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Original Article

Comparison between maternal and neonatal serum vitamin D levels in term jaundiced and nonjaundiced cases

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Abstract

Background: Neonatal jaundice is the result of an imbalance between the production and conjugation of bilirubin. Considering the multiple roles of vitamin D, lower levels of vitamin D in these cases may be associated with neonatal jaundice. The present study was undertaken for the purpose of comparing serum vitamin D levels in healthy term jaundiced and nonjaundiced newborns and their mothers.
Methods: This case–control study was conducted in 60 term newborns and their mothers from a teaching and referral children's hospital in the southwestern region of Iran, from December 22, 2013 through March 22, 2014. Neonatal and maternal blood samples were obtained and sent to the laboratory.
Results: The mean serum 25-hydroxy vitamin D levels of newborns and their mothers in both the case and the control groups were not significantly associated with their serum bilirubin levels. The mean of laboratory indices (calcium, phosphorus, alkaline phosphates, parathyroid hormone, and 25-hydroxy vitamin D) in mothers and newborns of the case group were nonsignificantly higher than that of the control group, but the mean vitamin D level was significantly lower among newborn cases compared with the controls ($p < 0.05$).
Conclusion: Newborn vitamin D levels were significantly lower in jaundiced cases compared with those in the nonjaundiced healthy groups, which may reveal an association between indirect hyperbilirubinemia and serum vitamin D levels. We suggest that more studies should be conducted including follow-up after 15 days of age, when jaundice has typically been resolved, and before starting vitamin D supplementation.

Keywords: hyperbilirubinemia; jaundice; mothers; newborns; vitamin D

1. Introduction

In neonates, jaundice generally results from an imbalance between the production and conjugation of bilirubin.[1,2] Overall, up to 60% of term newborns have clinical jaundice in the 1st week of life.[3] Although some factors such as blood groups and/or Rh incompatibility and sequestration had been reported as reasons of neonatal jaundice, the majority of reasons for this condition have not yet been clearly defined. Liver tissue is involved in vitamin D synthesis and plays an important role in indirect to direct bilirubin conversion and hyperbilirubinemia pathophysiology.

Vitamin D deficiency was accompanied by cardiovascular problems, neoplastic diseases, diabetes, obesity, metabolic syndrome, and colorectal and breast cancers. Vitamin D deficiency has also been reported to have a relationship with the maternal, fetal, and placental health.[4] However, it was reported that more than 80% of Iranian pregnant women had low levels of vitamin D, and the mean 25-hydroxy vitamin D test results in most of their neonates were immeasurably low.[5]

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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Although several studies had been performed on the treatment of hyperbilirubinemia among newborns using phototherapy and/or blood exchange and medications, only a few studies have investigated the role of vitamin D in neonatal jaundice. High economic expenditure and social problems of hospitalization of neonatal jaundice discourage investigators from finding a new therapeutic method.

There are several generally recognized causes of neonatal jaundice; however, despite numerous studies, the cause remains unknown in 10–50% of infants hospitalized with jaundice. However, considering the multiple roles of vitamin D, lower levels of vitamin D may be associated with neonatal jaundice in these cases.[3,4]

The present study was performed to compare the serum vitamin D levels in healthy term jaundiced and nonjaundiced newborns and their mothers.

2. Methods

2.1. Study participants

This case–control study was conducted in 60 term newborns (38–42 gestational weeks) and their mothers from a teaching and referral children's hospital in the southwest of Iran, between December 22, 2013 and March 22, 2014. This study was approved by the Ahvaz Jundishapur University of Medical Sciences Ethical Committee, and all parents signed the informed consent prior to enrollment.

2.2. Inclusion criteria

Jaundiced healthy term newborns (newborns with indirect hyperbilirubinemia) ranging in age from 2 days to 10 days, with birth weights between 2.5 kg and 4 kg, and their mothers were included as the case group. Nonjaundiced healthy term newborns with similar age and birth weight ranges and their mothers were considered as the control group. The case group consisted of newborns with a bilirubin level of >15 mg/dL, and the control group included newborns with nonvisible jaundice.

2.3. Exclusion criteria

Newborns with pathological causes for their hyperbilirubinemia such as blood group mismatch, infection, polycythemia, glucose-6-phosphate dehydrogenase deficiency, and cephalic hematoma; a history of asphyxia; or congenital anomalies were excluded. Additionally, newborns whose mothers had a history of chronic hepatic or renal disorders, gestational diabetes, or hypertension and used anticonvulsant drugs were excluded.

2.4. Study measurements

Blood samples were taken from the newborns and their mothers, and thereafter sent to the laboratory. After measurement of serum bilirubin levels, the blood samples were centrifuged using SELECTA devices at 4000 *g* and the extracted serum was maintained at −20°C. Then, samples were transferred on a weekly basis to the university reference laboratory and were stored at −70°C. Moreover, 25-hydroxy vitamin D, parathyroid hormone (PTH), calcium, phosphorus, and alkaline phosphates (ALPs) were measured. In our study, 25-hydroxy vitamin D and PTH were measured using the enzyme-linked immunosorbent assay method and ILB kit (Germany). Other tests such as calcium, phosphor, and alkaline phosphatase were carried out using Pars Azmoon kits (Pars Azmoon, Tehran, IR Iran). According to the reference level of those kits that were used in this study, individuals with serum vitamin D levels of <30 nmol/L were reported as vitamin D deficient, 30–75 nmol/L as vitamin D insufficient, and >75 nmol/L as those with a normal value of vitamin D.

2.5. Statistical analysis

The study data were collected and analyzed using the SPSS, version 19.0. To compare two quantitative and qualitative variables with normal distribution, independent sample *t* test and chi-square tests were used. Additionally, the Mann–Whitney *U* test was used for variables without normal distribution. All p values < 0.05 were considered significant.

Table 1
Maternal and neonatal demographic characteristics of the study cases and controls.

Variables		Case group ($n = 30$)	Control group ($n = 30$)	p
Maternal age (y), mean ± SD		27.00 ± 5.21	27.07 ± 3.55	0.954
Delivery type, *n* (%)	C/S	22 (74)	16 (54)	0.11
	SVD	8 (16)	14 (46)	
Male/Female, *n* (%)		22/8	22/8	>0.99
History of consanguineous marriages	Yes	12	13	0.79
	No	18	17	
Maternal BMI (kg/m^2), mean ± SD		26.06 ± 5.22	23.70 ± 3.24	0.041
Residency	City	26	26	>0.99
	Urban	4	4	
Neonatal body weight (g), mean ± SD		3120 ± 495.36	3120 ± 353.58	0.993
Head circumference in newborn (cm), mean ± SD		34.53 ± 0.927	34.46 ± 0.955	0.78
Body length of newborn (cm), mean ± SD		50.32 ± 1.60	49.95 ± 1.74	0.40

BMI = body mass index; SD = standard deviation.

3. Results

Maternal and neonatal demographic characteristics of the study case and control groups are shown in Table 1. There was no significant association in terms of maternal age between the two study groups ($p = 0.95$). There was no significant association between the type of delivery and hyperbilirubinemia in newborns ($p = 0.11$). Twelve mothers in the case group and 13 in the control group had a history of consanguineous marriages. There was no significant association between consanguineous marriage and hyperbilirubinemia in newborns ($p = 0.79$).

The body mass index for the mothers of the case group was significantly higher than that for the mothers in the control group ($p = 0.041$). The mean newborn head circumference showed no significant difference between both study groups ($p = 0.78$). The mean newborn body length of the case group was nonsignificantly higher than that of the newborns of the control group ($p = 0.40$).

Furthermore, the mean serum 25-hydroxy vitamin D levels of the newborns and their mothers in the case and control groups were not significantly associated with their serum bilirubin levels. Lastly, the mean levels of laboratory indices (calcium, phosphorus, ALPs, PTH, and 25-hydroxy vitamin D) in mothers and newborns of the case group were nonsignificantly higher than that in the control group, but the mean level of vitamin D was significantly lower among newborn cases compared with the controls ($p < 0.05$; Table 2).

4. Discussion

The present study was performed to compare serum vitamin D levels of healthy term jaundiced and nonjaundiced newborns and their mothers, which showed significant differences in the serum vitamin D levels of term jaundiced newborns in spite of a nonsignificant difference in the vitamin D levels of their mothers. To the best of our knowledge, there has been only one other study also reporting that the serum vitamin D levels in mothers of term jaundiced newborns were not significantly different from those in mothers of healthy term nonjaundiced newborns.[6]

Typically, there should be a negative correlation between vitamin D level and serum ALPs and PTH, because serum ALP and PTH levels are normal or high during vitamin D deficiency.[7–9] We observed a nonsignificantly lower PTH level among healthy term nonjaundiced newborns compared with the jaundiced group. Furthermore, serum calcium and phosphorus levels should be normal or lower in patients suffering from vitamin D insufficiency and deficiency. Interestingly, our findings showed nonsignificantly higher serum calcium and phosphorus levels among term jaundiced newborns. Overall, a study of serum vitamin D levels in Iranian pregnant women reported that in almost 85% of the cases, the serum 25-hydroxy vitamin D level was <25 mol/L. Another study showed that 86% of mothers and 75% of their infants, and 46% of mothers and 35% of their infants had vitamin D deficiency during the winter and summer seasons, respectively.[5,10] According to a geographically lower level of normal limit (35 ng/mL for mothers and 26 ng/mL for newborns), 26.1% of mothers and 53.4% of newborns in Iran had vitamin D deficiency.[6,11]

Previous studies indicated a significant association between vitamin D deficiency and obesity.[12–14] The results of the present study also showed that obesity was more prevalent in mothers of term jaundiced newborns compared with healthy nonjaundiced term newborns.

In a study by Dijkstra et al,[10] it was shown that there was a significant difference in the prevalence of vitamin D deficiency between black newborns and their mothers, who were considered as high-risk and low-risk groups, respectively. Zhuang et al, in a study on pregnant women (30–37-weeks gestational age) and the placental tissue of their newborns, reported that vitamin D deficiency had been found in 88% of mothers and 91.2% of their newborns. They revealed that serum vitamin D levels were subject to seasonal changes and that pregnant women had the highest vitamin D level in the fall. Overall, there was a positive correlation between the serum levels of vitamin D in mothers and their newborns.

In the current study, jaundice in newborns was associated with a lower serum vitamin D level in their mothers. In the literature, only one study on pregnant women in Turkey was considerably similar to our study. Although vitamin D metabolism and bilirubin metabolism were performed on two separated pathways, both had a common pathway in the liver. By contrast, changes in metabolism or synthesis of each of them might have an impact on the other product. Normal values of vitamin D are related to parameters such as calcium, phosphorus, alkaline phosphatase, and parathormone. Nonsignificant differences in serum vitamin D levels between newborns with jaundice and healthy newborns suggested that the lower level of vitamin D might be a result of hyperbilirubinemia.

Table 2
Comparison of study characteristics among case and control newborns and their mothers.

Variables	Mothers ($n = 60$)		Children ($n = 60$)	
	Mean ± SD	p	Mean ± SD	p
Calcium (mg/dL)		0.561		0.932
Case ($n = 30$)	9.60 ± 0.65		9.6333 ± 0.97780	
Control ($n = 30$)	9.56 ± 0.75		9.6133 ± 0.81017	
Phosphorus (mg/dL)		0.219		0.947
Case ($n = 30$)	4.36 ± 0.58		4.6167 ± 0.84734	
Control ($n = 30$)	4.18 ± 0.58		4.6033 ± 0.69752	
ALP (U/L)		0.668		0.087
Case ($n = 30$)	283.3 ± 64		513 ± 180	
Control ($n = 30$)	275.3 ± 7.8.7		437 ± 159	
PTH (pg/mL)		0.933		0.683
Case ($n = 30$)	46.50 ± 22.93		41.84 ± 20.14	
Control ($n = 30$)	46.04 ± 19.49		39.77 ± 19.02	
25OHD (nmol/L)		0.986		<0.001
Case ($n = 30$)	22.49 ± 80.30		84.38 ± 29.29	
Control ($n = 30$)	80.19 ± 26.26		110 ± 22.62	

ALP = alkaline phosphatase; PTH = parathyroid hormone; SD = standard deviation; 25OHD = 25-hydroxy vitamin D.

Newborn vitamin D levels were significantly lower in jaundiced cases compared with the nonjaundiced healthy groups, which revealed that there is an association between indirect hyperbilirubinemia and serum vitamin D levels. The findings of this study need to be confirmed by future research, including studies with larger sample size and repetition of vitamin D measurements with a follow-up until the age of 15 days, when jaundice is resolved, and before starting vitamin D supplementation.

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