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Vitamin D Status in Mongolian Pregnant Women and Birth Outcomes

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Objectives: Vitamin D deficiency and insufficiency in pregnancy can lead to gestational diabetes, preeclampsia, and eclampsia, as well as newborns having Vitamin D deficiency. This study was performed to determine the amount of maternal, neonatal Vitamin D, and consequences of Vitamin D deficiency on birth outcomes. **Methods:** Hospital-based prospective research was conducted on 528 participants which included 264 mothers and 264 neonates. Pre-delivery maternal venous blood and neonatal cord blood samples were collected and total 25(OH)D concentration was measured. After checking the normality of data distribution, methods of result presentation and statistical analyses were applied. **Results:** The average level of 25(OH)D in the mother's blood was 16.53 ± 6.5 ng/ml. The total Vitamin D deficiency in mothers was 191 (72.3%), insufficiency was 63 (23.9%), and 10 (3.8%) registered levels of sufficiency. Maternal serum 25(OH)D was significantly correlated with cord blood 25(OH)D ($r = 0.87$, $p < 0.01$). **Conclusion:** 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's blood and in the umbilical cord blood of the newborn. Complications of pregnancy are not associated with Vitamin D status in mother's blood.

Keywords: 25(OH)D, Umbilical Cord, Apgar Score, Newborn Measurements, Rickets

Introduction

It is globally recognized that Vitamin D deficiency affects not only musculoskeletal metabolism but also affects susceptibility to communicable and non-communicable diseases. Prevalence of Vitamin D deficiency is 7- 100% worldwide and it is different in each country [1]. Vitamin D deficiency in pregnancy can lead to gestational diabetes, preeclampsia, and eclampsia, as well as newborns having Vitamin D deficiency [2]. At birth, umbilical cord 25(OH)D levels are directly correlated with maternal levels [3, 4]. The mother's nutrition, lifestyle, and vitamin intake during pregnancy affect Vitamin D levels, and Vitamin D plays an important role in mother-child health, both skeletally and non-skeletally. A systematic review by Thorne-Lyman et al. demonstrated protective effects of supplementation on low birthweight, and non-significant but suggestive effects of daily supplementation on small-for-gestational age in five randomized trials [5]. Another study of a population-based prospective cohort in Netherlands also revealed that mothers with 25(OH)D concentrations in the lower quartiles had offspring with third-trimester fetal growth restriction leading to a smaller head circumference, shorter body length, and lower body weight at birth (all $p < 0.05$). Further, mothers which had 25(OH)D concentrations in the lowest quartile had an increased risk of preterm delivery (OR: 1.72; 95% CI: 1.14, 2.60) and children who were small for gestational age (OR: 2.07; 95% CI: 1.33, 3.22). The authors concluded that low maternal 25(OH)D concentrations are associated with proportional fetal growth restriction and with an increased risk of preterm birth and small size for gestational age at birth. A double-blind trial of vitamin D supplements in pregnant Asian women by Brooke et al showed that when calciferol (ergocalciferol, 1000 IU/day) was administered to 59 women and placebo to 67 controls during the last trimester, mothers in the treatment group gained weight faster in the last trimester than those in the control group, and at term they and their infants all had adequate plasma 25-OHD concentrations. On the other hand, mothers and infants in the control group had low plasma concentrations of 25-OHD, raised plasma alkaline phosphatase activity, and five of these infants developed symptomatic hypocalcaemia. Further, infants in the control group had larger fontanelles, suggesting impaired ossification of the skull.

Generally, exogenous sources of Vitamin D include fish, seafood, mushrooms, and eggs, and endogenous sources include 7-dehydrocholesterol, a precursor of Vitamin D, which is synthesized in the skin by the action of ultraviolet β-radiation (290- 315 nm) of sunlight [6]. However, due to its geographical region at 42- 50 degrees north latitude, Mongolia has an extremely cool climate with a sunlight angle of less than 90^0. Additionally, traditional Mongolian foods are low in Vitamin D so the conditions for the production of Vitamin D from endogenous sources are limited. According to the study in 2009 by Ganmaa. D and others, 99 out of 100 women in Mongolia were deficient in vitamin D. This study also demonstrated that the content of vitamin D3 (25 OH) is very low in the diet, endogenous D-vitamin synthesis does not occur until March, and vitamin D levels peak between April and July [7]. In a study published in 2020, conducted on 8851 children living in Ulaanbaatar, 95.6% of children had a baseline serum 25(OH)D level of less than 20 ng per milliliter [8].

There is a high prevalence of Vitamin D deficiency in women of reproductive age [7, 9], pregnant women [10], and children in Mongolia [8, 11, 12], but a study to determine the level of Vitamin D in pregnant women and umbilical cord blood in neonatals, has not been performed until now. The cause of vitamin D deficiency and sufficiency in a newborn is based on the mother's 25(OH) D levels during pregnancy. Therefore, this study aims to detect early vitamin D deficiency in the newborn and to identify some of the birth outcomes that may contribute to vitamin D deficiency in pregnancy. The novelty of the study was some of the factors contributing to maternal Vitamin D levels; and was the first time in Mongolia that Vitamin D levels were determined based on umbilical cord blood samples.

Materials and Methods

The study was conducted using a hospital-based prospective study model and random sampling, involving 264 mothers who gave birth in July and August 2019 at the Urguu Maternity Hospital in Ulaanbaatar, along with their newborns. Samples were collected from the veins of the pregnant woman during follow-up in the delivery room before giving birth, and from the umbilical vein after the umbilical cord clamping, and samples were then transported on ice to the laboratory for measurement. Concentration of 25 (OH) D3 was determined via ELISA (VIDAS 25 OH Vitamin D total). Based on the criteria of the Medicine and Endocrine Society, Vitamin D levels were classified as deficient $<$ 20 ng/ml, insufficient 21- 29, sufficient $\geq$ 30 ng/ml or excess $>$ 100 ng/ml.

A questionnaire was taken from mothers who agreed to participate in the study. We excluded preterm and late term births, multiple gestations, and infants with fetal anomalies. The following maternal and neonatal data were collected. Maternal demographic characteristics included mother's age, education, BMI before pregnancy, marital status and household type. Birth outcome Vitamin D status was compared with birth outcomes and complications of pregnancy.

Statistical analysis

For categorical variables, chi-square and Fisher's exact tests were carried out. Multiple linear regression was performed. Cohen's kappa coefficient was used to match the grouping variables of the mother's vitamin D levels at birth and the agreement between the groupings of the newborns' vitamin D levels at birth. All p-values less than 0.05 were defined as statistically significant. Data analyses were performed using IBM SPSS V25.0 software (SPSS Inc., Chicago, IL).

Ethical statement

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

Results

In total, 264 mother-neonate pairs participated and 528 blood samples were collected in this study. Table 1 details the demography of participants and the distribution of Vitamin D levels.

Maternal Vitamin D levels varied with age, educational level, BMI, marital status and household types. There was no significant correlation between any of the demographic variables and 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). Table 2 details 191 (72.3%) women were 25(OH) D deficient, 63 (23.9%) were insufficient, 10 (3.8%) had sufficient 25(OH)D levels. The results for neonatal Vitamin D deficiency are as follows: there were 232 (87.9%) deficient neonates, insufficient neonates numbered 28 (10.6%), and sufficient neonates a total of 4 (1.5%).

Table 3 shows the multivariate linear regression analysis, and there was no association between neonatal Vitamin D level and other related factors.

We further tested possible associations between birth outcomes and Vitamin D deficiency. Mothers with Vitamin D deficiency had more pre-eclampsia which is generally characterized by hypertension as well as increased levels of protein in the urine (Table 4). Further, studies revealed that

Table 1. Distribution of maternal demographic characteristics.

Variables	Deficiency n = 191	Insufficiency n = 63	Sufficiency n = 10	Total n = 264
Maternal age, years	N (%)	N (%)	N (%)	N (%)
<24	40 (20.4)	6 (12.2)	3 (30.0)	49 (18.6)
25-29	46 (23.5)	24 (33.8)	1 (10.0)	71 (26.9)
30-34	61 (31.9)	16 (20.3)	2 (20.0)	79 (29.9)
≥35	44 (23.0)	17 (26.2)	4 (40.0)	65 (24.6)
Education				
Secondary education or below	55 (28.8)	14 (19.4)	3 (40.0)	72 (27.3)
Vocational education	12 (6.3)	7 (35)	1 (10.0)	20 (7.6)
Graduate	124 (64.9)	42 (24.4)	6 (60.0)	172 (65.2)
Pre-pregnancy BMI				
Underweight	12 (6.3)	6 (31.6)	1 (10.0)	19 (7.2)
Normal	114 (59.7)	37 (23.3)	8 (80.0)	159 (60.2)
Overweight	43 (22.5)	15 (25.9)	-	58 (22)
Obesity	22 (11.5)	5 (17.9)	1 (10.0)	28 (10.6)
Marital status				
Unmarried	49 (25.7)	20 (27.4)	4 (40.0)	73 (27.7)
Married	124 (64.9)	40 (23.5)	6 (60.0)	170 (64.4)
Others	18 (9.4)	3 (14.3)	-	21 (8.0)
Household type				
Ger (Yurt)	24 (12.6)	12 (30.8)	3 (30.0)	39 (14.8)
House	51 (26.7)	14 (21.5)	-	65 (24.6)
Apartment	116 (60.7)	37 (23.1)	7 (70.0)	160 (60.6)

Table 2. The amount of Vitamin D in the mother-child.

Variables	Maternal Vitamin D level			
	Deficient n = 191	Insufficient n = 63	Sufficient n = 10	Total n = 264
Cord Vitamin D	N (%)	N (%)	N (%)	N (%)
Deficient	189 (99.0)	43 (68.3)	-	232 (87.9)
Insufficient	2 (1.0)	19 (30.2)	7 (70.0)	28 (10.6)
Sufficient	-	1 (1.6)	3 (30.0)	4 (1.5)

Table 3. Multivariate linear regression.

Variables	Unstandardized Coefficients		95.0% CI for B				p-value
	B	Std. Error	Lower Bound	Upper Bound	t	VIF	
Maternal Vitamin D level	0.692	0.027	0.64	0.744	15.1	1.6	0.000
Secondary education or below	0.627	0.37	-0.102	1.355	-18.3	5.9	0.091
Vocational education	0.592	0.591	-0.571	1.756	-1.76	3.8	0.317
Graduate	Ref						
Family income >₮500,000	-0.572	0.612	-1.778	0.633	-2.16	8.3	0.351
Family income ₮500,001-1,000,000	-0.575	0.33	-1.224	0.075	3.15	1.4	0.082
Family income < ₮1,000,000	Ref						
Vitamin D intake during pregnancy	0.109	0.367	-0.614	0.832	-3.91	4.4	0.767
(Constant)	2.898	0.488	1.938	3.859			0.000
							0.125*

F-statistics: 101.45, adjusted $R^2 = 0.269$; *p-value for F-statistics

Table 4. Birth outcomes according to Vitamin D status.

Variables	Deficiency n = 191	Insufficiency n = 63	Sufficiency n = 10	Total n = 264	p-value
Threatened abortion	N (%)	N (%)	N (%)	N (%)	
Yes	24 (12.6)	8 (12.7)	1 (10.0)	33 (12.5)	0.972
No	167 (87.4)	55 (87.3)	9 (90.0)	231 (87.5)	
Preeclampsia					
Yes	111 (58.1)	30 (47.6)	6 (60.0)	147 (55.7)	0.334
No	80 (41.9)	33 (52.4)	4 (40.0)	117 (44.3)	
Severe headaches					
Yes	44 (39.6)	8 (26.7)	3 (50.0)	55 (37.4)	0.346
No	67 (60.4)	22 (73.3)	3 (50.0)	92 (62.6)	
Edema					
Yes	72 (64.9)	22 (73.3)	3 (50.0)	97 (66.0)	0.481
No	39 (35.1)	8 (26.7)	3 (50.0)	50 (34.0)	
Hypertension					
Yes	40 (36.0)	9 (45.0)		49 (33.3)	
No	71 (64.0)	21 (55.0)	6 (100.0)	98 (66.7)	
Proteinuria					

Continued

Yes	10 (9.0)	4 (13.3)		14 (9.5)	
No	101 (91.0)	26 (86.7)	6 (100.0)	133 (90.5)	
Postpartum hemorrhage					
Yes	8 (4.2)	1 (1.6)		9 (3.4)	
No	183 (95.8)	62 (98.4)	10 (100.0)	255 (96.6)	
Mode of birth					
Normal	61 (31.9)	20 (31.7)	5 (50.0)	86 (32.6)	0.578
Abnormal	63 (33.0)	21 (33.3)	4 (40.0)	88 (33.3)	
C-section	67 (35.1)	22 (35.0)	1 (10.0)	90 (34.1)	
Apgar score 1-minute					
0-3	-	-	-	-	
4-6	10 (5.2)	4 (6.3)	-	14 (5.3)	
7-10	181 (94.8)	59 (93.7)	10 (100.0)	250 (94.7)	
Apgar score 5-minute					
0-3	-	-	-	-	
4-6	5 (2.6)	1 (1.6)	-	6 (2.3)	
7-10	185 (97.4)	62 (98.4)	10 (100.0)	257 (97.7)	

maternal Vitamin D deficiency is a risk factor for delivery by C-section.

It has been suggested that there is approximately a 2-fold increased risk of C-section for prolonged labor. In our study, mothers with Vitamin D deficiency had more delivery complications. On the other hand, no association was found between Maternal Vitamin D deficient, insufficient or sufficient levels and birth outcomes, also. A significant correlation was observed between maternal and neonatal 25(OH)D concentrations (Pearson r square = 0.78) in Figure 1.

Discussion

Numerous studies demonstrated that maternal Vitamin D deficiency has been associated with various adverse pregnancy outcomes such as pre-eclampsia and gestational diabetes. Further, there is a significant impact of maternal Vitamin D deficiency on birth outcomes, including impaired bone developments, multiple sclerosis, diabetes mellitus as well as impaired function of the immune system of the fetus. On the other hand, it has also been suggested that both vitamin D concentrations and birth outcomes are significantly different in different ethnic groups. Bodnar et al. showed that there was a U-shaped relation between serum 25(OH)D and risk of small-for-gestational age births among white mothers, while there was no relation among black mothers. Further, one single nucleotide polymorphisms (SNP) in the Vitamin D receptor gene among white women and 3 SNP in black women were significantly associated with small-for-gestational age births [13]. Similar studies have been done in the United States, Europe, and Asia which show that mother-child Vitamin D deficiency is prevalent in the population. In the study by Ginde et al, the National Health and Nutrition Examination Survey 2001– 2006 of United States showed that average level of Vitamin D of pregnant women in the first trimester was 26 ng/ml, which is similar to nonpregnant women, despite a higher proportion taking vitamin D supplementation [14]. While in Italy in 2012- 2013, in total 533 mothers and children participated and the average level of Vitamin D was 11.28 ± 7.68 ng/ml for mothers, and 15.96 ± 8.4 ng/ml for newborns, which is close to the results of our study. In another study of the Pakistan population, it has been demonstrated that a maternal Vitamin D supplementation group had increased 25OHD (18.3 ± 11 ng/dL vs 8.82 ± 11.84 ng/dL (p = .001) compared with a group who had 200 mg ferrous sulfate and 600 mg calcium daily (6.9 ± 7.0 ng/dL vs 6.32 ± 3.97 ng/dL, p = .06). Also, neonatal 25OHD levels were significantly higher in the Vitamin D supplementation group (19.22 ± 12.19 ng/dL vs 6.27 ± 5.2 ng/dL). Further, one- and 5-minute Apgar scores were significantly higher in a Vitamin D supplementation group (7.10 ± 0.66 vs 6.90 ± 0.50, p = .026, and 8.53 ± 0.68 vs 8.33 ± 0.81, p = .051, respectively). In our study, there was a significant correlation between maternal and neonatal serum concentrations (r = 0.883, p < 0.001). This finding has been reproduced in several studies [4, 13, 15-18]. Concentrations of 25(OH)D are generally low in fetal blood, compared to levels in maternal blood [3, 19].

International studies have shown that factors such as education, income, and BMI are statistically significant factors contributing to Vitamin D deficiency [1, 20]. A study of the BMI of 360 pregnant women in the United States compared with Vitamin D levels found that a 1 kg/m2 increase in BMI decreased Vitamin D to 0.40 ng/ml [21]. However, no statistically significant correlation (p > 0.05) was observed in our study. In addition, maternal Vitamin D deficiency has been associated with adverse pregnancy outcomes. Vitamin D deficiency results in proximal muscle weakness and decreased lower extremity muscle function, perhaps contributing to the risk of C-section delivery [22]. The present study also revealed that the type of delivery had a significant association with Vitamin D levels [23- 25].

The evidence linking Vitamin D and Apgar scores is conflicting and controversial; two studies reported a positive correlation [26, 27]. Another two studies found Vitamin D levels did not predict Apgar score [25, 28]. The latter result was obtained in our study. In a 2012 systematic review and meta-analysis, pooled analysis of all five trials on mean birthweight suggested no significant overall effect and other which showed a significant decrease in birthweight [29-32]. There is no statistically difference in correlation between Vitamin D status and newborn anthropometry conducted in our study.

Our hospital-based study was held in July and August of 2020. The Urguu maternity hospital is reserved for Ulaanbaatar city's 4 districts. Only 3.8% of total participants had sufficient 25(OH)D in serum even though blood samples were drawn in summer. Abnormal distribution of Vitamin D level was the main reason for statistically insignificant results. According to the results of the study, maternal vitamin D deficiency leads to neonatal vitamin D deficiency, thus pregnant women need to take additional vitamin D especially in their 3rd trimester of pregnancy.

Our study has some limitations. At first, vitamin D deficiency can be associated with a range of chronic health conditions or behavioral factors of individuals. In this study, we did not include such parameters for the analysis. Second limitation is that our sample size of the data was small. We conducted this study in one Maternal Hospital of Ulaanbaatar. Another limitation is that the study conduction period was during the summer season, which significantly influences data outcomes. Thus, future studies are needed to further delineate the factors including participants' lifestyle, and chronic illness as well as the external factor such as the limited sun exposure during the winter season.

Conclusions

We conclude that Vitamin D deficiency is high among mothers and newborns and there is a significant correlation between them. However, birth outcomes are not associated with low Vitamin D levels. Therefore, Vitamin D supplements have an important role in pregnant women in decreasing the risk of neonatal Vitamin D deficiency.

Conflict of Interest

The authors declare no conflict of interest.

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