ORIGINAL RESEARCH

To investigate the correlation between acute respiratory distress syndrome (ARDS) and serum 25(OH) vitamin D3 levels in pediatric patients

[1]Arshdeep Saggi, [2]Sukhjiwan Singh Bhandal, [3]Navjiwan Singh Bhandal

Corresponding Author
Arshdeep Saggi
Email: saggiarshdeep@gmail.com

Received: 16 January, 2023 Accepted: 22 March, 2023

ABSTRACT

Aim: To investigate the correlation between acute respiratory distress syndrome (ARDS) and serum 25(OH) vitamin D3 levels in pediatric patients. **Material and methods:** This prospective study included the enrolment of all preterm infants with a gestational age of 32 weeks or less who were admitted to the neonatal intensive care unit (NICU) at our hospital. The diagnosis of RDS was established through the assessment of both radiographic and clinical findings. The utilization of maternal 25-hydroxyvitamin D (25(OH)D) was categorized into three distinct groups.Blood samples from neonatal intensive care unit (NICU) patients were acquired within six hours after birth, while maternal blood samples were collected within the initial four hours following birth. The plasma derived from blood samples obtained from both the infants and mothers was stored at a temperature of -80°C. The samples underwent analysis utilizing a Shimadzu LC-20AT high-performance liquid chromatography system, which was equipped with a UV detector. **Results:** Out of the 100 participants enrolled in the study, respiratory distress syndrome (RDS) was detected in 70 individuals, while the remaining 30 participants did not exhibit any signs of RDS. The levels of 25(OH)D were found to be 7.33 ng/mL in the group with respiratory distress syndrome (RDS) and 10.01 ng/mL in the group without RDS. A statistically significant difference in the levels of 25(OH)D was observed between the two groups (p=0.03). There was no statistically significant correlation observed between maternal vitamin D levels and the development of respiratory distress syndrome (RDS). However, it is worth mentioning that the incidence of RDS in group 1, which consisted of patients with severe 25(OH)D deficiency, was higher at 85.71% . **Conclusion:** The deficiency of 25-hydroxyvitamin D (25(OH)D) is an autonomous risk factor for the development of respiratory distress syndrome (RDS) in premature infants. Conversely, elevated levels of 25(OH)D in neonates at birth may serve as a protective factor against RDS in premature infants.

Keywords: Respiratory distress syndrome, serum 25(OH) vitamin D3, Pediatric

INTRODUCTION

Vitamin D is classified as a fat-soluble vitamin and is known to have significant involvement in the regulation of calcium and phosphorus levels within the body, as well as in the maintenance of bone health and metabolism. The protein under consideration plays a role in both innate and acquired immune responses, as well as autoimmune responses. Additionally, it exerts inhibitory effects on the proliferation of cancer cells, regulates cardiovascular function, and modulates the activity of hormones such as insulin [1]. The production of vitamin D does not occur within the fetus; rather, the fetus obtains vitamin D from the maternal source. A neonate with a very low birth weight (VLBWI), defined as a birth weight below 1,500 grams, typically has a truncated gestational age, leading to diminished maternal transfer of vitamin D, inadequate nutritional provision, and limited exposure to sunlight while receiving care in the neonatal intensive care unit (NICU).

Hence, the prevalence of vitamin D deficiency is widespread, thereby amplifying the risk of neonatal morbidities and mortality [2-4]. The investigation is currently examining the association between vitamin D deficiency and various diseases in preterm infants, including sepsis [5,6], necrotizing enterocolitis (NEC) [7], respiratory distress syndrome (RDS) [8], and bronchopulmonary dysplasia (BPD) [9,10].

Respiratory distress syndrome (RDS) is found to be diagnosed in approximately 50% of very low birth weight infants (VLBWIs) and is a prevalent factor contributing to mortality among premature infants [11]. According to the cited source,

bronchopulmonary dysplasia (BPD) is responsible for 23% of very low birth weight infants (VLBWIs) and 52% of preterm infants weighing between 501 and 750 grams [12].

Nguyen et al. [13] have reported that vitamin D is implicated in the interactions between mesenchymal cells and alveolar epithelial cells, thereby contributing to the maturation of the fetal lung. Type II alveolar cells exhibit the presence of vitamin D receptor and play a role in the production and release of surfactants in response to the presence of vitamin D. The investigation of the impact of vitamin D on pulmonary development, maturation, and postnatal respiratory diseases has emerged as a novel area of research.

MATERIAL AND METHODS

This prospective study included the enrolment of all preterm infants with a gestational age of 32 weeks or less who were admitted to the neonatal intensive care unit (NICU) at our hospital. The exclusion criteria for this study encompassed several factors, namely the rejection of parental consent, the presence of significant congenital abnormalities or chromosomal anomalies in infants, the occurrence of cyanotic congenital heart disease, the occurrence of major maternal infection, and the presence of chorioamnionitis.

The diagnosis of RDS was established through the assessment of both radiographic and clinical findings. The treatment administered to all patients involved the use of nCPAP at a mean airway pressure of 7 cm H2O. In order to ensure that the arterial oxygen pressure remains above 60 mm Hg, it was necessary to administer a specific FiO2 to infants. For infants aged ≤26 weeks, the FiO2 requirement was 0.3, while for infants aged >26 weeks, the FiO2 requirement was 0.4. Infants who required a FiO2 greater than 0.4 were subjected to "early rescue therapy" and administered 200 mg/kg of poractant alfa. A second dose was administered to infants who did not exhibit clinical improvement during the follow-up period and required a FiO2 equal to or greater than 0.4, with a time interval of 6 hours following the initial dose. During the subsequent evaluation, a maximum of three doses of surfactant were administered as a result of respiratory distress syndrome (RDS). The researchers recorded the length of hospitalization, duration of mechanical ventilation, incidence of bronchopulmonary dysplasia, and rates of survival.

The researchers collected demographic information, including the age of the mothers, their level of education, socioeconomic status, and any existing maternal diseases. Gestational age, birth weight, gender, type of delivery, and birth period were documented for all infants in the study.

The utilization of maternal 25-hydroxyvitamin D (25(OH)D) was categorized into three distinct groups: individuals who abstained from its usage throughout pregnancy, individuals who used it sporadically for a duration of less than three months in total, and individuals who were consistent users for a duration of three months or more in total. The patients were categorized into three distinct groups based on their 25(OH)D levels. The first group, referred to as severe deficiency group (group 1), consisted of patients with 25(OH)D levels below 5 ng/mL. The second group, known as moderate deficiency group (group 2), included patients with 25(OH)D levels ranging from 5 to 15 ng/mL. Lastly, the third group, designated as mild deficiency group (group 3), comprised patients with 25(OH)D levels between 15 and 30 ng/mL.[14,15]

Blood samples from neonatal intensive care unit (NICU) patients were acquired within six hours after birth, while maternal blood samples were collected within the initial four hours following birth. The plasma derived from blood samples obtained from both the infants and mothers was stored at a temperature of -80°C. The samples underwent analysis utilizing a Shimadzu LC-20AT high-performance liquid chromatography system, which was equipped with a UV detector. This analysis was conducted at the Biochemistry Laboratory located within the hospital.

STATISTICAL DATA

The statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS) version 25.0 software, developed by SPSS Inc. in Chicago, IL, USA. In addition to conducting descriptive statistical analyses, such as calculating measures of central tendency (mean, median) and dispersion (standard deviation, range), the study data were subjected to two-group comparisons. Specifically, the Student's t-test was employed for comparing two groups with normally distributed data, while the Mann-Whitney U test was utilized for comparing two groups with non-normally distributed data. The one-way analysis of variance (ANOVA) was employed to compare three or more groups that exhibited a normal distribution. The researchers employed logistic regression analysis to investigate the risk factors that influence RDS. The statistical tests employed for the comparison of qualitative data included the Chi-square test, the Fisher-Freeman-Halton test, and Fisher's exact test. A significance level of less than 0.05 was used to determine statistical significance.

RESULTS

Out of the 100 participants enrolled in the study, respiratory distress syndrome (RDS) was detected in 70 individuals, while the remaining 30 participants did not exhibit any signs of RDS. Table 1 provides a summary of the demographic characteristics of patients both with and without Respiratory Distress Syndrome (RDS). The study revealed that RDS patients had significantly lower age in gestational

weeks and birth weights compared to non-RDS patients.

Table 1 Basic profile of the participants

	RDS Positive =70		RDS Negative =30		P value
Gender	**Number**	**Percentage**	**Number**	**Percentage**	**0.21**
Male	50	71.43	17	56.67	
Female	20	28.57	13	43.33	
Gestational age at birth, wk	29.71		30.74		0.001
Birth weight, g	1087		1441		0.001
Type of delivery					0.001
Normal vaginal delivery	2	2.86	8	26.67	
caesarean section	68	97.14	22	73.33	
Antenatal steroid					0.44
Used	31	44.29	12	40	
Not used	39	55.71	18	60	

Table 2 Types of deficiency

Groups		Number	Percentage
Severe deficiency	25(OH)D ≤ 5ng/ml	35	35
Moderete deficiency	25(OH)D 5–15ng/ml	50	50
Mild deficiency	25(OH)D 15–30 ng/ml	15	15

Upon categorizing the patients based on their vitamin D levels, no statistically significant distinctions were observed among the groups in relation to perinatal characteristics, including birth weight, gestational age, gender, ethnicity, delivery type, and antenatal steroid usage, which could potentially serve as risk factors for respiratory distress syndrome (RDS).

Table 3 correlation between demographic data and severity of vitamin D levels

	Severe=35	Moderete=50	Mild=15	P value
Gender				
Male	20	35	12	0.36
Female	15	15	3	
Gestational age at birth, wk	29.44	30.59	29.74	0.14
Type of delivery				0.43
Normal vaginal delivery	3	5	2	
caesarean section	32	45	13	
Antenatal steroid				0.37
Used	12	23	8	
Not used	23	27	7	

The levels of 25(OH)D were found to be 7.33 ng/mL in the group with respiratory distress syndrome (RDS) and 10.01 ng/mL in the group without RDS. A statistically significant difference in the levels of 25(OH)D was observed between the two groups (p=0.03) (Table 4). There was no statistically significant correlation observed between maternal vitamin D levels and the development of respiratory distress syndrome (RDS). However, it is worth mentioning that the incidence of RDS in group 1, which consisted of patients with severe 25(OH)D deficiency, was higher at 85.71% according to Table 4. There were no statistically significant differences observed between the groups that received RDS and those that did not receive RDS in terms of maternal age, educational attainment, maternal vitamin supplementation, and disease status.

Table 4 Maternal and infant 25(OH)D levels and RDS ratios of the study groups

	RDS Positive =70		RDS Negative =30		P value
	Number	**Percentage**	**Number**	**Percentage**	
Severe deficiency	30	85.71	5	14.29	0.07
Moderete deficiency	30	60	20	40	
Mild deficiency	10	66.67	5	33.33	
Maternal, 25(OH)D level (ng/ml)	11.85		10.41		0.63
Infant, 25(OH)D level (ng/ml)	7.33		10.01		0.03

The evaluation of the RDS group revealed a significant association between low levels of vitamin D and an extended duration of mechanical ventilation (p=0.002). Group 3, which exhibited mild vitamin D

deficiency, did not display any instances of BPD. In contrast, the BPD rate in group 1 was found to be 48.57% with a p-value of 0.3.

In the multiple regression analysis, the potential independent risk factors of gestational week, antenatal steroid use, and 25(OH)D levels were examined. The results indicated that higher levels of 25(OH)D in patients (odds ratio [OR] 0.91; 95% confidence interval [CI] 0.91–0.98; p=0.03) and greater gestational age (OR 0.60; 95% CI 0.38–0.79; p=0.002) were found to have a preventive effect on the development of respiratory distress syndrome (RDS).

The study conducted a multivariate analysis to evaluate the potential factors influencing the length of hospital stay. The variables considered in the analysis included late neonatal sepsis, bronchopulmonary dysplasia (BPD), and 25-hydroxyvitamin D (25(OH)D) levels, which were incorporated into the statistical model. Among these three factors, it was determined that Borderline Personality Disorder (BPD) had a notable impact on the length of hospital stay (odds ratio [OR] 69.89; 95% confidence interval [CI] 55.78–89.91; p<0.001).

DISCUSSION

This study aimed to examine the correlation between the development of respiratory distress syndrome (RDS) and levels of vitamin D, and our findings demonstrated that vitamin D deficiency is a distinct risk factor for the development of RDS. It is believed that 25(OH)D plays a role in the prevention of surfactant insufficiency by promoting the growth of type 2 pneumocytes and subsequently enhancing surfactant synthesis. This is considered a crucial factor in the pathophysiology of respiratory distress syndrome (RDS).The user has provided a numerical range, specifically [16,17].

The findings of our study align with the current body of literature, which has also observed a comparable association between vitamin D deficiency and respiratory distress syndrome (RDS). [18,19] In addition to vitamin D deficiency, age in gestational weeks is a significant risk factor for respiratory distress syndrome (RDS). Patients diagnosed with RDS tend to exhibit a lower age in gestational weeks and a lower birth weight. Nevertheless, even after controlling for gestational age, vitamin D deficiency was found to be a significant risk factor. Furthermore, an examination of the literature pertaining to risk factors for respiratory distress syndrome (RDS) indicates that both low birth weight and low levels of 25-hydroxyvitamin D (25(OH)D) are associated with heightened incidence and severity of RDS.[20]

The active form of 25-hydroxyvitamin D (25(OH)D) is recognized to have a crucial function in various tissues and epithelial barriers.[20] While the impact of vitamin D on the development of fetal and neonatal lungs lacks conclusive evidence, research conducted on animals has suggested a positive association between the proliferation of type 2 pneumocytes and fibroblasts, surfactant synthesis, and the upregulation of vitamin D receptors (VDRs) in pulmonary tissue. [21]

Surfactant serves to diminish surface tension and plays a role in the regulation of pulmonary inflammation. Surfactant synthesis is regulated by various factors, such as the release of cytokines, hormones, and growth factors. The administration of corticosteroids promotes the process of fetal lung maturation by facilitating the differentiation of type 2 pneumocytes and enhancing the release of surfactant. [22]

Vitamin D has been found to enhance the synthesis and release of surfactant-related phospholipids in type 2 pneumocytes. Additionally, studies have indicated that during the peak phase of alveolarization, 1,25(OH)2D exerts a positive influence on type 2 pneumocytes and fibroblasts by suppressing programmed cell death and promoting the secretion of surfactant-related phospholipids.[23]

The prevention of programmed cell death leads to a higher quantity of cells after birth.[24,25]

The study conducted by Sakurai et al. (year) demonstrated the significant involvement of 14 C-3 epimer, a metabolite derived from 1,25(OH)2D, in various essential processes such as antenatal lung maturation, lipofibroblast proliferation, and epithelial mesenchymal interaction mechanisms. The vitamin D levels of the patients with respiratory distress syndrome (RDS) in our study were found to be significantly lower, consistent with previous findings reported in the literature. It is important to highlight that there was a significant increase in the RDS rate among patients who exhibited severe vitamin D deficiency.In the present study, it was observed that the patients' age in gestational weeks and birth weights were lower than anticipated, while the rate of cesarean section births was higher in cases of respiratory distress syndrome (RDS).

Tochie et al. [26] conducted a study wherein they found that C/S was identified as a significant independent predictor for RDS. Consistent prenatal monitoring and the avoidance of unwarranted early elective cesarean sections (C/S) have the potential to decrease the occurrence of preterm births and respiratory distress syndrome (RDS).

The patients in group 1 exhibited a statistically significant prolongation in the duration of mechanical ventilation, as well as a 48.57% rate of bronchopulmonary dysplasia (BPD). Based on the potential benefits of elevated 25(OH)D levels on pulmonary maturation, it is plausible to hypothesize that individuals belonging to group 3 exhibited a more favorable prognosis in relation to respiratory distress syndrome (RDS). The speculation arises from the observation of a significantly shorter duration of mechanical ventilation and the absence of bronchopulmonary dysplasia (BPD) in all cases within group 3.

Cetinkaya et al. [27] recently reported a comparable finding, wherein they identified a significant deficiency of 25-hydroxyvitamin D (25(OH)D) in all premature patients with bronchopulmonary dysplasia (BPD). Bronchopulmonary dysplasia (BPD) is considered to be among the most severe morbidities observed in premature patients. Our study has revealed a noteworthy association between BPD and the length of hospital stay. The potential benefits of elevated 25(OH)D levels in the prevention of bronchopulmonary dysplasia (BPD) in premature infants show promise. The existing body of literature does not provide a definitive understanding of the appropriate levels of 25-hydroxyvitamin D (25(OH) D), particularly in the context of premature infants.

According to the definition provided by Fettah et al., 25-hydroxyvitamin D (25(OH)D) deficiency in premature infants is characterized by levels equal to or below 15 ng/mL. Similarly, within the scope of this research, we have established the categorization of vitamin D levels below 5 ng/mL as severe deficiency, while levels ranging from 5 to 15 ng/mL are classified as moderate deficiency. In the existing body of literature, it has been widely acknowledged that 25-hydroxyvitamin D (25(OH)D) levels exceeding 30 ng/ml are considered within the range of normalcy. Hence, the range of 15 to 30 ng/mL was established as the threshold for mild deficiency.[28,29]

It is standard practice in Turkey to routinely recommend multivitamin supplements containing 500 IU of vitamin D for pregnant women. In the present study, there was no observed disparity in maternal vitamin utilization between the RDS and non-RDS cohorts. In accordance with prior research, there was a notable association between the levels of 25-hydroxyvitamin D (25(OH)D) in mothers and neonates. Moreover, it was observed that both maternal and fetal concentrations of vitamin D frequently exhibited deficiencies.[30] Despite the recommendation for vitamin D supplementation during pregnancy, both neonatal and maternal vitamin D levels continue to be low, likely attributable to inadequate adherence to vitamin D supplement usage. Moreover, it is worth noting that premature infants with a gestational age of less than 32 weeks are at a higher risk of experiencing vitamin D deficiency. This can be attributed to their shorter gestation periods and inadequate vitamin D reserves.[31]

The findings of our research indicate that infants who experienced a significant deficiency in 25-hydroxyvitamin D (25(OH)D) displayed elevated rates of respiratory distress syndrome (RDS), a prolonged requirement for mechanical ventilation, and increased rates of bronchopulmonary dysplasia (BPD). Hence, the presence of vitamin D deficiency during the neonatal period could potentially increase the susceptibility of infants to complications associated with premature birth.

CONCLUSION

The deficiency of 25-hydroxyvitamin D (25(OH)D) is an autonomous risk factor for the development of respiratory distress syndrome (RDS) in premature infants. Conversely, elevated levels of 25(OH)D in neonates at birth may serve as a protective factor against RDS in premature infants.

REFERENCES

1. Di Rosa M, Malaguarnera M, Nicoletti F, Malaguarnera L. Vitamin D3: a helpful immuno-modulator. Immunology 2011;134:123–39.
2. Fares S, Sethom MM, Khouaja-Mokrani C, Jabnoun S, Feki M, Kaabachi N. Vitamin A, E, and D deficiencies in tunisian very low birth weight neonates: prevalence and risk factors. Pediatr Neonatol 2014;55:196–201.
3. Newhook LA, Sloka S, Grant M, Randell E, Kovacs CS, Twells LK. Vitamin D insufficiency common in newborns, children and pregnant women living in Newfoundland and Labrador, Canada. Matern Child Nutr 2009;5:186–91.
4. Sutherland ER, Goleva E, Jackson LP, Stevens AD, Leung DY. Vitamin D levels, lung function, and steroid response in adult asthma. Am J Respir Crit Care Med 2010;181:699–704.
5. Cetinkaya M, Cekmez F, Buyukkale G, Erener-Ercan T, Demir F, Tunc T, et al. Lower vitamin D levels are associated with increased risk of early-onset neonatal sepsis in term infants. J Perinatol 2015;35:39–45.
6. Gamal TS, Madiha AS, Hanan MK, Abdel-Azeem ME, Marian GS. Neonatal and maternal 25-OH vitamin D serum levels in neonates with early-onset sepsis. Children (Basel) 2017;4(5): pii: E37. https://doi.org/10.3390/children4050037.
7. Cetinkaya M, Erener-Ercan T, Kalayci-Oral T, Babayiğit A, Cebeci B, Semerci SY, et al. Maternal/neonatal vitamin D deficiency: a new risk factor for necrotizing enterocolitis in preterm infants? J Perinatol 2017;37:673–8.
8. Ataseven F, Aygün C, Okuyucu A, Bedir A, Kücük Y, Kücüködük S. Is vitamin d deficiency a risk factor for respiratory distress syndrome? Int J Vitam Nutr Res 2013;83:232–7.
9. Çetinkaya M, Çekmez F, Erener-Ercan T, Buyukkale G, Demirhan A, Aydemir G, et al. Maternal/neonatal vitamin D deficiency: a risk factor for bronchopulmonary dysplasia in preterms? J Perinatol 2015;35:813–7.
10. Joung KE, Burris HH, Van Marter LJ, McElrath TF, Michael Z, Tabatabai P, et al. Vitamin D and bronchopulmonary dysplasia in preterm infants. J Perinatol 2016;36:878–82.
11. Jobe AH. Animal models, learning lessons to prevent and treat neonatal chronic lung disease. Front Med (Lausanne) 2015;2:49.
12. Lemons JA, Bauer CR, Oh W, Korones SB, Papile LA, Stoll BJ, et al. Very low birth weight outcomes of the National Institute of Child health and human development neonatal research network, January 1995 through December 1996. NICHD Neonatal Research Network. Pediatrics 2001;107:E1.
13. Nguyen TM, Guillozo H, Marin L, Tordet C, Koite S, Garabedian M. Evidence for a vitamin D paracrine system regulating maturation of developing rat lung epithelium. Am J Physiol 1996;271(3 Pt 1): L392–9.

14. Misra M, Pacaud D, Petryk A, Collett-Solberg PF, Kappy M, Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society Vitamin D deficiency in children and its management: review of current knowledge and recommendations. Pediatrics. 2008;122(2):398–417.
15. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al.Endocrine Society Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011;96(7):1911–1930.
16. Nguyen M, Trubert CL, Rizk-Rabin M, Rehan VK, Besançon F, Cayre YE, et al. 1,25-Dihydroxyvitamin D3 and fetal lung maturation: immunogold detection of VDR expression in pneumocytes type II cells and effect on fructose 1,6 bisphosphatase. J Steroid Biochem Mol Biol. 2004;89–90(1–5):93–97.
17. Ballard PL, Ertsey R, Gonzales LW, Gonzales J. Transcriptional regulation of human pulmonary surfactant proteins SP-B and SP-C by glucocorticoids. Am J Respir Cell Mol Biol. 1996;14(6):599–607.
18. Yu RQ, Chen DZ, Hao XQ, Jiang SH, Fang GD, Zhou Q. Relationship between serum 25(OH)D levels at birth and respiratory distress syndrome in preterm infants. Zhongguo Dang Dai Er Ke Za Zhi. 2017;19(11):1134–1137.
19. Kazzi SNJ, Karnati S, Puthuraya S, Thomas R. Vitamin D deficiency and respiratory morbidity among African American very low birth weight infants. Early Hum Dev. 2018;119:19–24.
20. Kong J, Zhang Z, Musch MW, Ning G, Sun J, Hart J, et al. Novel role of the vitamin D receptor in maintaining the integrity of the intestinal mucosal barrier. Am J Physiol Gastrointest Liver Physiol. 2008;294(1):G208–G216.
21. Sakurai R, Shin E, Fonseca S, Sakurai T, Litonjua AA, Weiss ST, et al. 1alpha,25(OH)2D3 and its 3-epimer promote rat lung alveolar epithelial-mesenchymal interactions and inhibit lipofibroblast apoptosis. Am J Physiol Lung Cell Mol Physiol. 2009;297(3):L496–L505.
22. Di Renzo GC, Anceschi MM, Cosmi EV. Lung surfactant enhancement in utero. Eur J Obstet Gynecol Reprod Biol. 1989;32(1):1–11.
23. Lee P, Nair P, Eisman JA, Center JR. Vitamin D deficiency in critically ill patients. N Engl J Med. 2009;360(18):1912–1914.
24. Hansdottir S, Monick MM, Hinde SL, Lovan N, Look DC, Hunninghake GW. Respiratory epithelial cells convert inactive vitamin D to its active form: potential effects on host defense. J Immunol. 2008;181(10):7090–7099.
25. Barnett N, Zhao Z, Koyama T, Janz DR, Wang CY, May AK, et al. Vitamin D deficiency and risk of acute lung injury in severe sepsis and severe trauma: a case-control study. Ann Intensive Care. 2014;4(1):5.
26. Tochie JN, Choukem SP, Langmia RN, Barla E, Koki-Ndombo P. Neonatal respiratory distress in a reference neonatal unit in Cameroon: an analysis of prevalence, predictors, etiologies and outcomes. Pan Afr Med J. 2016;24:152.
27. Çetinkaya M, Çekmez F, Erener-Ercan T, Buyukkale G, Demirhan A, Aydemir G, et al. Maternal/neonatal vitamin D deficiency: a risk factor for bronchopulmonary dysplasia in preterms? J Perinatol. 2015;35(10):813–817.
28. Mulligan ML, Felton SK, Riek AE, Bernal-Mizrachi C. Implications of vitamin D deficiency in pregnancy and lactation. Am J Obstet Gynecol. 2010;202(5):429 e1–429 e9.
29. Cizmeci MN, Kanburoglu MK, Akelma AZ, Ayyildiz A, Kutukoglu I, Malli DD, et al. Cord-blood 25-hydroxyvitamin D levels and risk of early-onset neonatal sepsis: a case-control study from a tertiary care center in Turkey. Eur J Pediatr. 2015;174(6):809–815.
30. Hollis BW, Wagner CL. Assessment of dietary vitamin D requirements during pregnancy and lactation. Am J Clin Nutr. 2004;79(5):717–726.
31. Marshall I, Mehta R, Petrova A. Vitamin D in the maternal-fetal-neonatal interface: clinical implications and requirements for supplementation. J Matern Fetal Neonatal Med. 2013;26(7):633–638.