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Original article

Correlation Between Maternal-Neonatal Vitamin D Status and it's Related to Supplementation in Mongolian Pregnant Women

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Abstract

Background: Vitamin D deficiency and insufficient in pregnancy can lead to fetal deficiency that may affect chronic disease susceptibility childhood and adulthood. The aim of this study is to investigate the correlation between maternal and neonatal Vitamin D levels at birth and to identify other risk factors among pregnant women in Mongolia. **Methods:** Hospital-based study was conducted on 528 participants which included 264 mothers and 264 neonates. Pre-delivery maternal blood and neonatal cord blood samples were collected after birth. 25(OH)D concentration was analyzed in relation to neonatal Vitamin D status, maternal and neonatal characteristics, and maternal Vitamin D intake. **Results:** The majority of Vitamin D levels in both maternal (76.5%) and neonatal cord (90.5%) blood were in the deficiency range. Only 3.8% of mothers and 1.5% of neonates had levels in the sufficient range at the time of delivery. For maternal demographic factors, total income was significantly different between the groups (P=0.000). The maternal outcomes were no significant associations were found between groups, but neonatal outcomes were associated with maternal Vitamin D status. In terms of Vitamin D supplementation, 27% of women were taken during pregnancy. Of the not supplemented women, 80% were Vitamin D deficient. **Conclusions:** A high proportion of Vitamin D deficiency was found in both mothers and newborns in our study. There is a strong correlation between the amount of Vitamin D in the mother and in the newborn. A mother's Vitamin D intake is related to Vitamin D levels in the mother's blood.

Keywords: ***Vitamin D deficiency, low-income, umbilical cord, newborn measurements, Apgar score.***

Introduction

During pregnancy, a woman maintains her Vitamin D requirements to support her health and also needs the extra amount to support her fetus [1]. Vitamin D requirements during pregnancy must be met through dietary intake, supplements, and sun exposure [2]. Women who are pregnant at high-latitude locations or during winter are at increased risk of Vitamin D deficiency. Heckmatt et al supplemented 44 Asian mothers with 1000 IU Vitamin D daily 1-3 months before delivery and found that this significantly increased the plasma 25-hydrooxyvitamin D concentrations at delivery [3]. Iran, 80% of the mothers had 25(OH)D concentrations of less than 25 nmol/L (10 ng/mL), the mean cord serum 25(OH)D concentrations were very low (4.94±9.4 nmol/L) [4]. Meanwhile, in Saudi Arabia, the median concentrations of pregnant women 25(OH)D was 5-7 ng/mL, which has a highly significant correlation between maternal and cord blood [5]. These results demonstrate that even in Mediterranean climates hypovitaminosis in pregnant women is prevalent and neonatal serum vitamin levels are low. Vitamin D status of infants in the first months after birth then it would follow that low Vitamin D status in pregnant women would result in early Vitamin D deficiency of their newborn children. In addition, Vitamin D deficiency affects both the fetus and the mother since the fetus' nutrition is highly dependent on the mother [6].

Since Mongolia is a large, north Asian country at latitudes 42o-50o N, daytime in winter temperatures -20o-50oC are a significant disincentive to exposure of skin to light [7]. There is a high prevalence of Vitamin D deficiency in women of reproductive age [8,9], pregnant women [10] and children [11], hence a study to determine the level of Vitamin D in pregnant women before delivery and umbilical cord blood in neonatal, had not been performed until now. Therefore, this study aims to assess the correlation between maternal and neonatal Vitamin D levels at birth and identify other factors of Vitamin D deficient levels. The novelty of the study was to evaluate Vitamin D levels based on umbilical cord blood samples for the first time in Mongolia.

Materials and Methods

The study was conducted through a hospital-based study model and random sampling, involving 264 mothers at the Urguu Maternity

Hospital in Ulaanbaatar city along with their newborns. This hospital handles 12 000 deliveries each year, which would account for most of the childbirths in the city. The study was undertaken in the summer of 2019 (between July 1 and August 31) and 1860 mothers gave birth during this period. We excluded preterm and late-term births, multiple gestations, and infants with fetal anomalies. A questionnaire consisting of five groups with 64 questions, was taken from mothers who agreed to participate in the study. Written informed consent was obtained and conducted to determine the association between maternal-neonatal outcomes and Vitamin D status. Factors leading to Vitamin D deficiency have been identified.

Maternal and neonatal pairs (n=528) were randomly sampled. Samples were collected from the veins of the pregnant woman during follow-up in the delivery room before giving birth, and from the umbilical cord blood after the umbilical cord clamping. Samples were then transported on ice to the laboratory for measurement. Serum was stored at -70oC until they were analyzed for 25(OH)D. The concentration of 25(OH)D was measured via electrochemiluminescence immunoassay (VIDAS 25-OH Vitamin D Total Assay, Biomerieux, France). The measuring range is broad 8.1-126 ng/mL with excellent linearity. Twenty-three (8.7%) mothers with the values were below 8.1 ng/mL, neonates were 29 (10.9%) with lower limits of detection. Based on the criteria of the Medicine and Endocrine Society, Vitamin D levels were classified as deficient ≤20 ng/ml, insufficient 21-29, sufficient ≥30 ng/ml [12,13] and excess >100 ng/ml [14].

Maternal demographic characteristics included mother's age, education,[15] marital status, working condition, total income, and household type. Maternal health and obstetric outcomes included chronic illness, allergy, back pain, muscle pain, BMI (Body Mass Index) before pregnancy, pre-eclampsia (pre-eclampsia is defined as high blood pressure, excess protein in the urine after 20 weeks of pregnancy in a woman who previously had normal blood pressure) and C-section delivery. Some factors (sun exposure, diet, multivitamin, and Vitamin D supplementation intake) were identified by questionnaires at the base of the study. Neonatal outcomes were recorded such as birth weight, height, head circumference, Apgar score, and birth asphyxia.

Statistical analysis

Data analyses were performed using IBM SPSS V25.0 software (SPSS Inc., Chicago, IL). Values are presented as means±SD or mean (95% confidence interval CI) for variables with normal distribution. Grouping variables for materrnal Vitamin D levels at birth were calculated using Pearson's Chi-square test with general information (**Table 1**). Comparisons of normally distributed value among more than two groups were performed with one-way analysis of variance test (**Table 2**). Multivariate linear regression analysis was used to assess the association between maternal Vitamin D level and related factors. The correlation between maternal serum 25(OH)D at birth and neonatal umbilical cord 25(OH)D was calculated using Pearson's correlation coefficient (**Figure 2**). All p-values less than 0.05 were defined as statistically significant.

Results

In total, 264 mother-neonate pairs participated, and 528 blood samples were collected in this study. Most participants were between 30 and 34 years old (mean±SD 30.21±5.95) and the youngest mother was 15 years old and the oldest one was 43 years old. The demographic of participants and the distribution of Vitamin D levels are in Table 1. Maternal Vitamin D levels varied with age, educational level, marital status, working condition, total income, and household types. For maternal demographic factors, total income was significantly different between the groups (p=0.000). Figure 1 shows the distribution of maternal and cord blood Vitamin D levels. The overall range of maternal 25(OH)D was 8.1-41.8 ng/mL (mean±SD: 16.53 ± 6.5 ng/mL) and the neonatal 25(OH)D was 8.1-35.5 ng/mL (mean±SD: 14.25 ± 5.3). Twenty-three (8.7%) mothers of the values were below to 8.1 ng/mL while, 29 neonates (10.9%) were regarded within the lower limits of detection. Out of the 264 respondents, 202 of them (76.5%) have Vitamin D deficiency, while 52 (19.7%) were insufficiency, and 10 (3.8%) have sufficient 25(OH)D levels. The results for neonatal Vitamin D deficiency are as follows: there were 239 (90.5%) deficient neonates, insufficient neonates numbered 21 (8.0%), and sufficient neonates a total of 4 (1.5%). Cord serum 25(OH)D had a strong positive correlation with maternal serum 25(OH) before delivery (Pearson r =0.883, p=0.0001) in Figure 2. Association between maternal Vitamin D status and maternal-neonatal outcomes is displayed in Table 2. The maternal outcomes (chronic illness, allergy, back pain, muscle pain, and before pregnancy BMI, C-section, and pre-eclampsia) were no significant associations were found between groups, and neonatal outcomes such as head circumference (p=0.015), and a score of Apgar 5' (p=0.001) were associated with maternal Vitamin D status. The lowest level of Maternal Vitamin D was significantly associated with an increase in head circumference. Table 3 shows association between maternal Vitamin D level and life styles. The mother's prenatal vitamin intake, exposure to sunlight, egg and fish consumption did not differ significantly between maternal Vitamin D levels. One hundred and twenty-two (46.2 %) of the mothers had consumed cow milk. There was a difference in the maternal serum 25(OH)D levels between groups (p=0.006). In terms of fish consumption, 82.5% of the study participants did not eat fish at all, and 82.6 % of these women were Vitamin D deficient. From all these effects, a significant correlaton was observed between Vitamin D intake during pregnancy and maternal Vitamin D levels (p=0.000).

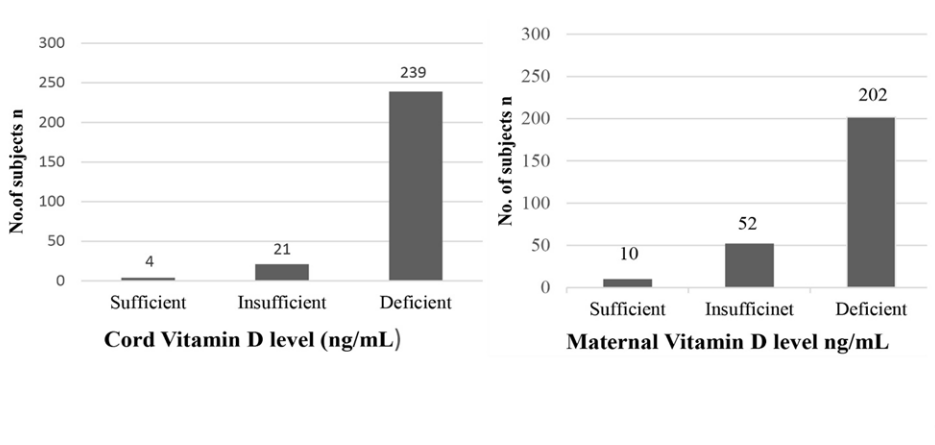

Figure 1: Distribution of maternal serum and neonatal cord blood 25(OH)D levels (N=264)

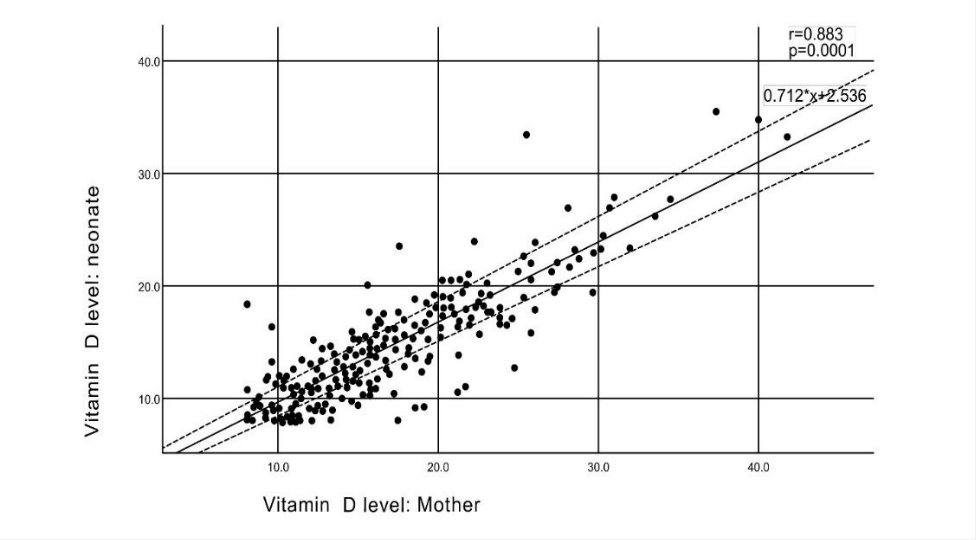

Figure 2: Correlation between maternal 25(OH)D level and neonatal 25(OH)D level

Table 1: Distribution of maternal demographic characteristics

Maternal characteristics	Total	Deficiency	Insufficiency	Sufficiency	*p*-value
	n (%)	n (%)	n (%)	n (%)	
Maternal age (years)					0.086
≤24	49 (18.6)	42 (20.8)	4 (7.7)	3 (30.0)	
25-29	71 (26.9)	49 (24.3)	21 (40.4)	1 (10)	
30-34	79 (29.9)	62 (30.7)	15 (28.8)	2 (20)	
≥35	65 (24.6)	49 (24.3)	12 (23.1)	4 (40)	
Education					0.392
Secondary education or below	72 (27.3)	58 (28.7)	11 (21.2)	3 (30)	
Short cycle tertiary	20 (7.6)	12 (5.9)	7 (13.5)	1 (10)	
Graduate	172 (65.2)	132 (65.3)	34 (65.4)	6 (60)	
Marital status					0.871
Single	73 (27.7)	53 (26.2)	16 (30.8)	4 (40)	
Married	170 (64.4)	130 (64.4)	34 (65.4)	6 (60)	
Divorced	5 (1.9)	5 (2.5)	0 (0)	0 (0)	
Widowed	1 (0.4)	1 (0.5)	0 (0)	0 (0)	
Cohabitant	15 (5.7)	13 (6.4)	2 (3.8)	0 (0)	
Working condition					0.703
Intellectual work	150 (56.8)	118 (58.4)	27 (51.9)	5 (50)	
Physical work	31 (11.7)	23 (11.4)	7 (13.5)	1 (10)	
Unemployed	71 (26.9)	50 (24.8)	17 (32.7)	4 (40)	
Other	12 (4.5)	11 (5.4)	1 (1.9)	0	
Total income					0.000
Low	17 (6.4)	12 (5.9)	1 (1.9)	4 (40)	
Middle	129 (48.9)	103 (51.0)	26 (50.0)	0 (0)	
High	118 (44.7)	87 (43.1)	25 (48.1)	6 (60.0)	
Household type					0.293
Ger (Yurt)	39 (14.8)	27 (13.4)	9 (17.3)	3 (30.0)	
House	65 (24.6)	53 (26.2)	12 (23.1)	0 (0)	
Apartment	160 (60.6)	122 (60.4)	31 (59.6)	7 (70.0)	
Total	264	202 (76.5)	52 (19.7)	10 (3.8)	

Table 2: Association between maternal-neonatal outcomes and Vitamin D status

Variables	Q1*		Q2*		Q3*		Q4*		*p-value*
	n	%	n	%	n	%	n	%	
Maternal outcomes									
Chronic illness	11	19.3	15	26.4	17	29.8	14	24.5	0.462
Allergy	5	20	4	16	9	36	7	28	0.303
Back pain	32	30.5	18	17.1	25	23.8	30	28.6	0.955
Muscle pain	11	19.6	15	26.8	15	26.8	15	26.8	0.420
C-section	21	23.3	21	23.3	25	27.8	23	25.6	0.562
Pre-eclampsia	30	25.6	25	21.4	29	24.8	33	28.2	0.472
BMI (kg/m^2)	26.2±21.7		23.2±3.8		24.0±4.3		24.2±4.6		0.494

Neonatal outcomes									
Asphyxia	3	21.4	2	14.3	6	42.9	3	21.4	0.624
Birth weight (g)	3552±430.5		3479±417.0		3556±412.3		3544±455.1		0.704
Birth heigh (cm)	50.8±1.5		50.2±1.8		50.8±1.5		50.8±1.7		0.125
Head circumference (cm)	34.8±1.4		34.4±1.9		34.7±1.3		36.4±2.0		0.015
Apgar 1’	6.9±0.4		6.9±0.2		6.8±0.6		6.9±0.3		0.173
Apgar 5’	7.6±0.5		7.8±0.3		7.5±0.7		7.8±0.5		0.001
Maternal 25(OH)D divided quartile: Q1<11.3 ng/mL, Q2 11.4-15.6 ng/mL, Q3 15.7-20.374 ng/mL, Q4 >20.375 ng/mL									

Table 3: Multivariate linear regression between Maternal Vitamin D level and life styles

Variables	Unstandardized Coefficients		95.0% CI for B			
	B	Std. Error	Lower bound	Upper bound	t	*p*-value
Maternal Vitamin D intake	0.370	0.069	0.234	0.506	5.364	0.000
Prenatal multivitamin intake	0.019	0.091	-0.160	0.199	0.210	0.834
Sun exposure	0.125	0.066	-0.005	0.255	1.893	0.059
Alcohol consumption	-0.076	0.067	-0.208	0.056	-1.135	0.258
Tobacco consumption	0.085	0.140	-0.190	0.360	0.609	0.543
Egg consumption	0.008	0.030	-0.051	0.066	0.265	0.791
Fish consumption	0.046	0.061	-0.074	0.167	0.758	0.449
Milk consumption	0.180	0.065	0.052	0.307	2.769	0.006

Discussion

The cause of varying levels of Vitamin D in newborns is based on the mother’s 25(OH)D levels during pregnancy. Our group showed that Vitamin D status at birth is closely related to that of the mother and it is lesser than the mother’s serum level. The data showed that the cord blood will contain approximately 50 percent to 60 percent of the maternal circulating 25(OH)D [16]. Many studies have shown a strong relationship between maternal and cord blood circulating 25(OH)D concentrations [12,17-19]. The nutritional Vitamin D status of the fetus and neonate is dependent on the Vitamin D stores of the mother,[20] thus, if the mother has hypovitaminosis D, her fetus will experience depleted Vitamin D exposure throughout the developmental period. Dietary supplements may prevent Vitamin D deficiency during pregnancy. Studies reporting a high prevalence of Vitamin D deficiency among pregnant women and their neonates are abundant, particularly in the United States. During delivery, vitamin D is deficiency is seen in 29.2% of the black women and 45.6% of the black neonates, 5% of the white women and 9.7% of the white neonates, respectively. Notably, low concentrations of 25(OH)D despite >90% of women reporting regular multivitamin use in the last trimester of pregnancy is seen [21]. The natural diet does not provide a good Vitamin D source, hence, the options of fortification and supplementation are critically important. The Endocrine Society Clinical Practice Guideline suggests that pregnant and lactating women require at least 600 IU/d of Vitamin D and recognize that at least 1500-2000 IU/d of Vitamin D may be needed to maintain a blood level of 25(OH)D above 30 ng/mL [14]. The Health Council of the Netherlands (latitude 52oN) recommends a higher amount of Vitamin D for pregnant than nonpregnant women [22]. Of the mothers who participated in our study (n=264), almost 27.3 % reported taking a Vitamin D supplement during the pregnancy. In terms of Vitamin D intake, 7 (2.6%) were taken during the first trimester of pregnancy, 16 (6.1%) were in the second trimester, and 49 (18.6%) were used during the last trimester of pregnancy.

There is evidence that adults, as well as children, may not be adequately fed because of increased poverty during the past 20 years. To identify any special factors that may be promoting Vitamin D deficiency in Mongolia, the Nutritional Research Center in Ulaanbaatar has conducted a 2-year survey of different population groups. The surveyed women ate diets consisting mainly of flour, rice, potato, and meat. Their intake of unbalanced food and micronutrients may also have been marginal in comparison to dietary recommendations for pregnancy [11]. The daily intake of calcium by pregnant women was found to be only about 35% of the recommended daily allowance of 400 mg/d [7]. Clinical Vitamin D deficiency in Mongolia in early childhood is associated not only with an inadequate supply of calcium but also with protein and energy malnutrition. In a total study group of 394 children under 5 years of age, 38.8% were stunted, with height for age Z-score values of less than 2 S.D. and 14.5% of all the children studied were significantly below accepted values for weight for age [11]. In the United States and Canada foods are fortified with Vitamin D. Sweden and Finland fortify milk, and many European countries add Vitamin D to cereals, bread, and margarine [13]. Vitamin D is almost non-existent in traditional Mongolian food, and some types of milk and yogurt are fortified with Vitamin D, but due to poverty, the families are incapable of buying milk, yogurt even meat, potato, flour, and rice. The latitudes above 37oN is too weak to induce sufficient cutaneous Vitamin D synthesis during winter [23]. In Mongolia, there is no Vitamin D production in the skin from October through April [24]. We would therefore presume the serum 25(OH)D concentrations in the July-August span the highest. Following too much exposure to direct sun rays, people are advised to use sunscreen to reduce the risk of sun damage to skin [25] and diseases such as skin cancer [26]. In our study, sunscreen usage was not common among the participants (n=106). Studies have shown that clouds, smoke, and air pollution reduce UV radiation [27, 28]. Thus, the conditions to produce Vitamin D from endogenous sources are limited. In a Harvard study, most of the demographic, lifestyle, reproductive, anthropometric, and dietary factors were not associated with 25(OH)D levels of reproductive-aged women in Mongolia [9]. Vitamin D deficiency is associated with increased risk of pregnancy complications such as pre-eclampsia and requirement of a primary C-section [29, 30]. Though no significant difference in maternal outcomes and Vitamin D levels in mother’s blood.

There are also other limitations in the present study. First, our study was a single-center study, and the generalizability of the results is low. Second, using only single measurements of each study participant and blood collection both made it impossible to evaluate fluctuations of vitamin D status during pregnancy. Third, information on dietary and supplemental vitamin D intake and sunlight exposure were collected by questionnaires, which may affect the statistical analysis.

Conclusions

In conclusion, we have confirmed our hypothesis that maternal and neonatal Vitamin D deficiency is high in Mongolia, and there is a significant correlation between mothers and their neonates. The lack of naturally Vitamin D rich food in the diet and limited sun production should be considered. We have also demonstrated that Vitamin D intake in pregnancy is the main role in the prevention of Vitamin D deficiency. The results provide a Vitamin D supplement that warrants consideration, well-designed prospective case-control or cohort studies involving multiple measurements are required.

Ethics approval

Ethical approval for the research was obtained from the Mongolian National University of Medical Sciences Research Ethics Board, under the protocol last May 24, 2019 (No. D-06). We acquired written informed consent from each participant.

Conflicts of Interest

The authors declare no conflict of interest.

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