk has been shown to contain very low amounts of vitamin D (25-78 IU/L), and an exclusively breastfed infant has a higher predisposition to have vitamin D deficiency[41]. Therefore, it is suggested that vitamin D deficiency should be considered a public health problem and that supplementation actions should be carried out, both at pregnancy and neonatal stage, by increasing the doses recommended by the Mexican Official Standard NOM-051-SCFI/SSA1-2010, which suggests a daily intake of 224 IU, based on recommendations of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán[14].

Performing prospective studies in Mexico is recommended, using different supplementation doses between 400 and 1000 IU/day in neonates and infants, including the different types of nutrition as variables, in order to establish an optimal dose in this population group.

Conclusions

There is a high prevalence of vitamin D deficiency in mothers and their newborns, regardless of factors such as maternal age, weight, time of solar exposure, latitude of place of residence, season of the year and skin phototype.

For future investigations, carrying out a larger population-based study, analyzing vitamin D-receptor gene most common polymorphisms and using different vitamin D supplementation schemes would be convenient.

Financial resources

This study was carried out with Universidad Autónoma de Nuevo León Hospital Universitario Dr. José Eleuterio González Pediatrics and Endocrinology Departments own resources. The authors declare there are no external financing sources to declare.

Acknowledgements

To Laura Jaqueline Cortés Gallardo, BSc in Clinical Biochemistry, Gloria Alejandra Jasso de la Peña, MBA, Brenda Leticia Méndez Guerrero, MD, and Neri Alejandro Álvarez Villalobos, MD, for their valuable collaboration.

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