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Original Article

Vitamin D Deficiency and Lower Respiratory Tract Infections in Newborn Infants

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Abstract

Purpose: There are reports that suggest vital and complex role of vitamin D in immune system function and regulation. The consequences of mild forms of vitamin D deficiency are less known. An association of subclinical vitamin D deficiency and acute lower respiratory infection in non-rachitic children has been reported. This study was conducted to determine serum concentrations of 25 hydroxy vitamin D in non-rachitic neonates with lower respiratory infections. ***Methods:*** This case control study was conducted in a university referral hospital. Forty admitted neonates with diagnosis of lower respiratory tract infection were enrolled in study as case group. Control group consisted of 40 healthy newborn infants who were seen in outpatient clinic without any respiratory symptoms. The serum 25(OH) D_3 was measured using a chemiluminesence immunoassay. ***Results:*** The mean concentration of vitamin D in neonates with pneumonia was 9.6±6.8 ng/ml and 14.7±9.3 ng/ml in control group (p=0.02).Vitamin D deficiency was determined in 37 neonates (92.5%) in case group and 26 neonates (65%) in control group (p=0.005). There was vitamin D deficiency in 36 (90%) mothers in case group and 23 (57.5%) mothers in control group (p=0.002). The concentration of vitamin D was below 10 ng/ml in 26 patients (65%), 10-20 ng/ml in 11 neonates (27.5%); and above 20 ng/ml in 3 cases (7.5%) of neonates in case group (p=0.001). ***Conclusion:*** This study shows vitamin D deficiency is a common problem in our community and infants with acute respiratory infections had lower vitamin D concentrations. Therefore, future studies needed to determine how to effectively improve vitamin D status and achieve its optimal function.

Key words Lower respiratory tract infections; Neonate; Vitamin D

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Introduction

The biochemical structure of vitamin D was discovered in the 1930. Vitamin D is a steroid hormone and plays a major role in regulation of calcium and phosphorus haemostasis, bone metabolism and bone development.[1,2] Sunshine exposure is important for endogenous synthesis of vitamin D. Vitamin D is also absorbed from dietary sources in the duodenum and jejunum. Both of them hydrolysed in the liver to form 25 hydroxy vitamin D, which is the most abundant vitamin D metabolite. Circulating 25(OH) D_3 concentrations provide a useful index of vitamin

D status that reflects both dietary intake and sunshine exposure. Its serum half-life is long (approximately 3 weeks). The measurement of 1,25 dihydroxy vitamin D provide little additional data about vitamin D status because it is tightly controlled by physiologic secondary hyperparathyroidism in a vitamin D deficient status. There is new information about the vitamin D role on glucose haemostasis, immune system, cardiovascular diseases and cancer. A severe vitamin D deficiency causes impaired mineralisation of bone tissue.[3] Vitamin D deficiency is associated with increased risk of many common cancers, type 1 and 2 diabetes, rheumatoid arthritis and multiple sclerosis in adults.[3-6]

There are reports that suggest vital and complex role of vitamin D in immune system function and regulation. The 1,25 dihydroxy vitamin D acts to promote the innate immature response to pathogens.[7] Clinical vitamin D deficiency that manifests as rickets was associated with pneumonia in different countries including Ethiopia,[8] Yemen[9] and Kuwait.[10] The consequences of mild forms of vitamin D deficiency are less known. Vitamin D insufficiency and deficiency have been associated with type 1 diabetes mellitus, allergies and atopic diseases in infants and children.[11,12] Subclinical vitamin D deficiency as identified by low serum concentration of 25 (OH) D_3 has been associated with increased risk of tuberculosis in adults. An association of subclinical vitamin D deficiency and acute lower respiratory infection in non-rachitic children was reported by Wayse in Indian children.[13] Epidemiologic studies have identified a link between inadequate vitamin D concentrations and respiratory infectious disease. There is little studies in this field in neonatal period. This study was conducted to determine serum concentrations of 25 hydroxy vitamin D in non-rachitic neonates with lower respiratory infections.

Methods

Study design: This case control study was conducted in a university referral hospital (children hospital, Tabriz. Iran) during March-September 2014.

Setting and sample: Forty admitted neonates of age 7 to 30 days with diagnosis of lower respiratory tract infection were enrolled in study as case group. Control group consisted of normal newborn infants who were seen in outpatient clinic without any respiratory symptoms. Acute lower respiratory tract infection (ALRI) was defined as the combination of clinical symptoms such as lower chest in drawing with respiratory rate more than 60 per minute and radiologic findings. Neonates with respiratory distress who diagnosed as transient tachypnea of newborn, respiratory distress syndrome, congenital pneumonia were excluded from study. Other exclusion criteria were chronic diseases and glucocorticoid therapy. In our country, it is recommended to start multivitamin supplementation for term newborns at age of 15 days that contains 400 IU vitamin D in each ml of droplet.

Ethical consideration: Ethic committee of Tabriz University of medical sciences approved the study. Written informed consent was obtained from parents.

Measurements: Venous blood specimens were collected from all enrolled neonates and their mothers. Collected specimens were stored at -20°C until analysis. The serum 25(OH) D_3 was measured using a chemiluminesence immunoassay. Vitamin deficiency is typically defined as circulating 25(OH) D_3 concentrations less than 20 ng/ml (50 nM/L).[14,15] No consensus on optimal serum 25(OH) D_3 exists. We considered both cut off 10 and 20 to define vitamin D deficiency.

Data analysis: Data were analysed using SPSS software version 13.0 for windows and presented as mean ± standard deviation (SD). The difference between mean values of both groups was compared using student's t test. Quantitative variables were compared by using the chi-square test. A *p* value of 0.05 or less was considered statistically significant.

Results

The neonates in case and control groups were similar with respect to gestation age and birth weight. Demographic characteristics of patients in both groups are showed in Table 1.

None of the neonates had clinical signs of rickets including craniotabes. The mean concentration of vitamin D was 9.6±6.8 ng/ml in neonates of case group, and 14.7±9.3 ng/ml in control group (p=0.02). There was vitamin D deficiency in 37 (92.5%) neonates in case group and 26 (65%) in control group. The concentration of vitamin D was below 10 ng/ml in 26 patients (65%), 10-20 ng/ml in 11 neonates (27.5%); and above 20 ng/ml in 3 cases (7.5%) of neonates in case group. There was vitamin D deficiency in 26 neonates (65%) in control group. It was less than 10 ng/ml in 11 neonates (27.5%), 10-20 ng/ml in 15 neonates (37.5%); and above 20 ng/ml in 13 (32.5) patients in control group, p=0.001 (Table 2).

The mean serum total calcium (laboratory reference range

Table 1 Demographic characteristics of patients

	Case group (neonates with ALRI) N=40	Control group (healthy neonates) N=40	*P value*
Gestation age, wk	38.7±1.7	39.3±0.9	0.16
Birth weight, gr	3168±503	3082±507	0.54
Current body weight, gr	3437±639	3547±676	0.55
Sex			
Male, n (%)	23 (57.5)	22 (55)	0.82
Age, days	16.6±7.3	13.3±7.6	0.11
Apgar score			
1 minute	8.85±0.49	8.95±0.22	0.43
5 minutes	9.94±0.23	10	0.28
Delivery			
Cesarean section, n (%)	21 (52.5)	20 (50)	0.82
Living location			
Industrial cities	24 (60)	25 (62.5)	0.81
Birth order			
First child	27 (67.5)	22 (55)	0.36
Maternal age, yr.	24.3±5.6	27.0±4.5	0.07
Maternal weight, kg	66.8±11.8	73.1±15.7	0.09

ALRI=acute lower respiratory tract infection

Table 2 Neonatal biochemical parameters and vitamin D status in mothers and neonates

Vitamin D concentration (ng/ml)	Case group (neonates with ALRI) N=40	Control group (healthy neonates) N=40	*P value*
Infants			
Less than 10	26 (65%)	11 (27.5%)	0.003
10-20	11 (27.5%)	15 (37.5%)	0.63
More than 20	3 (7.5%)	14 (35%)	0.005
Mothers			
Less than 10	25 (62.5%)	8 (20%)	<0.001
10-20	11 (27.5%)	15 (37.5%)	0.47
More than 20	4 (10%)	17 (42.5%)	0.001
Total calcium, mg/dl	8.98±1.52	9.15±2.14	0.86
Serum phosphorus, mg/dl	5.87±1.17	5.88±1.13	0.95
Alkaline phosphatase, U/Lit	585±191	685±374	0.19

ALRI=acute lower respiratory tract infection

8-10.8 mg/dl), phosphorous (5-7.8 mg/dl) and alkaline phosphatase levels (146-600 U/L) in neonates of two groups are shown in Table 2. Exclusive breast feeding was noted in 35 neonates (87.5%) in case group and 30 neonates (75%) in control group. The mean concentrations of vitamin D was 24.58±8.3 ng/ml in mothers of control group and it was 17.23±10.5 in mothers of case group (p=0.69). There was vitamin D deficiency in 36 (90%) mothers in case group and 23 (57.5%) mothers of neonates in control group, p=0.002 (Table 2). Vitamin D supplementation by multivitamin drops was started in 13 neonates (32.5%) in case group and 20 neonates (50%) in control group (p=0.17). White blood cell count was 10632±4256 in case group and 8190±2095 in control group, p=0.02. Platelet count was not significantly different between two groups. C reactive protein was positive in 95% patients with pneumonia. Blood culture was positive in 3 patients that were coagulase negative staphylococcus in 2 cases and staphylococcus aureus in one patient. Neither patient needed respiratory support with ventilator.

Discussion

In our study, vitamin D deficiency was determined in 92.5% in case group and 65% in control group. Few studies have published about the prevalence of vitamin D deficiency in newborn infants. One study in Netherlands, reported a high prevalence of vitamin D deficiency in newborn infants of dark skinned or veiled mothers. Their cut-off value for vitamin D deficiency was 25 nmol/L. It is necessary to multiply 25(OH) D concentrations in nano gram per mili litter by 2.496 to convert its concentrations to nano moles per liter. The reported prevalence of vitamin D deficiency was 63.3% and they had higher alkaline phosphatase concentrations that suggest increased bone turn over.[16] There is other report of severe vitamin D deficiency in non-European infants[17] without data on their pigmentation. Sachan found similar high prevalence in newborn infants and pregnant mothers in India, a country with abundant sunlight.[18]

In the study of Merewood and co workers, vitamin D deficiency was present in 58% of the newborns and 35.8% of the mothers at Boston.[19] In one study from Boston, vitamin D deficiency (cut off 12 ng/ml) was determined in 65% of neonates.[20] In another study from Pennsylvania, vitamin D deficiency was reported in 9.7% and vitamin D insufficiency in 56.4% of white neonates. Neonates were classified as vitamin D deficient (less than 15 ng/ml), vitamin D insufficient (15-32 ng/ml) or vitamin D sufficient (>32 ng/ml) in their study. Deficiency was more common in white neonates born in spring than those born in summer. Among black neonates, vitamin D deficiency and insufficiency were found in 45.6% and 46.8% of patients without seasonal effect.[21]

Sunlight exposure during spring, summer and fall for 5-15 minutes (from 10 AM to 3PM) provides adequate cutaneous vitamin D synthesis. Black persons and individuals with darker skin require 5-10 times longer sunlight exposure.[22,23]

In one study in Turkey, the serum 25(OH) D_3 levels less than 10 ng/ml was significantly more common in newborns with ALRI.[24] Vitamin D concentration was significantly lower in their mothers. In one study in Indian, 150 neonates aged 2-60 months were enrolled that 80 cases had ALRI. Serum 25 (OH) D_3 increased significantly with age and levels less than 22.5 nmol/L was significantly more common in children with ALRI. They obtained similar results when a 50 nmol/L cut off was used for normal vitamin D status.[13] A study in New Zealand found increased risk of respiratory infection by 3 months of age among infants who had cord blood 25(OH) D_3 concentrations less than 25 nmol/L.[25]

In our study, although serum vitamin D levels were low in most of neonates in both groups, it was significantly lower in patients with ALRI.

The vitamin D concentration in human milk is lower than its levels in regular formulas (20-60 IU/L vs. 400-600 IU/L). If breast feeding infants don't receive vitamin D supplementation, their vitamin D stores could be depleting within 8 weeks after birth.[26,27] Breast milk is ideal for enteral caloric source for infants. Infants born to mothers with vitamin D deficiency are at an increased risk to develop vitamin D deficiency if they have not supplementation with vitamin D. Most of studied neonates were exclusively breast feeding in our study. Low serum vitamin D was common in mothers of studied neonates. Breast milk may not provide enough vitamin D for neonates. The current recommendation for daily vitamin D supplementation may be inadequate, since over one third of studied neonates received vitamin D 400 IU/day from 15 days of birth. Future studies with larger number of patients and longer duration of patient follow up are recommended to determine the optimal daily vitamin D supplementation for prevention of vitamin D deficiency.

Conclusion

Our study results show vitamin D deficiency is a common problem in our community and infants with acute respiratory infections had lower vitamin D concentrations. Therefore, future studies needed to determine how to effectively improve vitamin D status and achieve its optimal function.

Conflict of Interest

None

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