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Adverse Effects of Quarantine on Maternal and Neonatal Vitamin D Levels

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ABSTRACT

Vitamin D deficiency, which is considered a global pandemic, has become an even more important problem during the COVID-19 quarantine period. Our aim with this study is to investigate the change in vitamin D levels in babies of pregnant women who could not benefit from UV-B rays during the quarantine period.

Retrospective study, and infants with hypocalcemia and low vitamin D levels (<20 ng/mL) hospitalized in the neonatal intensive care unit for any reason were included in the study. The patients were divided into two groups (study group and control group) and compared statistically. Study group of infants affected by the quarantine period (n:94); The control group was infants (38 infants) who were hospitalized in the neonatal intensive care unit for any reason before the quarantine.

After the coronavirus quarantine period, annual hospitalization rates with the diagnosis of vitamin D deficiency increased from 1.4% to 3% (*p:0.035*). There was a significant decrease in serum vitamin D levels of the babies in the study group (*p:0.001*). Calcium treatment durations of the babies in the study group were higher than the babies in the control group (*p:0.045*).

Although it is known that the application of vitamin D and calcium supplementation to women before pregnancy, during pregnancy, and lactation period leads to positive results, especially in newborns during the quarantine period, we should be alert to vitamin D deficiency especially, in newborns in this period.

Keywords: Quarantine, vitamin D, ultraviolet B rays

Introduction

Coronavirus disease (COVID-19) is a new infectious disease caused by strains of coronavirus (1). Although the effectiveness of the coronavirus epidemic has decreased recently, unfortunately, its effectiveness still continues. Although most infected individuals survive the disease asymptomatically, some patients may develop COVID-19 as a severe coronavirus disease (systemic hyper-inflammation, acute respiratory distress syndrome, and multi-organ failure) (2,3). In addition to creating negative situations related to multi-organ involvement in humans, COVID-19 infection also causes sociological and psychological negative situations (stress, anxiety, depression, frustration, boredom, insomnia, anger, post-traumatic stress and loneliness) (4,6). It has caused widespread anxiety and fear in humans, especially during the quarantine period (7,8). This state of anxiety is felt more especially in pregnant women who represent a high-risk population and who are concerned about protecting their own health and fetus (7,9-11). Anxiety disorders and stress during pregnancy are among the factors that may adversely affect the psychosocial health of mothers and babies (12,13). Because of these reasons; The COVID-19 period has caused extreme anxiety in pregnant women, causing these individuals to have more restrictions in their lives. Unfortunately, these restrictions have negatively affected the social life and health of pregnant women in many ways.We thought that because pregnant women were isolated at home during the COVID-19 quarantine period, they could not benefit from sunlight [UV-B (ultraviolet-B)] sufficiently, and therefore, vitamin D deficiency could be seen more frequently in pregnant women and their babies during the quarantine period. It is known that fetal vitamin D concentrations are directly related to maternal vitamin D concentrations, and it is known that the leading cause of vitamin D deficiency in infants is usually secondary vitamin D deficiency to the mother

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(14). For this reason, it is accepted as an inevitable result that the babies of pregnant women with vitamin D deficiency will also have vitamin D deficiency.

Although there are many studies on COVID-19 and vitamin D levels in the literature, as far as we know, there are no studies on quarantine-related vitamin D and calcium levels of pregnant women and newborn babies of these pregnant women. In this study, we aimed to investigate the rate of change in vitamin D and calcium levels of pregnant women and their babies due to quarantine and to investigate the response of patients to treatment.

Materials and Methods

Our study is a retrospective study and the study group consists of infants who were admitted to the neonatal intensive care unit for any reason between October 2020 and October 2021 and whose biochemical parameters were found to be treatable with hypocalcemia and vitamin D deficiency. The control group consisted of infants hospitalized in the neonatal intensive care unit for any reason before the COVID-19 epidemic period (between October 2018 and October 2019). The ethics committee approval of our study was obtained from the ethics committee of our hospital (2020-KAEK-141/274). The records of the patients included in the study were obtained from our hospital's automation system. Demographic characteristics (week of gestation, birth weight, mode of delivery, gender), clinical outcomes (coexistence of hypocalcemia clinic, relationship between vitamin D deficiency and seasonal variation, time of detection of hypocalcemia, calcium treatment dose, magnesium or cholecalciferol treatment requirements) of the patients were recorded.

Hypocalcemia in laboratory tests during hospitalization in neonatal intensive care unit [Serum total calcium level <8 mg/dL (2 mmol/L) in term infants, <7 mg/dL (1.75 mmol/L) infants in preterm infants), ionized calcium 3-4.4 mg/L (0.75-1.1 mmol/L)] and low $25(OH)_2D_3$ (25 hydroxyvitamin D_3) levels (<20 ng/mL) were included in the study (15). A $25(OH)_2D_3$ level was defined as <10 ng/ml severe vitamin D deficiency. $25(OH)_2D_3$, calcium, ionized calcium, and phosphorus levels were routinely inspected by the mothers of babies who were started on calcium therapy due to vitamin D deficiency in our intensive care unit, to determine the etiology, and were also recorded in case report forms retrospectively. Hypocalcemic newborns of diabetic mothers, newborns of pregnant women who took vitamin D supplements during pregnancy, newborns with hypocalcemia but normal vitamin D levels, and newborns of mothers who were pregnant during the pre-quarantine period were excluded from the study.

Statistical Analysıs: Statistical analysis were performed using the SPSS 26.0 software package (SPSS Inc, Chicago, Illinois). Descriptive statistical analysis was performed on demographic data. Normality of outcome distribution was evaluated with the Kolmogorov-Smirnov test. Continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range, IRR), while categorical variables were detailed as frequency (n) and percentage (%). Student t test or Mann Whitney U test was used for ordinal outcome in pairwise comparisons in independent groups, and chi-square test was used in the analysis of categorical data. All analytical procedures were carried out with a 95% confidence interval, and a p value <0.05 was interpreted as significant.

Results

In the one-year period before the coronavirus quarantine period, the number of infants followed up in the neonatal intensive care unit with the diagnosis of hypocalcemia and vitamin D deficiency was 38, and the annual hospitalization rate was 1.4%. After the quarantine period, this number increased to 94 and the annual hospitalization rate increased to 3% (p:0.034). Seasonal differences were not found to be effective in the rates of hospitalization in the intensive care unit in infants with vitamin D deficiency and hypocalcemia (*p>0.05*) (Table 1.).

While the biochemical calcium values taken in the early period (postnatal 12th hour) of the babies in the study group were normal, it was found that hypocalcemia occurred later. There was no statistically significant difference between the two periods in terms of the initiation time of calcium treatment (started between the 3rd and the 5th day) (*p>0.05*) (Table 2).

We observed a statistically significant decrease in vitamin D levels of newborns affected by the COVID-19 quarantine period compared to the pre-COVID-19 period. (*p:0.001*). The decrease in vitamin D levels during the quarantine period was associated with an increase in severe vitamin D deficiency (*p:0.002*). In addition, it was determined that the duration of calcium treatment was longer in infants with severe vitamin D deficiency who were affected by the COVID-19 quarantine period (*p:0.045*) (Table2). As a complication of vitamin D deficiency and hypocalcemia in the patients included in the study; vitamin D level was <10 ng/mL and calcium

Table 1: Demographic Characteristics Of Patients With Vitamin D Deficiency Before and After The COVID-19 Quarantine Period

	Before the quarantine period	Quarantine period	p value
Newborns with hypocalcemia and vitamin D deficiency / Patients admitted to the NICU	38/2734	94/3190	0.034
Ratio of patients with hypocalcemia and vitamin D deficiency to all hospitalized patients (%)	1.4	3	0.034
Gestation week (weeks)	36,9 ± 1.9	36.9 ± 2.1	>0.05
Gestational weight (gram)	3074 ± 02	2849 ± 612	>0.05
Cesarean section n (%)	29 (76)	63 (67)	>0.05
Male n (%)	25 (66)	63 (67)	>0.05
Seasonal distribution of vitamin D deficiency (%)	Spring-Summer (58) Autumn-Winter (42)	Spring-Summer (50) Autumn-Winter (50)	>0.05

NICU: Neonatal intensive care unit

level was 5 mg/dL in 1 baby who was found to be positive for COVID-19 and died during follow-up. In addition, calcitriol treatment was required for 2 patients who were hospitalized in the intensive care unit and were given calcium support for 30 days during the pandemic period. There was no difference between the two periods in terms of complications that may develop due to vitamin D deficiency.

Discussion

In this study, we found a significant increase in the rates of hypocalcemia due to vitamin D deficiency in the NICU during the COVID-19 quarantine period compared to the pre-epidemic period. In addition, we found that the babies of pregnant women who were affected by the quarantine period had lower vitamin D levels and needed longer-term calcium support treatment due to vitamin D deficiency.

One of the necessary conditions for the continuation of human life is sunlight. Based on numerous studies on vitamin D, he concluded that "without the ultraviolet (UV) part of the sunlight spectrum, there would be no vitamin D on earth" (13). Sun rays and vitamin D are indispensable for supporting the bone-muscle health of our body, maintaining metabolic functions and a strong immune system (16). Angeline et al found that the percentage of vitamin D_3 produced from epidermal 7-DHC increased significantly with time and dose of UV-B radiation exposure (17). For adequate vitamin D production, it is recommended that the arms and legs receive 15-30 minutes of sunlight during the day (18). In previous studies, it is known that vitamin D_3 levels resulting from sun exposure and dietary D_2 levels affect the total circulating vitamin D level. It has been observed that most of the vitamin D is obtained by exposure to sunlight, the effect of dietary intake is low, and dietary D2 levels are insufficient (19). In our study, vitamin D levels were thought to be associated with direct UV-B rays, since pregnant women who took oral vitamin D supplements were excluded from the study.

Reports of vitamin D deficiency are increasing in pregnant women who do not get enough sunlight, do not take vitamin D supplements, who have vitamin D deficiency during pregnancy but cannot be detected, and infants fed only with breast milk. The milk of healthy, lactating women contains relatively small amounts of vitamin D. Therefore, exclusively breastfed babies are more prone to vitamin D deficiency if their exposure to sunlight is limited (20). In our study, it was observed that the number of babies diagnosed with hypocalcemia and vitamin D deficiency in the neonatal intensive care unit during the quarantine period increased 2.5 times compared to the pre-quarantine period. These results show that the rate of pregnant women benefiting from

Table 2: Clinical Outcomes of Newborns With Hypocalcemia and Vitamin D Deficiency, Their Mothers

	Before Quarantine Period (2019-2020) (n=38)	Quarantine Period (2020-2021) (n=94)	p value
Mother			
25(OH)2vitamin D3 (ng/mL)	9 (7.2-11.3)	8.4 (6.4-11.2)	>0.05
iCa (mmol/L)	1.23±0.09	1.32±0.12	>0.05
Albumin (g/dL)	4.09±0.58	3.62±0.71	> 0.05
P (mg/dL)	3.75±0.71	3.79±0.83	>0.05
Newborn			
25(OH)2vitamin D3 (ng/mL)	11.65 (9.4-16)	7.9 (4.3-13.6)	0.001
Early calcium value (at postnatal 12th hour) (mg/dL)	8.7±0.6	8.75±0.65	>0.05
Ca (mg/dL)	7.1(6.7-7.4)	7.1(6.6-7.4)	>0.05
iCa (mmol/L)	0.95±0.06	0.95±0.09	>0.05
Albumin(g/dL)	3.31±0.39	3.1±0.4	>0.05
P (mg/dL)	7.02±1.44	6.2±1.4	>0.05
Newborn			
Ca treatment duration (days)	4.2±2.28	6±4.69	0.045
Time to start Ca treatment (postnatal day)	3.97±4.2	4.26±5.5	>0.05

(iCa: ionized calsium, Ca: calsium, P: phosphorus)
Statistical analysis: Student t test or Mann Whitney U test was used

sunlight has decreased considerably during the quarantine period.

Maternal deficiency is the most important factor in low vitamin D concentrations in infants (13). Vitamin D deficiency usually manifests as asymptomatic hypocalcemia in infants. They are diagnosed as idiopathic during newborn intensive care unit admissions. Although asymptomatic neonatal hypocalcemia often resolves spontaneously over time, it should be treated as adverse effects of hypocalcemia on the brain and cardiovascular system have been reported (15). In addition to the higher number of pregnant women with vitamin D deficiency during the quarantine period, the severity of vitamin D deficiency in newborn babies born in this period was also higher than in newborns in the pre-quarantine period. In addition, the response of these babies to hypocalcemia treatment was later. We interpreted this situation as being related to the severity of vitamin D deficiency in the baby.

The strength of this study is that it is a study investigating the effects of sociological and lifestyle changes on vitamin D values of pregnant women and their babies during the COVID-19 quarantine period. It is important because it is the first study to clinically investigate the inability of pregnant women and their babies to benefit from UV-B rays and indirectly the effect of UV-rays on vitamin D levels during the quarantine period applied with the epidemic. The weakness of the study is that it is a retrospective study and the criteria affecting the vitamin D levels of mothers could not be standardized (it could not be questioned whether pregnant women benefit from sunlight during the quarantine period and how dress pregnant women).

Pregnant women, fetuses and newborn babies constitute the most risky population in terms of both the vitamin D deficiency and the COVID-19 epidemic. It should be taken into account that the benefit of sunlight by all people, especially pregnant women, may decrease during possible quarantine periods that may develop in the coming years. It should be considered that possible vitamin D deficiency that may develop in this population, which constitutes a sensitive population, may cause neonatal

morbidity and mortality. Additionally, giving vitamin D supplements to these populations is an important issue that requires sensitivity by clinicians.

References

1. Güner Ö, Öztürk R. Psychological and social impact and lifestyle changes among pregnant women of COVID-19 pandemic: A qualitative study. Archives of psychiatric nursing 2022;36:70-77.
2. Liu Y, Sawalha AH, Lu Q. COVID-19 and autoimmune diseases. Current opinion in rheumatology 2021;33:155-162.
3. Kim JS, Lee JY, Yang JW, et al.Immunopathogenesis and treatment of cytokine storm in COVID-19. Theranostics 2021;11:316-329.
4. Bao Y, Sun Y, Meng S, et al. 2019-nCoV epidemic: address mental health care to empower society.Lancet (London, England) 2020;395:37-38.
5. Erdoğan A, Hocaoglu A. Psychiatric aspect of infectious diseases and pandemic: A review. KlinikPsikiyatri Dergisi-Turkish Journal Of Clinical Psychiatry 23, 2020.
6. Kackin O, Ciydem E, Aci OS, et al. Experiences and psychosocial problems of nurses caring for patients diagnosed with COVID-19 in Turkey: A qualitative study.
7. The International journal of social psychiatry 2021;67:158-167.
8. Serafini G, Parmigiani B, Amerio A, et al. The psychological impact of COVID-19 on the mental health in the general population. QJM: monthly journal of the Association of Physicians 2020;113:531-537.
9. Tee ML, Tee CA, Anlacan JP, et al. Psychological impact of COVID-19 pandemic in the Philippines. Journal of affective disorders 2020;277:379-391.
10. Ravaldi C, Wilson A, Ricca V, et al. Pregnant women voice their concerns and birth expectations during the COVID-19 pandemic in Italy. Women and birth: journal of the Australian College of Midwives 2021;34:335-343.
11. Wu Y-T, Zhang C, Liu H, et al. Perinatal depression of women along with 2019 novel coronavirus breakout in China2020.
12. Dashraath P, Wong JLJ, Lim MXK, et al. Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. American journal of obstetrics and gynecology 2020;222:521-531.
13. Körükcü Ö, Deliktaş A, Aydin R, et al. Gebelikte psikososyal sağlık durumu ile doğum korkusu arasındaki ilişkinin incelenmesi. Clinical and Experimental Health Sciences2017;7:159-165.
14. Güner Ö, Öztürk R. Psychological and social impact and lifestyle changes among pregnant women of COVID-19 pandemic: A qualitative study. Archives of psychiatric nursing2021.
15. Zhao R, Zhou L, Wang S, Yin H, Yang X, Hao L. Effect of maternal vitamin D status on risk of adverse birth outcomes: a systematic review and dose-response meta-analysis of observational studies. Eur J Nutr. 2022 Sep;61(6):2881-2907.
16. Namgung R, Tsang RC. Perinatal calcium and phosphorus metabolism. Nephrology andfluid/electrolyte physiology, neonatology questions and controversies (3rd ed). Philadelphia, Elsevier 2019; 65-84.
17. Wacker M, Holick MF. Sunlight and Vitamin D: A global perspective for health. Dermato-endocrinology 2013; 5: 51-108.
18. Angeline J. Veronikis, Muhammet B. Cevik, Rachel H. Allen et al. Evaluation of a Ultraviolet B Light Emitting Diode (LED) for Producing Vitamin D3 in Human Skin.Anticancer Research 2020; 40(2): 719-722.
19. Hossein-nezhad A, Holick MF. Vitamin D for health: a global perspective. Mayo Clinic proceedings. Elsevier 2013;720-755.
20. Morita D, Nishida Y, Higuchi Y. Short-range ultraviolet irradiation with LED device effectively increases serum levels of 25(OH)D. J Photochem Photobiol B 2016; 164: 256-263.
21. Yoon Ju Bae, Juergen Kratzsch. Vitamin D and calcium in the human breast milk,Best Practice & Research Clinical Endocrinology & Metabolism 2018; 32: 39-45.