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The association of serum 25-hydroxyvitamin D levels with early neonatal morbidity and mortality in late preterm infants monitored in the neonatal intensive care unit

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ABSTRACT

Objective: We aimed to determine the association of serum vitamin D levels with early neonatal mortality/morbidity in late-preterm (LP) infants (born between 34 0/7 and 36 6/7 weeks of gestational age) monitored in the neonatal intensive care unit (NICU).

Patients and Methods: This retrospective study was conducted by reviewing live-born LP neonates from singleton pregnancies. The infants were monitored and treated in our hospital's NICU between June 2016 and June 2019.

Results: Maternal age at delivery was higher among infants with adequate vitamin D levels than among those with deficient vitamin D levels (P=0.007). A weak positive correlation was found between maternal age at childbirth and neonates' vitamin D levels (r=0.296). The rate of low-birth-weight deliveries was greater in babies with sufficient vitamin D levels than in those with deficient levels. There was a weak negative association between the number of stools on the day that the infants' serum 25-hydroxyvitamin D (25-OHD) levels were taken and their vitamin D level (P=0.027, r=-0.244).

Conclusions: A significant correlation was shown between serum 25-OHD levels and maternal age and low birth weight in LP neonates. Upon examining the influence of vitamin D levels on the number of defecations per day, no significant difference was detected; however, a weak negative association was identified between them.

Keywords: Late preterm, Mortality, Early morbidity, Vitamin D deficiency

1. INTRODUCTION

Infants with a gestational week (GW) of 34 0/7–36 6/7 or who were born between the 239th-259th postconceptional days are called late preterm (LP) infants [1]. For babies delivered without enduring the last 6 weeks of pregnancy, which is an important period related to the completion of foetal maturation, their major morbidity and mortality rates in the early neonatal period are higher than their rates in the term period. In contrast to term newborns, the resuscitation requirements at birth, respiratory problems during the neonatal period (respiratory distress syndrome (RDS), transient tachypnoea of the newborn (TTN), pneumonia), apnoea, hypoglycaemia, hyperbilirubinemia, sepsis, feeding intolerance, various neurological problems, and frequency of the need for rehospitalization are increased for LP neonates [2-4].

Vitamin D, being one of the fat-soluble vitamins, can be described as a group of sterols that have important roles in the bone-skeletal metabolism of the body and are also hormones and hormone precursors that are produced in the body [5]. The production of vitamin D occurs after its sterol derivative precursors in the skin are under the influence of sunlight, and the precursors transform into the active substance form by being converted in the liver and kidney. Vitamin D is regarded as a vitamin with hormonal properties due to its involvement in many important pathways, such as calcium (Ca) phosphorus (P) metabolism, cell growth, proliferation, development, anti-inflammatory processes, and insulin synthesis [6,7].

The vitamin D levels of premature infants are particularly low, as vitamin D has a short intrauterine half-life. Therefore, these infants are at risk for vitamin D deficiency. The third trimester is especially critical for the placental transfer of vitamin D [8].

Although, there are numerous publications in the literature that have investigated the relationship between 25-hydroxyvitamin D (25-OHD) levels of term and preterm infants and their different morbidities (newborn respiratory distress, bronchopulmonary

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dysplasia (BPD), acute lower respiratory tract infections, RDS, necrotizing enterocolitis (NEC), late-onset neonatal sepsis, retinopathy of prematurity), we were unable to find a study involving only LP infants [9-19]. Therefore, we aimed to determine the association of serum vitamin D levels with early neonatal mortality/morbidity in LP infants.

2. PATIENTS and METHODS

After the approval for this study was obtained from University of Health Sciences Istanbul Bakirkoy Dr. Sadi Konuk Training and Research Hospital Clinical Trials Ethics Committee dated 22.04.2019, and the protocol number was 2019/178; we retrospectively evaluated the medical records of LP neonates treated in the neonatal intensive care (NICU) between June 2016 and June 2019.

Live-born LP infants from singleton pregnancies who were between 34 0/7 and 36 6/7 weeks of gestational age admitted to the NICU were included in this study. Multiple birth babies, those with chromosomal anomalies determined via genetic tests and those diagnosed with perinatal asphyxia were excluded. A total of 83 newborns were included in the study.

The demographic characteristics of the patients, maternal data, anthropometrical and the newborns' clinical parameters that were recorded in the delivery room, clinical data from the NICU, and laboratory data were obtained from our hospital's electronic health record system, the NICU physician and nurse clinical record files, and the delivery room newborn close follow-up baby registration forms.

Serum concentrations of 25-OHD, Ca, P, Mg, and alkaline phosphatase (ALP) were obtained from the data collected in the biochemistry laboratory of our hospital by reviewing the electronic records retrospectively.

When calculating the cumulative vitamin D replacement (parenteral/enteral) dose (IU) that was administered to the baby, on the day the serum 25-OHD level was measured, the doses of any oral multivitamin supplements, along with any vitamin D supplementation that was given intravenously to the neonate through total parenteral nutrition (TPN), were taken as the basis. The amount of vitamin D contained in these drugs was recorded from the original package insert information.

By dividing the LP infants included in the study into 3 groups according to their serum 25-OHD level, the infants were categorized as vitamin D deficient (< 20 ng/ml), insufficient (20-30 ng/ml), and adequate (30-100 ng/ml), and the data were compared statistically.

Statistical Analysis

Data were analysed with SPSS for Windows version 21.0. The distribution of the variables was evaluated with the coefficient of skewness, kurtosis coefficient and the Kolmogorov–Smirnov test. As the continuous variables did not follow a normal distribution in at least one of the groups, nonparametric tests were utilized. For descriptive statistics, the median (min-max) was used to describe continuous variables, and the categorical variables were described with numbers and percentages. The significance of the difference between more than two independent groups was examined using the Kruskal–Wallis test. In the pairwise comparisons between groups, the Mann–Whitney U test was performed to evaluate the variables after the application of the Bonferroni correction. Regarding evaluating the categorical variables, the differences between the groups were assessed via the Pearson's chi-square test and Fisher's exact test. For relationships between nonnormally distributed variables, the correlation coefficients and statistical significance were determined using Spearman's test. All calculations were two-tailed, and a p value of <0.05 was considered statistically significant.

3. RESULTS

Of the 83 infants included in the study, 37 (44.6%) were girls, and 46 (55.4%) were boys. The mean length of gestation was 34.9±0.83 weeks. Twenty-five (30.1%) LP infants were born via spontaneous vaginal birth, and 58 (69.9%) were born by c-section. The average age of the mother at childbirth was 29.9±6.8 years. The mean birth weight of the LP infants was 2471±530.1 g, their mean length was 45.2±2.4 cm, and their average head circumference was 32.5±1.6 cm on average.

The mean APGAR scores of the babies at 1 minute and 5 minutes were 7.1±1.2 and 8.4±0.95, respectively. The indications for admission to the NICU were subclassified as respiratory system diseases, infections, nutritional problems, neonatal jaundice, infant of a diabetic mother and other indications. The most commonly identified indication for hospitalization was respiratory system diseases (congenital pneumonia, TTN, RDS, pneumothorax), involving 68.7% of the infants (n=57).

The average postnatal age of the newborns on admission to the NICU was 15.29±44.9 hours. The mean length of their NICU stay was 17±8.5 days. Noninvasive respiratory support (continuous positive airway pressure (CPAP)/intermittent mandatory ventilation (nasal IMV)) (44.6%) was the method of respiratory support that was most frequently applied. The mean time duration of receiving TPN support was 6.1±4.3 days, that of antibiotic administration was 12±6.7 days and that of phototherapy was 4.1±2.7 days on average. Blood samples from the babies for serum 25-OHD levels were collected on approximately the 9.5±4.3th day of hospitalization. The mean daily urinary frequency of the infants on the day of the serum 25-OHD level measurement was detected was 7.6±1.2, and the daily average number of stools was 3.6±1.7. Upon discharge from the NICU, all of the neonates could feed on their mother's breast.

The mean serum 25-OHD level of the babies was 18.8±12.1 ng/ml, and the simultaneous obtained values of Ca, P, Mg, and ALP on average were 9.7±1 mg/dl, 5.8±1.3 mg/dl, 1.9±0.2 mg/dl, and 250.4±107 U/L, respectively.

Vitamin D was shown to be deficient (group 1) (n=54) in 65.1% of the infants, insufficient (group 2) (n=17) in 20.5%, and sufficient (group 3) (n=12) in 14.5%.

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The maternal demographic, clinical and obstetric data were compared according to the infants' vitamin D levels (Table I). The age of the mother at childbirth was revealed to be significantly different in the 3 groups based on the vitamin D levels (P=0.025). The maternal age at the time of delivery was found to be higher in the infants with sufficient vitamin D levels than in the infants with deficient levels, and this difference was statistically significant (P=0.007). A weak positive correlation was detected between the age of the mothers at childbirth and the vitamin D level (P=0.007 and r=0.296). The vitamin D levels increased with increasing maternal age. There was no statistically meaningful difference between the maternal clinical and obstetric data and the vitamin D levels (P>0.05) (Table I).

Table I. *Comparison of the maternal demographic, clinical and obstetric data of late preterm infants based on serum 25-hydroxyvitamin D levels*

Characteristics	Group 1 (n = 54)	Group 2 (n = 17)	Group 3 (n = 12)	P value
Age of the mother at childbirth (mean ± SD)	28.6 ± 6.5	30.5 ± 7.2	34.5 ± 5.8	0.025*
Mode of delivery				0.83**
NSD	16 (29.6)	6 (35.3)	3 (25)	
C-Section	38 (70.4)	11 (64.7)	9 (75)	
Presence of maternal illness prior to pregnancy[1]				0.09***
No	41 (85.4)	11 (73.3)	7 (58.3)	
Yes	7 (14.6)	4 (26.7)	5 (41.7)	
Presence of maternal gestational diseases and pregnancy-related complications[2]				0.76**
No	28 (58.3)	8 (50)	7 (63.6)	
Yes	20 (41.7)	8 (50)	4 (36.4)	
Oral multivitamin replacement during pregnancy				0.75**
No	25 (47.2)	9 (52.9)	7 (58.3)	
Yes	28 (52.8)	8 (47.1)	5 (41.7)	
Smoking during pregnancy				0.1***
Absent	41 (85.4)	15 (100)	9 (75)	
Present	7 (14.6)	0 (0)	3 (25)	

Values are given as n (%).
**Kruskal–Wallis test, **Pearson's chi-square test, ***Fisher's exact test*
[1]Presence of maternal illness prior to pregnancy: Diabetes, hypertension, thyroid dysfunction (hypothyroidism), kidney diseases, digestive conditions (gastritis and gastroesophageal reflux disease (GERD)), rheumatic disorders, haematological findings (thrombocytopenia), neurological conditions (migraine, epilepsy), respiratory disorders (asthma), cardiovascular diseases.
[2]Maternal gestational diseases and pregnancy-related complications: Preeclampsia, eclampsia, placental abruption, placenta previa, gestational hypertension, gestational diabetes, gestational cholestasis, urinary tract infection during pregnancy, anaemia during pregnancy, hypothyroidism during pregnancy
Group 1: Vitamin D deficiency of the infants, Group 2: Vitamin D insufficiency of the infants, Group 3: Vitamin D sufficiency of the infants

The birth weights of the babies were divided into 2 groups: normal (2500-3999 g) and low birth weight (<2500 g). In group 3, 91.7% of the infants with adequate vitamin D had a low-birth-weight rate, 64% of them in group 2 had a low-birth-weight rate and insufficient levels, 51.9% of the infants in group 1 had a low birth weight rate and vitamin D deficiency, and a statistically significant difference was observed between the groups (P=0.036). The percentage of low-birth-weight infants in group 3 was greater than that in group 1. A weak negative correlation was identified between the vitamin D level and birth weight (P=0.01 and r=-0.280).

The sex, gestational age, birth weight (g), birth length (cm), birth head circumference (cm) and subclasses of these measurements in accordance with the Fenton curve, such as appropriate for gestational age (AGA), large for gestational age (LGA), and small for gestational age (SGA), were compared between the groups, and no statistically remarkable difference was detected (P>0.05).

No statistically significant difference was detected in the comparison of the infants' APGAR scores at 1 and 5 minutes after delivery (P>0.05).

The indications for admission to the NICU (respiratory diseases (congenital pneumonia, TTN, RDS, pneumothorax), infections (early-onset neonatal sepsis, late-onset neonatal sepsis, omphalitis, urinary tract infection), nutritional issues (feeding intolerance), neonatal jaundice (indirect hyperbilirubinemia), baby of a diabetic mother, others (intrauterine growth restriction (IUGR), major congenital anomaly, polycythaemia, congenital metabolic disease, neonatal convulsion, early neonatal transient hypoglycaemia) were contrasted across the groups based on their vitamin D levels, and no statistically meaningful difference was demonstrated (p> 0.05).

Comparisons of the number of daily bowel movements based on the day babies' serum 25-OHD levels were taken between the groups with respect to the vitamin D status, and no remarkable difference was detected (P=0.06) (Table II). However, a weak negative correlation was noted between the number of stools on the day of serum 25-OHD level measurement and the vitamin D level (P=0.027 and r=-0.244).

While reporting the type of hospital discharge from the NICU, most infants in the groups with deficient and insufficient vitamin D levels were discharged with improvement/full recovery, and the medical support requirement at the time of discharge persisted for 1 patient in the group with sufficient vitamin D levels (Table II).

There was no considerable difference identified across the groups when the clinical and laboratory data of the babies in the NICU were compared according to the serum 25-OHD levels (P>0.05) (Table II).

Table II. *Comparison of the neonatal intensive care unit clinical and laboratory data of late preterm infants according to the serum 25-hydroxyvitamin D levels*

Characteristic	Group 1 (n = 54)	Group 2 (n = 17)	Group 3 (n = 12)	P value
Age on admission to the NICU (hours)	13 ± 37	28 ± 73	8 ± 19	0.61*
Weight on admission to the NICU (g)	2500.6 ± 503.7	2325.3 ± 503.1	2249.6 ± 482.4	0.1*
Length of NICU stay (days)	17 ± 9.5	18.3 ± 7.1	15.3 ± 4.7	0.50*
Recurrent NICU admissions status, n (%)				0.15**
Present	1 (1.9)	2 (11.8)	0 (0)	
Absent	53 (98.1)	15 (88.2)	12 (100)	
Respiratory support requirement, n (%)				0.17*
None	11 (20.4)	6 (35.3)	2 (16.7)	
Free-flow blended oxygen	5 (9.3)	2 (11.8)	1 (8.3)	
CPAP/NIV	23 (42.6)	5 (29.4)	9 (75)	
Invasive mechanical ventilation	15 (27.8)	4 (23.5)	0 (0)	
TPN support (day)	6 ± 4.5	6.5 ± 4.8	6.1 ± 3	0.84*
Age at initiation of enteral nutrition (day)	2.6 ± 2.4	2.8 ± 2.9	2.2 ± 0.8	0.96*
Transition time to full enteral feeding (150–160 ml/kg/day)	8.9 ± 5.3	8.4 ± 6.1	8.3 ± 3.3	0.99*
Transition time to full at-breast feedings	9 ± 7.9	9.2 ± 7.4	8.3 ± 6.9	0.98*
Duration of antibiotic therapy (day)	12.5 ± 7.6	11.9 ± 5.7	10 ± 2	0.71*
Duration of phototherapy (day)	3.6 ± 2.2	5.5 ± 3.1	4.1 ± 3.3	0.08*
Mean arterial blood pressure value on test day (at 9 am) (mmHg)	52.9 ± 7.7	52.2 ± 9.2	47.3 ± 9.2	0.46*
Oxygen saturation on test day (SpO2) (%)	98.2 ± 1.9	98.3 ± 1.8	97.9 ± 3.2	0.89*
Heart rate on test day (beats/min)	137.2 ± 12.7	141.6 ± 14	136.5 ± 13.7	0.35*
Daily urinary frequency on test day	7.6 ± 1.1	7.2 ± 1.7	7.9 ± 0.3	0.54*
Number of daily bowel movements on test day	3.9 ± 1.6	2.9 ± 1.8	3.2 ± 1.5	0.06*
Age on test day (day)	9 ± 4.1	11.4 ± 5.7	8.7 ± 1.9	0.21*
Total vitamin D supplementation on test day (IU)	1521.6 ± 1742.2	1731.8 ± 1525.4	1165 ± 735	0.71*
Concurrent laboratory tests on test day				
Ca (mg/dl)	9.6 ± 1	9.7 ± 1	10.1 ± 0.8	0.33*
P (mg/dl)	5.6 ± 1.2	6.2 ± 1.2	6.1 ± 1.6	0.08*
Mg (mg/dl)	1.9 ± 0.2	1.9 ± 0.2	1.9 ± 0.3	0.80*
ALP (U/L)	263.4 ± 116.3	221.8 ± 86.6	234 ± 84.5	0.36*

*Values were given as the mean ± standard deviation. Test day refers to the day of the serum 25-OHD level measurement. *Kruskal–Wallis test, **Fisher's exact test*

4. DISCUSSION

The age of the mother at childbirth was shown to be significantly different in the 3 groups that were based on the vitamin D levels. It was established that the age of the mother at the time of delivery was higher in those with sufficient vitamin D levels than in those with vitamin D deficiency. A weak positive correlation was demonstrated between the age of mothers at childbirth and their vitamin D levels. Consistent with our results, it has been reported in the literature that vitamin D deficiency, as measured using cord blood, is more common in babies who are born to younger mothers [20, 21]. In a study published in 2019, unlike our findings, mothers of newborns with low vitamin D levels were revealed to be older at the time of delivery [10]. There are also studies that did not identify a significant relationship between maternal age at childbirth and the serum 25-OHD levels of the mothers and the 25-OHD levels in the cord blood of their infants [8, 9, 15, 22-26].

In our study, we allocated neonates into two groups: normal (2500-3999 g) and low (<2500 g) birth weights. The rate of low birth weight was demonstrated to be 91.7% in group 3, where the patients had sufficient vitamin D, 64.7% in group 2 with insufficient levels, and 51.9% in group 1 with vitamin D deficiency, and a statistically significant difference was observed across the groups. The percentage of low birth weight was found to be higher in those who had sufficient vitamin D than in those with deficient levels. With regard to our study, a weak negative correlation was detected between vitamin D level and birth weight. Thus, it was shown that birth weight decreased as the

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vitamin D levels increased. In contrast to our findings, studies that have revealed a positive correlation between birth weight and serum vitamin D levels exist in the literature, and it is stated in these studies that maternal vitamin D deficiency during pregnancy elevates the risk of low birth weight and increases the number of SGA newborns [23, 24, 27-29]. However, there are also studies that have also identified no relationship between the serum 25-OHD levels of the mother during pregnancy or the serum 25-OHD levels in their infant's cord blood and the presence of normal or low birth weight [8, 15, 22]. Nevertheless, in a large-scale retrospective cohort study published in Southern China in 2021, it was established that the risk of macrosomic (birth weight ≥4000 g) births increases in babies whose mothers have low vitamin D levels during the second trimester of pregnancy [30]. This study supports our results.

When investigating the association of bowel movements per day, as a marker of intestinal motility [31], with serum 25-OHD levels, a weak negative correlation was detected between the number of stools on the day that the vitamin D level was measured and the serum vitamin D concentration. As the vitamin D level increased, the number of stools decreased. There was no study in the literature that has explored the relationship between serum 25-OHD levels and bowel movements of newborns, but the data indicating that VDR plays a role in cell proliferation, differentiation, and induction of apoptosis within the intestinal system endorse our findings [32].

On reviewing the relationship between the discharge from the NICU and the serum 25-OHD levels of infants in our study, discharge with improvement/full recovery was noted to be 100% in the groups with vitamin D deficiency and insufficiency. For the group with sufficient serum vitamin D concentrations, 91.7% were discharged with improvement/full recovery and 8.3% had other types of discharge (Orogastric tube, MV support, oxygen support). In our study, the mortality rate of the LP babies in the NICU was detected as 0%. That is, we have discharged all of our infants in the groups with different vitamin D levels home from the hospital; consequently, we cannot comment on the association of vitamin D levels with mortality. Upon examination of the literature, in a study conducted on very low birth weight (1250 g and below) newborns, discharge home with oxygen support was observed to be statistically higher among those with deficient 25-OHD vitamin levels. In the same study, no correlation was identified between the serum 25-OHD level and mortality rate at the hospital [9]. Another study, in which babies with a birth weight of less than 1500 g were included, reported that the death rate before discharge increased as the vitamin D level decreased [10].

In the comparisons of the maternal clinical characteristics, obstetric data and mode of delivery across the groups according to the serum 25-OHD level of the LP babies, no statistically remarkable difference was revealed in our study. Additionally, there are studies in the world literature demonstrating results similar to our data [8-10, 13, 15, 20, 21]. However, among different studies contrasting identical characteristics based on the 25-OHD vitamin levels, there are also studies that have presented significant results [24, 27, 33]. In our study, no statistically meaningful difference was noted between the maternal use of multivitamin supplements during pregnancy and the serum 25-OHD levels of LP infants. In a study investigating the relationship between vitamin D supplementation during pregnancy and the cord blood 25-OHD levels of newborns, no difference was identified, which is consistent with our study [21]. Contrary to our findings, in a study conducted with women who took low levels of vitamin D supplementation during pregnancy, the serum 25-OHD levels were found to be deficient in both the mothers and in the cord blood of their babies [26]. With respect to another study, a negative correlation was established between maternal vitamin D supplement intake during pregnancy and the serum 25-OHD level of the baby [10]. No statistically significant difference was found in our study between smoking during pregnancy and the serum 25-OHD levels of LP newborns, and these results are compatible with the literature [21].

In our study, no statistically meaningful difference was established comparing the sex of LP babies and their gestational age at delivery based on the serum 25-OHD levels. According to neonatal studies conducted at different gestational weeks, no correlation was detected between sex and the gestational age of the infant and maternal and newborn cord blood 25-OHD levels [8-10, 13, 15, 20-23, 26, 34]. Unlike our data, there are also studies in the world literature revealing significant results [35, 36].

When comparing the birth weight (g), birth length (cm), birth head circumference (cm) of LP babies and the subcategorized groups of these measurements between the groups and according to the Fenton curve using the AGA, LGA, SGA with serum 25-OHD levels of LP infants, there was no statistically significant difference observed across the groups in our study. In the literature, other studies have had similar [9, 10, 21, 26, 34] and dissimilar [10, 20, 27, 28] results compared to our study.

In our study, when the 1 – and 5-minute APGAR scores were compared based on the serum 25-OHD levels of LP babies, no statistically significant difference was found between the groups. Similarly, in the literature, no relationship was demonstrated between the APGAR scores at 1 and 5 minutes after birth and the serum 25-OHD levels of newborns [9, 15, 21]. In contrast, in one study, the 1-minute APGAR score diminished as the vitamin D level decreased, and the 5-minute Apgar score did not change [10].

In our study, when the indications for admission to the NICU were compared between the groups according to the serum 25-OHD levels of LP babies, no statistically significant difference was found. There are studies in the world literature similarly showing no association [8, 10, 19, 21, 34, 37, 38]. However, significant statistical results were also established in many studies that have investigated the relationship between different disease groups (RDS, BPD, pneumonia, sepsis, NEC, IUGR) and the serum 25-OHD levels of newborns, worldwide and in our country, in different age groups [9-13, 15, 16, 18, 34].

On review of the association between the NICU clinical data of LP babies and serum 25-OHD levels, different results were noted for each parameter. First, there was no statistically significant

difference detected between the groups when comparing LP infants in terms of age on admission to the NICU, weight on admission, recurrent admissions status, and length of NICU stay according to the serum 25-OHD levels. In local and international studies, similar results to our study [8, 9, 21] and other studies [10, 13, 39] have been reported.

In our study, comparing the respiratory support requirement of LP babies in NICU, duration of receiving TPN support, time at initiation of enteral nutrition, transition time to full enteral feeding, transition time to full breast feedings, durations of antibiotic treatment and phototherapy between the groups based on the 25-OHD levels, no statistically remarkable difference was observed. In many studies, such as our study, no relationship was found between the need for respiratory support and the serum 25-OHD levels of newborns [8, 9, 13, 39]. In another study, it was demonstrated that with decreasing serum 25-OHD levels of infants, the length of stay on mechanical ventilation as well as the durations of receiving noninvasive ventilation and total supplemental oxygen support were increased [10]. Additionally, no correlation was identified between the 25-OHD level of cord blood and the rate of phototherapy in the literature [21].

Serum creatinine, blood urea nitrogen and urinary frequency are indicators of kidney function [40]. In our study, we also reviewed the relationship between the number of times that the LP infants urinated on the day that the serum 25-OHD levels were taken and the vitamin D levels, and we did not find a statistically significant difference. There was no study identified in the literature that has investigated the relationship between the serum 25-OHD levels of newborns and urinary frequency.

On examination of the association between discharge from the NICU and the serum 25-OHD levels of LP babies, 100% of the patients in the group with vitamin D deficiency had discharge with improvement/full recovery, as for the group with sufficient serum vitamin D levels, 91.7% were discharged with improvement/full recovery and 8.3% had other forms of hospital discharge (Orogastric tube, MV support, oxygen support). In our study, the mortality rate of LP newborns in the NICU was detected as 0%. When the infants with very low birth weight (1250 g and below) were compared according to the serum 25-OHD levels, those with vitamin D deficiency were found to be discharged home more often with supplemental oxygen. Moreover, in this study, no correlation was detected between the serum 25-OHD levels and mortality at the hospital [9]. Contrary to our data, in a study conducted with babies with a birth weight of <1500 g, it was demonstrated that the mortality rate prior to discharge increased as the vitamin D levels decreased [10].

In our study, when the NICU clinical and laboratory data of LP babies were compared between the groups according to the 25-OHD levels, no statistically significant difference was found, and no study that has investigated this relationship was found in the literature.

There was no statistically remarkable variation detected in our study. When the LP babies' postnatal age on the day that the serum 25-OHD level was taken, the total vitamin D supplementation (IU) and simultaneous laboratory tests (Ca, P, Mg, ALP) were compared with respect to the vitamin D levels. In line with our study, no correlation was noted between the vitamin D levels and serum concentrations of Ca, P, Mg, and ALP in two studies [20, 26].

Conclusion

We examined the association of maternal and neonatal demographic and clinical data with the serum 25-OHD levels in LP infants. By reviewing the parameters, we determined that the serum vitamin D levels of the babies rose with increasing maternal age. Higher vitamin D levels were observed in infants born with low birth weight in comparison to those delivered with a normal birth weight. We demonstrated a weak negative correlation between the number of stools per day and the vitamin D level. A limitation of our study is that the vitamin D levels of the neonates were not measured from cord blood because of the retrospective nature of the study.

Compliance with Ethical Standards

Ethical approval: Ethical approval was obtained from University of Health Sciences Istanbul Bakirkoy Dr. Sadi Konuk Training and Research Hospital Clinical Trials Ethics Committee dated 22.04.2019, and the protocol number was 2019/178. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

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