Evaluation of Patients with Hypocalcemia in Pediatric Emergency Department

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Abstract

Objective: We aimed to evaluate the demographic, clinical, and laboratory findings of patients who presented to the pediatric emergency outpatient clinic of our hospital and whose tests revealed hypocalcaemia, and to determine whether the coronavirus disease 2019 pandemic affected the frequency of hypocalcemia.

Methods: Between 1 March 2019 and 1 March 2021, the gender, age, gestational age, gestational week, birth weight, history of comorbidities, presenting complaint, physical examination findings, diet, duration of breastfeeding, duration of vitamin D intake were recorded in patients aged 0-18 years who presented with various complaints and were found to have hypocalcemia. All data were divided into two periods as pre-pandemic and pandemic period and compared within themselves.

Results: The mean age of the 35 patients in the study was 6.3 years and 18 of them were male. The rate of regular and adequate vitamin D use was 22.86%. In etiological diagnoses, vitamin D insufficiency was 11.43% and vitamin D deficiency was 74.28%. When the etiological diagnoses were evaluated according to seasonal distribution before the pandemic and seasonal distribution after the pandemic, no significant difference was found in both groups.

Conclusion: Vitamin D deficiency and insufficiency was found to be the most common etiological cause in patients with hypocalcemia in pediatric emergency department. The rate of regular and adequate use of vitamin D supplementation was also found to be low, and in order to increase this rate, it should be planned to increase compliance with the vitamin D supplementation program in primary health care institutions.

Keywords: Hypocalcemia, pediatric emergency, 25-hydroxy vitamin D, pandemic

Introduction

Calcium (Ca) is a mineral used in many vital functions in our body. Contraction of muscles, nerve transmission, bone metabolism, and coagulation are the main roles of calcium.^{1,2} Normal serum Ca concentration varies according to age intervals in childhood: it decreases immediately after birth, increases again after the first week, and reaches normal levels; it is slightly higher in the neonatal period compared to childhood.³ Hypocalcemia in children may be asymptomatic or may be seen with a wide range of signs and symptoms. Very young age groups present more frequently with symptoms such as weakness, feeding problems, facial contractions, tremors, or seizures because the complaints cannot be expressed accurately.⁴ Older age groups may present with tetany, paresthesia, and tingling in the mouth and fingers, which are findings of neuromuscular irritability. In chronic hypocalcemia, mild irritability may be observed or it may be asymptomatic.⁵

Calcium homeostasis is maintained by multiple organ systems. The parathyroid glands sense hypocalcemia via membrane-bound receptors and rapidly produce parathormone (PTH). PTH promotes

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e-mail: drsedacevik@hotmail.com DOI: 10.5152/cjm.2024.24024 bone resorption towards calcium release. PTH increases urinary Ca retention in the kidneys and renal activation of 1,25-dihydroxy vitamin D. Finally, normalization of calcium inhibits PTH release by feedback.⁶ The formation of 1,25-dihydroxy vitamin D requires adequate amounts of precursor vitamin D from the diet or through exposure to ultraviolet (UV) light. Most of the vitamin D we need is obtained from short-term sun exposure, even during daily activities; therefore, sunlight plays an important role in maintaining calcium homeostasis.⁷ The main role of this vitamin is to increase intestinal calcium absorption.⁶

Risk factors for hypocalcemia have been identified through global and regional studies. Researchers in India reported that low vitamin D levels, staying indoors during the daytime, living in metropolitan areas with high-rise buildings, and sunscreen use contributed significantly to hypocalcemia.8 Khan et al. reported that the consumption of fresh unfortified milk, lack of sun exposure, lack of maternal education, and living in large crowded families may be potential causes of hypocalcemia.9 Infants' consumption of cow's milk or formula milk containing large amounts of phosphate may also cause hypocalcemia.¹⁰ Among all these causes, the most important etiology leading to hypocalcemia is vitamin D deficiency.¹¹ It has long been known that severe vitamin D deficiency leads to rickets, bone deformities, and poor bone mineralization. 11-13 The prevalence of nutritional rickets, which is a problem in both developing and developed countries, is reported to be between 1.6% and 19.0% in our country.14 In Türkiye the Ministry of Health initiated a nationwide campaign in 2005 to give

400 IU/day of vitamin D to all children aged 0-1 year to eliminate nutritional rickets.¹⁵ After the campaign, the incidence of nutritional rickets decreased below 1% in eastern Türkiye between 2007 and 2008.¹⁶

In this study, we aimed to evaluate the demographic, clinical, and laboratory findings of patients who presented to the pediatric emergency outpatient clinic of our hospital and whose tests revealed hypocalcemia, and to determine whether the Covid-19 pandemic affected the frequency of hypocalcemia.

Methods

In our study, the data and patient files of 35 patients aged 0-18 years who presented to the pediatric emergency outpatient clinic of our hospital between 1 March 2019 and 1 March 2021 with various complaints and whose tests revealed hypocalcemia were retrospectively analyzed from the hospital automation system. Ethics Committee approval was obtained from Prof. Dr. Cemil Tascioglu City Hospital before the study (Approval no:183, Date: November 6, 2013). This study was conducted in accordance with the Declaration of Helsinki, and informed consent was obtained from all participants and their parents. Gender, age, gestational week, birth weight, history of comorbidities, presenting complaint, physical examination findings, diet (breast milk, breast milk and formula, breast milk and supplementary food), duration of breast milk intake, and duration of vitamin D intake were recorded. Ca, ionized calcium (iCa), phosphorus (P), alkaline phosphatase (ALP), magnesium (Mg), albumin (alb), PTH, and 25-hydroxy vitamin D (25-OHD) levels measured at admission were recorded.

A serum calcium level below 8.5 mg/dL was considered hypocalcemia.³ Vitamin D deficiency was considered vitamin D deficiency if 25-OHD level was <12 ng/ml and vitamin D insufficiency if 25-OHD level was 12-20 ng/ml.¹⁷ Patients with low serum Ca and high serum P levels and normal or low PTH levels were diagnosed as hypoparathyroidism.¹⁸

All data were divided into the pre-pandemic period between 1 March 2019 and 12 March 2020, and pandemic period between 13 March 2020 and 1 March 2021, and compared within themselves.

Statistical Analysis

The Statistical Package for Social Sciences version 25.0 software (IBM Corp.; Armonk, NY, USA) was used for statistical analysis of the data. Categorical measurements were summarized as number and percentage, and continuous measurements were summarized as mean and standard deviation (median and minimum-maximum where necessary). Chi-square test was used for comparisons of categorical expressions. Shapiro–Wilk test was used to determine whether the parameters in the study showed normal distribution. Mann–Whitney *U*-test was used for the parameters that did not show normal distribution. Spearman's rho correlation test was used to determine the relationship between continuous measurements. Statistical significance level was taken as 0.05 in all tests.

Results

In our study, 35 patients who presented to the pediatric emergency outpatient clinic of our hospital between 1 March 2019 and 1 March 2021 with various complaints and were found to have hypocalcemia were evaluated. The mean age of the patients was 6.3 years (0-16.9 years) and 51.43% of them were male. The mean birth weight was 3177.4 \pm 542.6, 2 (5.7%) were preterm, 33 (94.29%) were term, 1 was low birth weight (2000 g), and 1 was macrosomic (5000 g). When analyzed in terms of presenting complaints, the most common complaint was seizure with a rate of 40%. 31.43% of patients had a history of comorbidity. The

rate of vitamin D use was low, with only 22.86% used vitamin D regularly and in adequate doses. A mixed diet was the most preferred diet, with a rate of 45.71%. Laboratory findings showed a mean serum calcium (Ca) level of 6.65±0.9 mg/dL (normal range: 8.5-10.5 mg/dL), ionized calcium (iCa) level of 0.84±0.1 mmol/L (normal range: 1.12-1.32 mmol/L), phosphorus (P) level of 4.33 ± 1.8 mg/dL (normal range: 4-7 mg/dL), ALP level of 594.9±479.9 U/L (normal range: 50-420 U/L), albumin (Alb) level of 4.08 ± 0.6 g/dL (normal range: 3.5-5.5 g/dL), and 25-OHD level 8.31 ± 6.4 ng/mL (normal range: 20-100 ng/mL). Clinical and sociodemographic characteristics, as well as laboratory findings of the patients included in the study, are shown in Table 1.

The most common etiological diagnosis was vitamin D deficiency with a rate of 74.28%. Vitamin D insufficiency, hypoparathyroidism, and hypomagnesaemia were found with rates of 11.43%, 11.43% and 2.86%, respectively. The etiological diagnoses of the patients included in the study, are shown in Table 2.

In Table 3, clinical and sociodemographic characteristics, as well as laboratory data of patients admitted before and during the pandemic period are compared. When the biochemical parameters of the patients admitted before and during the pandemic period were compared, no significant difference was observed between the groups (P > .05) (Table 3).

The etiological diagnoses of patients admitted before and during the pandemic were compared, and no significant difference was found when evaluated according to seasonal distribution (p=0.31). When the etiological diagnoses were evaluated according to seasonal distribution before the pandemic and seasonal distribution after the pandemic, no significant difference was found in both groups (p=0.32, p=0.39, respectively) (Table 4).

Discussion

In our study, 68.57% of the patients were previously healthy and did not have any disease that would impair calcium absorption or vitamin D metabolism. This shows that hypocalcemia and vitamin D deficiency are not limited to certain disease groups and are important problems in the general pediatric population. In this context, the importance of vitamin D supplements for all children for the prevention and treatment of hypocalcemia should be emphasized, and health policies should be developed in this regard. Calcium, an important mineral, makes up a large proportion of bones and teeth and keeps tissues firm, strong, and flexible, allowing normal body movements. The ionized calcium pool in the circulatory system, intercellular fluid, and various tissues regulates the contraction and dilatation of blood vessels, muscle function, blood clotting, nerve conduction, and hormonal secretion. 19,20 Neglect of adequate calcium intake or low calcium levels in childhood may lead to serious health problems, including hypocalcemia in children.

In our study, the data of patients who presented to the pediatric emergency outpatient clinic of our hospital and were found to have hypocalcemia over a 2-year period, 1 year before the COVID-19 pandemic and 1 year during the COVID-19 pandemic period when curfews were imposed, were presented. It was shown that the most common cause of hypocalcemia was vitamin D deficiency, and the rate of regular vitamin D use in accordance with the vitamin D supplementation program was low with 22.86%.

Vitamin D is important for bone development, especially in infancy when growth is very rapid, and prophylactic doses of vitamin D are necessary to prevent possible complications in this period. Hypocalcemia is one of these complications, and the mean age of the patients with hypocalcemia in our study was 6.3 years (range 0-16.9 years). Karataş et al. reported the mean age

Table 1. Clinical and Sociodemographic Characteristics and Laboratory Findings of the Patients

	Number (n)	Percentage (%)
Gender		
Female	17	48.57
Male	18	51.43
Age at presentation (years) [median (lower–upper limit)]	6.3 (0-	16.9 years)
Week of gestation		
Term	33	94.29
Preterm	2	5.71
Nutrition		
Mixed diet	16	45.71
Breast milk	1	2.86
Breast milk and formula	3	8.57
Breast milk and supplementary food	1	2.86
Unknown	14	40.0
Duration of breastfeeding		
Unknown	3	8.57
Did not receive	6	17.14
<6 months	12	34.29
>6 months	14	40.0
Duration of vitamin D use		
Unknown	4	11.43
Not used	16	45.71
Irregular	7	20.0
Regular and adequate dosage	8	22.86
Application Complaint		
Seizures	14	40.0
Gastrointestinal complaints (vomiting, diarrhea, abdominal pain)	4	11.43
Respiratory distress	3	8.57
Other*	14	40.0
Additional Illness		
None	24	68.57
Epilepsy	2	5.71
Cerebral palsy	2	5.71
Di George syndrome	1	2.86
Down syndrome	1	2.86
		(Continued)

Table 1. Clinical and Sociodemographic Characteristics and Laboratory Findings of the Patients (Continued)

Thidings of the Fatients (Continued)							
	Number (n)	Percentage (%)					
Sturge Weber syndrome	1	2.86					
Other**	4	11.42					
Physical Examination							
Normal	23	65.71					
Expiratory length+crepitant rales	4	11.43					
Motor mental retardation	2	5.71					
Other***	6	17.14					
Laboratory findings	Mean ± SS	Med (Minimum– Maximum)					
Ca (mg/dL) (N: 8.5-10.5)	6.65 ± 0.9	6.53 (5.1-8.4)					
iCa (mmol/L) (N: 1.12-1.32)	0.84 ± 0.1	0.83 (0.62-1.09)					
P (mg/dL) (N: 4-7)	4.33 ± 1.8	3.79 (2.42-10.66)					
ALP (U/L) (N: 50-420)	594.9 ± 479.9	458 (63-1956)					
Mg (mg/dL) (N:1.8-2.5)	2.13 ± 0.4	2.1 (1.2-2.98)					
Albumin (g/dL) (N: 3.5-5.5)	4.08 ± 0.6	4.19 (2.5-5.0)					
PTH (pg/ml) (N: 15-65)	227.1 ± 156.6	199 (9.7-622)					
25-OHD (ng/ml) (N: 20-100)	8.31 ± 6.4	5.89 (3-35)					

25-OHD, 25 hydroxy vitamin D; Ca, calcium; iCa, ionized calcium; P, phosphorus; ALP, alkaline phosphatase; Mg, magnesium; PTH, parathormone.

*Numbness in lips and hands (n = 5, 14.29%), scorpion sting (n = 2, 5.71%), growth retardation (n = 1, 2.86%), swelling in eyes (n = 1, 2.86%), decreased sucking (n = 1, 2.86%), constipation (n = 1, 2.86%), urticaria (n = 1, 2.86%), dizziness (n = 1, 2.86%), fever (n = 1, 2.86%). **Single kidney agenesis (n = 1, 2.86%), Hashimoto thyroiditis (n = 1, 2.86%), Niemann-Pick disease (n = 1, 2.86%), dilated cardiomyopathy (n = 1, 2.86%), ***petechiae (n = 1, 2.86%), abdominal distension (n = 1, 2.86%), nystagmus (n = 1, 2.86%), port-wine stain (n = 1, 2.86%), rachitic rosary (n = 1, 2.86%), urticaria (n = 1, 2.86%).

 Table 2. Etiological Diagnoses of the Patients

Diagnosis	Number (n)	Percentage (%)
Vitamin D insufficiency	4	11.43
Vitamin D deficiency	26	74.28
Hypoparathyroidism	4	11.43
Hypomagnesaemia	1	2.86

of patients with hypocalcemia as 131 months.²¹ In our study, no significant difference was found in terms of gender, as in the study of Naz et al.²²

In our study, the most common cause of hypocalcemia was found to be vitamin D deficiency and insufficiency, with a rate of 85.71%. In Yıldız et al.'s study, moderate or severe vitamin D deficiency was found in all patients.²³ Prevention of hypocalcemia and nutritional rickets can be provided by three methods,

Table 3. Clinical and Sociodemographic Characteristics and Laboratory Data of Patients Admitted Before and During the Pandemic

	Pre-pandemic	Post-pandemic	P
Gender (n (%))			
Female	8 (44.4)	9 (52.9)	.615
Male	10 (55.6)	8 (47.1)	
Gestational week ((n (%))			
Term	16 (88.9)	17 (100)	.367
Preterm	2 (11.1)	-	
Birth weight (Mean ± SS)	3075±707.9	3285.9±262.4	.085
Laboratory findings	Mean ± SD	Med (Minimum– Maximum)	
Ca (mg/dL) (N: 8.5-10.5)	6.65±0.91	6.65±0.97	.856
iCa (mmol/L) (N: 1.12-1.32)	0.82 ± 0.15	0.86 ± 0.12	.597
P (mg/dL) (N: 4-7)	4.15 ± 1.41	4.51 ± 2.07	.908
ALP (U/L) (N: 50-420)	643.38 ± 468.5	543.5 ± 500.9	.391
Mg (mg/dL) (N:1.8-2.5)	2.10 ± 0.3	2.16 ± 0.4	.869
Albumin (g/dL) (N: 3.5-5.5)	4.13 ± 0.6	4.04 ± 0.7	.959
PTH (pg/mL) (N: 15-65)	251.4 ± 166.0	20.3 ± 146.6	.391
25-OHD (ng/mL) (N: 20- 100)	9.00 ± 7.6	7.57 ± 5.0	.409

P < .05, chi-square, Mann–Whitney U.

25-OHD: 25 hydroxy vitamin D; ALP, alkaline phosphatase; Ca, calcium; iCa, ionized calcium; Mg, magnesium; P, phosphorus; PTH, parathormone.

including exposure to sunlight, food supplementation, and vitamin D supplementation. Vitamin D supplementation of 400 IU/day under the age of one year and 600 IU/day between the ages of 1 and 18 years and in adults is recommended for the prevention of rickets. ^{17,24,25} The percentage of regular vitamin D use was found to be low, at 22.86%, in our study. In one study, it was suggested that the reason for not using vitamin D was that families did not know

the importance of vitamin D and did not comply with its use.²⁶ In order to increase this rate, increasing compliance with the vitamin D supplementation program in primary health care institutions is important for the prevention of nutritional rickets.

In our study, the most common presenting complaint was seizure with a rate of 40%. Tetany, muscle spasms, laryngeal spasm, and generalized seizures may be observed as a result of neuromuscular stimulation due to hypocalcemia.^{27,28} Yıldız et al.²³reported that the most common presenting complaint was seizure with a rate of 50% in their study. In a study by Khan et al.,²⁹ it was found that the frequency of hypocalcemia was 68.3% in children presenting with afebrile seizures.

In a study by Yıldız et al.²³ on patients hospitalized with a diagnosis of nutritional rickets, it was reported that 28.6% had curvature of the legs and delayed walking. In our study, rickets was found on physical examination in only one patient, and physical examination findings were normal in 65.71% of the patients. The fact that bone findings related to hypocalcemia were not frequent in our patients was attributed to the fact that the patients presented to the pediatric emergency department for different reasons and were incidentally found to have hypocalcemia.

Eleven (31.42%) of the patients had a history of comorbidities, and 24 (68.57%) of them were previously healthy and did not have any diseases that would impair Ca absorption or vitamin D metabolism. According to our study, vitamin D deficiency and hypocalcemia can also be a problem in healthy children, and in this context, the importance of vitamin D supplements for the prevention and treatment of hypocalcemia in all children should be emphasized. In health policies, measures should be taken to increase children's daily vitamin D intake, and parents and health-care professionals should be made aware.

Extraordinary circumstances, such as the COVID-19 pandemic, may affect children's dietary habits, physical activity, sun exposure, and thus have a negative impact on calcium and 25-OHD metabolism. In such cases, more attention should be paid to meet the 25-OHD needs of children, and 25-OHD supplements should be increased if necessary. Karataş et al.²¹ found only low Ca and high PTH levels to be statistically significant during the restriction period, but no significant difference was found between vitamin D levels. In our study, when the pre-pandemic and post-pandemic periods were analyzed, no significant difference was found in both calcium levels and the frequency of vitamin D deficiency or insufficiency. We attributed this to the fact that our study was not a community survey and included only patients who presented

Table 4. Comparison of the Diagnoses of Patients Admitted before and During the Pandemic According to Seasonal Distribution

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	Pre-pandemic					Post-pandemic					р
Diagnosis	Sp* n	Su** n	Au*** n	Wi**** n	Total n (%)	Sp* n	Su** n	Au*** n	Wi**** n	Total n (%)	0.31
D vit insufficiency	-	-	1	2	3 (16.67)	-	-	1	-	1 (5.88)	
D vit deficiency	2	1	4	4	11 (61.1)	-	4	4	7	15 (88.24)	
Hypoparathyroidism	-	1	2	-	3 (16.67)	-	-	1	-	1 (5.88)	
Hypomagnesaemia	1	-	-	-	1 (5.56)	-	-	-	-	-	
Р			.32					.39			

*Spring.

^{**}Summer.

^{***}Autumn.

^{****}Winter.

to the pediatric emergency department and were found to have hypocalcemia.

The limitations of our study include the retrospective collection of data and the small number of patients. This may limit the generalization of our results. Therefore, conducting prospective cohort studies and using larger sample groups from different geographical regions may help us better understand the incidence and risk factors of hypocalcemia in children.

Availability of Data and Materials: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Prof. Dr. Cemil Tascioglu City Hospital (Approval no:183, Date: November 6, 2023).

Informed Consent: Informed consent was obtained from the patients and their parents.

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