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Original Article

Vitamin D deficiency in pregnant women with pih and neonates and their correlation

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Abstract: Objective: To explore the correlation between the 25-hydroxy vitamin D (vitamin D) levels in pregnant women with pregnancy-induced hypertension (PIH) and the level in neonates, and investigate the effects of vitamin D levels in pregnant women with PIH on neonates with vitamin D deficiency. Methods: A retrospective analysis was performed on 249 pregnant women with preeclampsia and their neonates. Vitamin D concentrations in the serum of pregnant women and neonates were measured using LC-MS/MS. Vitamin D levels in neonates born to pregnant women with PIH at different vitamin D levels were compared, and the correlation of vitamin D levels between pregnant women and their neonates were analyzed. Results: The expression level of pregnant women in the vitamin D sufficient group was 38.24±7.62 ng/mL, which was significantly higher than that of PIH pregnant women with inadequate and deficient vitamin D levels ($P<0.05$). The expression level of neonates in the vitamin D sufficient group was 24.57±4.26 ng/mL, which was significantly higher than that of neonates with inadequate and deficient vitamin D levels ($P<0.05$). Vitamin D levels in pregnant women and neonates were positively correlated ($r=7.45$, $P<0.05$). The critical value of vitamin D (≤27.55 ng/mL) for pregnant women with PIH was used to predict the sensitivity of neonatal vitamin D expression levels at 94.82%, with a specificity of 76.95%. Conclusion: Vitamin D level of pregnant women with PIH is positively correlated with that of the neonates, and whether neonates have vitamin D deficiency can be effectively determined based on the vitamin D level of pregnant women with PIH.

Keywords: Vitamin D, pregnant women, neonates, pregnancy-induced hypertension

Introduction

Vitamin D is a kind of fat-soluble vitamin that belongs to sterol derivatives, which is indispensable to the human body [1]. It is also a very important influencing factor in the development of newborns which determine the normal growth of newborns. The vitamin D deficiency is currently an increasingly serious clinical problem with more and more newborns suffering from vitamin D deficiency after birth, among which, pregnant women with pregnancy-induced hypertension (PIH) are more likely to experience vitamin D deficiency. PIH is an endemic and extremely common disease [1]. According to the statistical results by Veerbeek et al. [2], the incidence of PIH was as high as 12.8% in 2015, which was much higher in India and Africa. Until this year, studies [3, 4] have shown a steady upward trend in the incidence of PIH. It is predicted that by 2050, PIH will become the largest gestational disease faced by pregnant women worldwide. According to the statistical analysis by Watanabe et al. [5], approximately 15.6% of pregnant women suffer from miscarriage due to PIH, and 30.5% of them are unable to become pregnant again. Research on PIH is committed to finding an effective preventive and treatment methods in the clinic and has made significant breakthroughs this year [6, 7]. Through effective clinical treatments and interventions, the threat posed by PIH has been greatly reduced. However, at present, there is a lack of relevant research literature on the vitamin D deficiency in neonates born to pregnant women with HIP. More and more research reports [8-10] show that Vitamin D deficiency has become the pri-

Table 1. Vitamin D deficiency in pregnant women with PIH and neonates [n (%)]

n=249	Pregnant women with PIH	Neonatal
Adequate vitamin D	89 (35.74)	19 (7.63)
Adequate vitamin D	96 (38.55)	69 (27.71)
Inadequate Vitamin D	64 (25.70)	161 (64.66)

mary health problem for new born babies. Vitamin D is an extremely important substance in the human body and can not only promote bone growth and development but also improve the body's immunity to various diseases [11]. The risk of neonatal vitamin D deficiency will not only cause slow growth but also increase the incidence of various types of infectious diseases. According to Kemse et al. [12], the chance of vitamin D deficiency in newborns delivered by pregnant women with PIH is as high as 24.3%, which has become a new clinical challenge. However, this situation has not yet been reported and accurately demonstrated at home and abroad.

Therefore, through this experimental analysis, the correlation between pregnant women with PIH and neonatal vitamin D levels will be determined, which provides reference and guidance for effective prevention and treatment of these conditions in the future clinical practice.

Materials and methods

Normal information

A total of 249 pregnant women with PIH (age range, 22-40 years) and their newborns admitted to Xingtai People's Hospital affiliated to Hebei Medical University were retrospectively analyzed. The inclusion criteria are as follows: all pregnant women diagnosed with PIH based on the 2013 diagnostic criteria [13], gestational age of ≥37 weeks, delivery was completed in our hospital, single-birth pregnant women, willing to cooperate with our hospital staff's arrangements, and with complete case information. Exclusion criteria are as follows: pregnant women with tumors, cardiovascular and cerebrovascular diseases, organ failures, parathyroid disease, liver and kidney disease, and drug allergies; newborns with congenital and hereditary diseases and deformities; and those who were transferred to the hospital. All patients have signed informed consents.

Methods

Two mL of venous blood and 4 mL of neonatal umbilical cord blood were collected from pregnant women one week before delivery, centrifuged for 5 min (4000 dpm/min), and detected by LC-MS/MS (Shanghai Guduo Biotechnology Co., Ltd.). The concentration of vitamin D in pregnant women with PIH and neonates was measured, and the level of vitamin D in neonates born by pregnant women with different vitamin D levels was compared. The correlation between vitamin D levels in pregnant women with PIH and neonates was also analyzed.

Judgment standard

With reference to the 2012 Vitamin D Metabolism Guidelines [14], maternal serum total vitamin D level of ≤20 ng/mL is regarded as deficient; serum total vitamin D level of >20 ng/mL but ≤30 ng/mL is regarded as inadequate; serum total vitamin D level of >30 ng/mL is considered adequate. Neonatal serum total vitamin D level of ≤15 ng/mL is regarded as deficient; serum total vitamin D level of >15 ng/mL, but ≤20 ng/mL is regarded as inadequate; and vitamin D level of >20 ng/mL is regarded as adequate.

Statistical method

SPSS 22.0 statistical software was used to analyze and process the data. The count data such as Vitamin D deficiency and age were expressed as % using chi-square test; Analysis of variance was used for comparison among groups and t test was used for comparison between two groups; the linear correlation analysis was used to compare vitamin D expression levels in pregnant women with PIH and neonates; the receiver operating characteristic (ROC) curve is used to predict vitamin D deficiency in newborns based on the vitamin D level in pregnant women with PIH. $P<0.05$ is considered statistically significant.

Results

Vitamin D deficiency

The average vitamin D level of 249 pregnant women with PIH is 27.85±10.17 ng/mL; 35.74% (89 cases) of them had adequate, 38.55% (96 cases) had inadequate, and 25.70% (64 cases) had deficient vitamin D levels. The average vita-

Table 2. Comparison of clinical information between pregnant women with PIH

	Sufficient vitamin D (n=89)	Insufficient vitamin D (n=96)	Vitamin D deficiency (n=64)	F	P
Age	26.72±4.33	27.04±5.01	27.12±4.86	0.16	0.85
Body weight (KG) before production	72.34±16.34	73.52±15.48	74.52±15.33	0.36	0.69
Pregnancy week	45.11±5.21	46.12±5.82	46.74±6.08	1.63	0.20
Whether it is first production				0.26	0.78
Yes	62 (69.66)	68 (70.83)	42 (65.63)		
No	27 (30.34)	28 (29.17)	22 (34.38)		
Residence				0.76	0.53
City	54 (60.67)	60 (62.50)	38 (59.38)		
Rural	35 (39.33)	36 (37.50)	26 (40.63)		

Table 3. Comparison of three groups of neonatal clinical information

	Sufficient vitamin D (n=19)	Insufficient vitamin D (n=69)	Vitamin D deficiency (n=161)	F	P
Body weight (KG)	3.24±1.24	3.50±1.23	3.04±1.47	2.66	0.72
Production methods				1.24	0.46
Virginal delivery	10 (52.63)	37 (3.62)	86 (53.42)		
Planning caesarean	9 (47.37)	32 (46.38)	75 (46.58)		
Gender				5.82	0.09
Boy	12 (63.16)	45 (65.22)	104 (64.60)		
Girl	7 (36.84)	24 (34.78)	57 (35.40)		

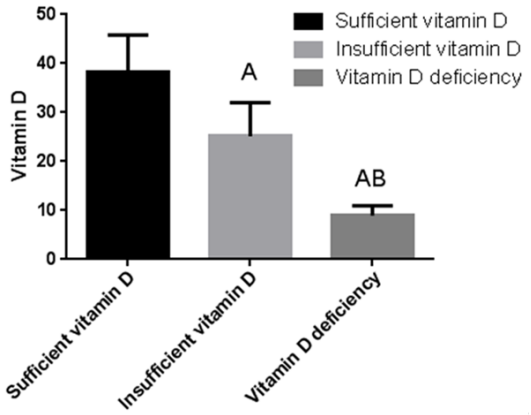

Figure 1. Level of vitamin D expression in pregnant women with PIH. A represents P<0.05 compared with pregnant women with PIH in the vitamin D sufficient group. B represents P<0.05 compared with pregnant women with vitamin D deficiency. The vitamin D expression levels of pregnant women with PIH in the three groups were highest in those with adequate vitamin D, followed by those with vitamin D deficiency.

min D level of 249 neonates is 13.26±6.07 ng/mL; 7.63% (19 cases) had adequate, 27.71% (69 cases) had inadequate, and 64.66% (161 cases) had deficient vitamin D levels (**Table 1**).

Patient clinical information

Comparing the ages, the weight before delivery and place of residence, there was no significant difference (P>0.05), which proved that the three groups of pregnant women with PIH were comparable (**Table 2**). There was no significant difference in the weight, delivery methods, and gender among the three groups of newborns (P>0.05), demonstrating that the newborns of the three groups were also comparable (**Table 3**).

Vitamin D expression

The expression level of pregnant women with PIH in the sufficient vitamin D group is 38.24±7.62 ng/mL, those in the inadequate vitamin D group is 25.16±6.84 ng/mL, and those in the vitamin D deficient group is 8.94±2.04 ng/mL, with the vitamin D deficient group having the lowest level among all groups, followed by vitamin D inadequate group (P<0.05). The V_D level of neonates in the sufficient vitamin D group is 24.57±4.26 ng/mL, those in the inadequate vitamin D group is 17.24±2.68 ng/mL, and those in the vitamin D deficient group is 5.24±1.27 ng/mL, with the

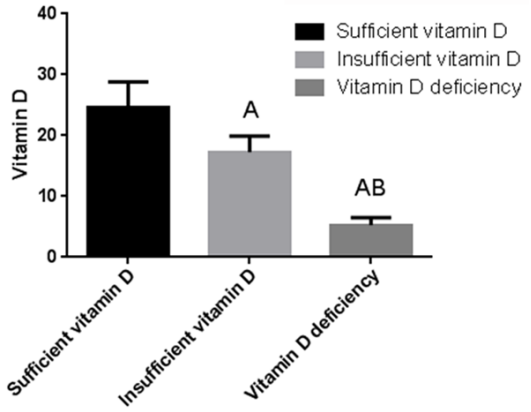

Figure 2. Level of neonatal vitamin D expression. A represents P<0.05 compared with neonates in the vitamin D sufficient group. B represents P<0.05 compared with neonates with vitamin D deficiency. The vitamin D expression levels of newborns in the three groups were highest in those with vitamin D supplementation, followed by those with vitamin D deficiency.

Table 4. Levels of vitamin D expression in neonates of three groups of pregnant women

Groups	Neonatal Vitamin D
Sufficient vitamin D (n=89)	26.14±5.17
Insufficient vitamin D (n=96)	15.43±3.86*
Vitamin D deficiency (n=64)	4.08±1.55#
F	572.71
P	<0.001

Note: *represents comparison with neonatal Vitamin D of pregnant women in vitamin D sufficient group, P<0.05. #represents neonatal Vitamin D of pregnant women in Insufficient vitamin D group, P<0.05.

vitamin D deficient group having the lowest level among all groups, followed by vitamin D inadequate group (P<0.05) (**Figures 1** and **2**).

Correlation analysis of vitamin D levels in neonates and pregnant women with PIH

Linear correlation analysis showed that vitamin D levels in pregnant women with PIH and neonates were positively correlated (r=7.45, P<0.05). The higher the vitamin D levels in pregnant women with PIH are, the higher the vitamin D level in neonates will be (**Table 4**, **Figure 3**).

The predictive value of vitamin D levels in pregnant women with PIH for the neonates

ROC curve analysis showed that the predictive value of vitamin D in pregnant women with PIH

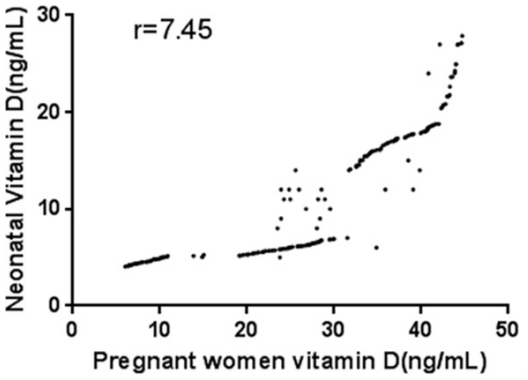

Figure 3. Correlation analysis of vitamin D expression levels in pregnant women with PIH and neonates. Vitamin D level in pregnant women with PIH was positively correlated with neonatal vitamin D expression (r=7.45, P<0.05). The higher the vitamin D level of pregnant women with PIH, the higher the vitamin D level of neonates.

for the neonates was 0.84 under the ROC curve, with the critical value of 27.55 ng/mL, and the sensitivity and specificity reached 94.82% and 76.95%, respectively (**Table 5**, **Figure 4**).

Discussion

Vitamin D is a fat-soluble vitamin and has a crucial physiological role in the formation and development of human bones [15]. At present, the mechanism of vitamin D on bone mineralization has not yet been clarified. Bauer et al. [16] demonstrated that vitamin D mineralizes bones by promoting the absorption of calcium and phosphorus. It is not only an essential nutrient but also a sensitive indicator of danger. A number of studies at home and abroad [17, 18] have shown that vitamin D is closely related to many chronic diseases during pregnancy, such as diabetes, anemia, and bacterial vaginosis. Because a pregnant woman requires a lot of nutrients for the fetal development, the blood volume and pressure will increase, which can easily cause various adverse reactions, and vitamin D deficiency is one of them, which can not only cause great burden to pregnant women but also may be a threat to the newborns' health [19].

The lack of vitamin D potentially causes neonatal rickets [20], and disorders related to calcium and phosphorus metabolism directly results in incomplete bone development and decreases resistance in newborns [21]. The lack of vita-

Table 5. ROC test results

Project	Value
Sensitivity	94.82%
Intentionality	76.95%
OR	1.72
95% CI	1.05~2.83
Area under the curve	0.84

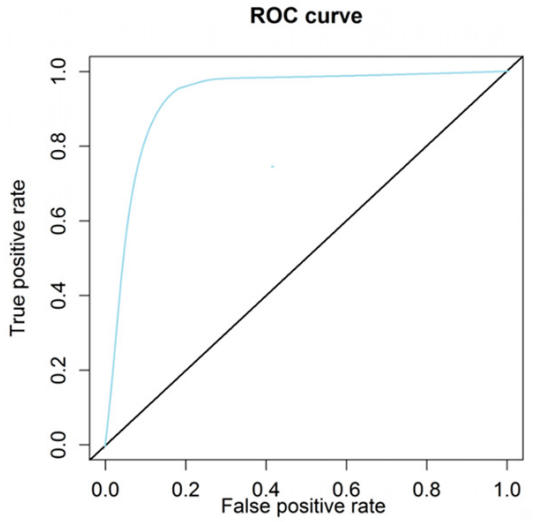

Figure 4. Predictive value of vitamin D deficiency in neonates for the detection of vitamin D levels in pregnant women with PIH. The area under the ROC curve was 0.84. The threshold value of vitamin D in pregnant women with PIH was ≤27.55 ng/mL. The sensitivity and specificity of the neonatal vitamin D expression level were 94.82% and 76.95%, respectively.

min D may also easily slowdown the neonatal cerebral cortex functional reflex and cause blood supply dysfunction, which leads to various blood diseases [22]. This condition has no accurate treatment available in clinical practice. Therefore, prophylaxis and treatment are advocated. The ambiguous relationship between the two results causes the lack of an effective reference limit in predicting vitamin D levels in neonates. Neonatal vitamin D deficiency has no accurate control and treatment measures as well; therefore, the relationship between them remains to be elucidated. According to the 2012 Vitamin D Metabolism Guideline as a reference value for vitamin D deficiency, this study investigated the correlation between vitamin D levels in pregnant women with PIH and that in neonates and studied the value of predicting vitamin D level in neonates by testing vitamin D in pregnant women, which aimed to provide a reliable reference for the prevention and treatment of neonatal vitamin D deficiency in the future.

The results of this experiment show that 24.70% of 249 pregnant women with PIH are vitamin D deficient, while vitamin D deficiency in neonates is as high as 64.66%, indicating that vitamin D deficiency in neonates born to pregnant women with PIH is a common phenomenon. Further analysis of the ROC curve showed that vitamin D level of ≤227.55 ng/mL is a critical value that can predict the presence of vitamin D deficiency in newborns with a sensitivity and specificity of 94.82% and 76.95%, respectively. This is a higher diagnostic value, indicating that the above methods can detect whether the newborn has vitamin D deficiency, promptly guide pregnant women to take vitamin D supplements, and reduce the incidence of neonatal complications. According to Cantorna et al. [23], the detection of neonatal vitamin D level can be a precondition that prevents pediatric rickets; its clinical operability is extremely poor and does not apply to a large area of the census. However, the method of predicting vitamin D deficiency in neonates by measuring vitamin D levels in pregnant women is simple, convenient, and can be universally used in clinical practice, which can be effectively avoided by taking supplements to increase the maternal vitamin D levels. According to Martineau et al. [24], pregnant women should take approximately 100,000 IU of vitamin D supplements per week during pregnancy, choose foods high in vitamins and proteins and gain knowledge on pregnancy-related diseases that may occur in newborns, which finally achieve optimal production conditions, reduce the chance of neonatal vitamin D deficiency, and improve the quality of newborns' survival.

In this study, the correlation between vitamin D levels in pregnant women with PIH and neonates was investigated. Testing vitamin D levels in pregnant women with pregnancy-induced hypertension was important in determining neonatal vitamin D deficiency. However, due to limited experimental conditions, deficiencies, such as a relatively small study base and single-center research population, existed. Due to the limited number of experimental samples,

repeated experiments cannot be performed to obtain the best test results. We will conduct longer-term follow-up surveys on the subjects of this study and will continue to refine and improve our experiments in the future.

In conclusion, the vitamin D level of pregnant women with preeclampsia is positively correlated with that of newborns, and whether vitamin D deficiency in newborns can be effectively determined based on the vitamin D level of pregnant women with PIH.

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Disclosure of conflict of interest

None.

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