ORIGINAL ARTICLE

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Vitamin D Status and Its Relationship with Clinical Presentation Characteristics in Children with the Diagnosis of Type 1 Diabetes

Tip 1 Diyabet Tanısı Alan Çocuklarda D Vitamini Durumu ve Klinik Başvuru Özellikleri ile İlişkisi

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ABSTRACT

Aim: This study is conducted to examine the correlation between vitamin D deficiency and type 1 diabetes since diabetes incidence is rising and recent studies have revealed extra osseous effects of vitamin D.

Materials and Methods: Eighty patients with newly diagnosed type 1 diabetes and 30 patients with no systemic disease were included in the study. Serum 25-hydroxyvitamin D (25-OHD), parathormone (PTH), calcium (Ca), phosphorus (P), and alkaline phosphatase (ALP) samples were obtained from both groups. Blood gas parameters were also obtained from the diabetic group. Information concerning vitamin D usage during pregnancy and infancy was acquired through personal interviews with patient's mothers.

Results: 25-OHD levels were lower in the diabetic group than in the controls (24.43±16.25 ng/mL vs. 34.55±15.03 ng/mL, respectively, p=0.001), but the difference was not significant when seasonal variation was taken into consideration (33.44±17.23 ng/mL, vs. 34.55±15.03 ng/mL, p>0.05). Vitamin D levels were similar between the groups with diabetic ketoacidosis and non-acidotic group (p>0.05, for all). Ca, P, ALP and PTH levels were also similar at the time of diagnosis in the acidotic and non-acidotic groups (p>0.05, for all). The relationship between vitamin D use during pregnancy and infancy and the development of type 1 diabetes was similar between the diabetic and control groups (p>0.05).

Conclusion: No significant effects of vitamin D deficiency/insufficiency on the development of diabetes and clinical status at admission was detected. Vitamin D intake in infancy and pregnancy exhibited no protective effect against the progression of diabetes. Therefore, it does not seem possible to reach a definitive conclusion about the relationship of vitamin D and type 1 diabetes.

Keywords: Type 1 diabetes, diabetic ketoacidosis, vitamin D

ÖZ

Amaç: Bu çalışma, diyabet insidansının artması ve D vitamininin ekstra osseöz etkilerini ortaya koyması nedeniyle D vitamini eksikliği ile tip 1 diyabet arasındaki ilişkiyi incelemek amacıyla yapılmıştır.

Gereç ve Yöntem: Çalışmaya yeni tanı almış tip 1 diyabetli 80 hasta ve sistemik hastalığı olmayan 30 hasta dahil edildi. Her iki gruptan da serum 25-hidroksivitamin D (25-OHD), parathormon (PTH), kalsiyum (Ca), fosfor (P) ve alkalen fosfataz (ALP) örnekleri alındı. Diyabetik gruptan kan gazı parametreleri de alındı. Gebelik ve bebeklikte D vitamini kullanımı, hastaların annelerinden karşılıklı görüşme ile öğrenildi.

Bulgular: 25-OHD düzeyi diyabetik grupta kontrollere göre daha düşüktü (sırasıyla 24,43±16,25 ng/mL, 34,55±15,03 ng/mL, p=0,001), ancak mevsimsel değişkenlik dikkate alındığında fark anlamlı değildi (33,44±17,23 ng/mL, 34,55±15,03 ng/mL, p>0,05). (D vitamini düzeyleri ketoasidoz olan gruplar ve asidoz olmayan grup arasında benzerdi (p>0,05, hepsi için). Asidoz olan ve olmayan grupta tanı anında Ca, P, ALP ve PTH düzeyleri de benzerdi (p>0,05, hepsi için). Gebelik ve bebeklik döneminde D vitamini kullanımı ile tip 1 diyabet gelişimi arasındaki ilişki diyabetli ve kontrol grupları arasında benzerdi (p>0,05).

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Sonuç: D vitamini eksikliği/yetersizliğinin diyabet gelişimi ve başvuru anındaki klinik durum üzerinde anlamlı bir etkisi saptanmamıştır. Bebeklik döneminde ve gebelikte D vitamini alımı diyabetin ilerlemesine karşı koruyucu bir etki göstermemiştir. Bu nedenle D vitamini ve tip 1 diyabet ilişkisi hakkında kesin bir sonuca varmak mümkün görünmemektedir.

Anahtar Kelimeler: Tip 1 diyabet, diyabetik ketoasidoz, D vitamini

INTRODUCTION

In children, type 1 diabetes is one of the most common chronic diseases, the incidence of which is growing. Despite the improvements in science and technology, the factors involved in the etiopathogenesis of type 1 diabetes are still not fully understood in all respects. This has encouraged the performance of further studies on type 1 diabetes. Accordingly, research has investigated the genetic factors involved in the pathogenesis of type 1 diabetes and environmental factors triggering the disease in the presence of genetic factors[1].

Vitamin D deficiency has been implicated in the pathogenesis of diabetes as an environmental factor[1,2]. In addition to many current studies of the relationship between vitamin D and type 1 diabetes, knowledge obtained from studies on vitamin D receptor (VDR) knock-out mice has strengthened the possibility of such a relationship. The immune system has been shown to increase the risk of the development of autoimmune diseases such as type 1 diabetes and inflammatory bowel disease in the presence of triggering factors in "roughly" normal cases with knockout VDRs or vitamin D deficiency[3].

Recent studies have observed low levels of vitamin D at the time of diagnosis in patients with type 1 diabetes. Vitamin D deficiency causes cellular cytotoxicity and cellular destruction as a result of its effects on the immune system, leading to diabetes by impairing the synthesis and secretion of insulin[4]. It also predisposes to infections and facilitates the presentation of patients with diabetic ketoacidosis (DKA). Vitamin D deficiency also increases the tendency to DKA, while on the other hand, acidosis in DKA causes low levels of vitamin D by reducing the conversion of 25-hydroxyvitamin D (25-OHD) to its active form and the synthesis of vitamin D-binding proteins[5].

In the light of this role of vitamin D in the pathogenesis of diabetes, studies have investigated the protective role of sufficient vitamin D levels against the development of diabetes. Research has focused on vitamin D supporting programs and the importance of babies using vitamin D in the first year of their lives. The use of supplements including vitamin D by mothers during pregnancy also affects serum levels of vitamin D in early infancy[6].

The objective of this study was to evaluate vitamin D levels in newly diagnosed patients with type 1 diabetes, and to examine the effects of vitamin D levels according to clinical manifestations at presentation. This study was conducted to evaluate vitamin D levels at presentation in patients newly diagnosed with type 1 diabetes, and the relationship between clinical presentation characteristics and vitamin D levels, and to assess the status of vitamin D intake by mothers during pregnancy and by infants in the first year of life, between a diabetic patient group and a control group.

MATERIALS AND METHODS

This study was performed in Kocaeli University Medical Faculty Department of Pediatrics. The patient group consisted of 80 patients who were admitted to the pediatric endocrinology and diabetes outpatient clinics, pediatric clinics, or pediatric emergency departments with newly diagnosed type 1 diabetes during 20 months between March 1, 2009 and November 1, 2010. The control group consisted of 30 patients admitted to pediatric clinics for various reasons during 3 months in the summer between June 1, 2010 and September 1, 2010. The members of the control group were selected from patients with no chronic disease capable of affecting vitamin D metabolism (renal failure, liver disease, gastrointestinal resection, hyperparathyroidism etc.), and not receiving drugs affecting that metabolism (such as phenytoin, phenobarbital, insulin, and thyroid hormone).

A questionnaire investigating the use of vitamin D during infancy and maternal use of vitamin D and similar supplements during pregnancy was performed. Vitamin D intake during infancy was evaluated based on the duration of intake and regularity of use.

Body mass indices (BMI) [weight (kg)/height (m^2)] were calculated in all patients and controls.

Laboratory Measurements

Venous blood glucose, blood ketone, and blood gas parameters were studied in patients with newly diagnosed type 1 diabetes. Patients were divided into two groups - those with and without DKA. The degree of DKA was evaluated based on pH values and 2006-2007 consensus guidelines of the International Society for Pediatric and Adolescent Diabetes (ISPAD). pH values <7.3 were classified as mild DKA, pH<7.2 as moderate DKA, and pH<7.1 as severe DKA[7].

Levels of calcium (Ca), phosphorus (P), alkaline phosphatase (ALP), parathormone (PTH), and 25-OHD were studied in both the patient and control groups.

The reference values for 25-OHD recognized by the American Academy of Pediatrics and the Pediatric Endocrinology Society are used to evaluate vitamin D status in the human body. Accordingly, 25-OHD>100 ng/mL was regarded as excess, 20-100 ng/mL as normal (sufficiency), 15-20 ng/mL as insufficiency, 5-15 ng/mL as deficiency, and <5 ng/mL as severe deficiency[8]. The study were approved by the Kocaeli University Faculty of Medicine of Local Ethics Committee [protocol number: 24.02.09-(5/17), date: 21.03.2011-(1/6)]. Informed consent was obtained from children and their parents.

Statistical Analysis

The study data were analyzed using Statistical Package for the Social Sciences 13.0 for Windows software. Normal distribution of the variables, variance homogeneity, and numbers of subjects were examined, and appropriate tests were applied. The Student's t-test, and the Mann-Whitney U, chi-square, and Kruskal-Wallis tests were used in the analysis. P<0.05 values were considered statistically significant.

RESULTS

Eighty patients with newly diagnosed type 1 diabetes were included in the patient group and 30 patients in the control group. No significant difference was found between the patients with type 1 diabetes and the control group in terms of demographic characteristics except for BMI (p=0.002). However, the mean 25-OHD and PTH values differed significantly between the two groups (p=0.001) (Table 1).

Since the control group was investigated in summer, that group was compared with diabetic patients diagnosed in summer in order to determine whether the difference between the groups was seasonal in nature. The mean 25-OHD levels were 33.44±17.23 ng/mL in the patient group and 34.55±15.03 ng/mL in the control group, the difference was not statistically significant (p>0.05). However, the mean PTH values differed significantly between the patient and control groups (p=0.020) (Table 2).

The rates of regular vitamin D intake in the first year of life and during pregnancy were similar between the patients with type 1 diabetes and the control group (p>0.05) (Table 3).

No significant correlation was found between vitamin D levels and pH, HCO_3, osmolarity, Na values, or duration of symptoms (p>0.05) (Table 4).

In terms of the relationship between clinical manifestations at presentation and vitamin D levels, 25 (31%) patients presented with mild DKA, 10 (12.5%) patients with moderate DKA, 13 (16%) patients with severe DKA, and 32 (40%) patients without developing metabolic acidosis. The mean 25-OHD was <15 ng/mL in 26% of patients and 15-20 ng/mL in 21% of patients.

Table 1. Comparison of demographic features and Ca, P, ALP, 25-OHD, and PTH parameters between the patient and control groups

	Patients with type 1 diabetes Number / (%)	Controls* Number / (%)	p
Gender			
Male	44 / (55.0)	15 / (50.0)	>0.050
Female	36 / (45.0)	15 / (50.0)	
Age			
<5 years	21 / (26.2)	10 / (33.3)	
5-10 years	25 / (31.2)	8 / (26.6)	
10-15 years	32 / (40.0)	9 / (30.0)	
>15 years	2 / (2.5)	3 / (10.0)	
Mean age (years)	8.38±4.25	8.45±5.39	>0.050
BMI	16.08±2.90	18.72±5.68	**=0.002**
Ca (mg/dL)	9.41±0.58	9.65±0.50	0.970
P (mg/dL)	4.26±1.01	4.62±0.60	0.690
ALP (U/L)	231.76±99.31	203.57±110.77	0.142
25-OHD (ng/mL)	24.43±16.25	34.55±15.03**	**0.001**
PTH (pg/mL)	25.29±15.01	40.02±14.6**	**0.001**

*Investigations were performed in summer in the control group.

**The Mann-Whitney U test was used since this was not normally distributed.

Ca: Calcium, P: Phosphorus, ALP: Alkaline phosphatase, 25-OHD: 25-hydroxyvitamin D, PTH: Parathormone, BMI: Body mass index

Table 2. Mean vitamin D and PTH values in patients with type 1 diabetes who were diagnosed in the same season as the controls

	Patients with type 1 diabetes (n=20)	Controls (n=30)	p
25-OHD (ng/mL)	33.44±17.23	34.55±15.03	>0.050
PTH (pg/mL)	28.87±20.28	40.02±14.65	**0.020***

*Mann-Whitney U test, Student's t-test.

25-OHD: 25-hydroxyvitamin D, PTH: Parathormone

Table 3. Evaluation of regular vitamin D intake in the first year of life and during pregnancy

	Patients with type 1 diabetes Number / (%)	Controls Number / (%)	p
Regular vitamin D intake in the 1st year (Yes)	29 / (44.6)	15 / (68.1)	>0.050
Regular vitamin D intake in the 1st year (No)	36 / (55.4)	7 / (31.9)	>0.050
Vitamin supplements intake during pregnancy (Yes)	35 / (51.5)	9 / (37.5)	>0.050
Vitamin supplements intake during pregnancy (No)	33 / (48.5)	15 / (62.5)	>0.050

There was no statistically significant difference between the patient and control groups when vitamin D levels were classified according to their serum concentration. Fourteen patients in our study had acidosis presented with vitamin D levels <15 ng/mL, and 34 patients with acidosis had vitamin D >15 ng/mL. Metabolic acidosis existence ratio values were also similar between the patients with mean 25-OHD< 15 ng/mL and those with mean 25-OHD>15 ng/mL among the patients with type 1 diabetes (p>0.05) (Table 5).

There was no significant difference between the patients and control groups in terms of the relationship between DKA status and 25-OHD, Ca, P, ALP, or PTH (p>0.05) (Table 6).

DISCUSSION

The increasing incidence of type 1 diabetes with increasing incidence of vitamin D deficiency also supports the idea that vitamin D deficiency may be a potential factor in the pathogenesis of type 1 diabetes. Accordingly, several studies have been conducted on the subject. Data obtained from animal studies about the relationship between type 1 diabetes and vitamin D have most commonly been obtained from non-obese diabetic (NOD) mice[3]. Mathieu and Badenhoop[9] showed that the incidence of autoimmune diabetes decreased from 56% to 8% after 200 days in NOD mice after using active vitamin D analogues. Similar results were obtained by Zella and DeLuca[10], who reported that Ro-262198, a vitamin D analogue, was effective in the control of type 1 diabetes and led to improvement in the clinical manifestation of the disease. In Finland, a northern country with a cold climate during the long months of winter, the incidence of type 1 diabetes was 18/100,000 and the recommended dose of vitamin D was 4500 IU/day before 1964 and the prophylaxis dose was reduced to 2000 IU/day in 1965. Since, the incidance of type 1 diabetes was 64/100,000 in 2005, vitamin D was addes to the formulae, and the incidance continued to decrease[11]. Infante et al.[12] also suggested an inverse relationship between vitamin D levels and the prevalence of type 1 diabetes. However, Reinert-Hartwall et al.[13] stated that these findings did not support a crucial role of circulating 25-OHD as a regulator of beta-cell autoimmunity.

Table 4. Relationships between vitamin D levels and blood gas and biochemical parameters and duration of symptoms

	Vitamin D			
	Normal or excess (n=42)	Insufficiency (n=17)	Deficiency and severe deficiency (n=21)	p
pH	7.24±0.13	7.25±0.18	7.23±0.14	p>0.050
HCO_3 (mg/dL)	12.63±6.62	14.35±7.21	13.41±6.23	p>0.050
Osmolarity (osm)	293.98±10.62	296.74±10.58	296.92±9.82	p>0.050
Na (mEq/L)	137±4.7	137.4±4.2	137±4.0	p>0.050
Duration of symptoms (day)	23.90±23.27	33.00±24.38	36.43±26.86	p>0.050

HCO_3: Bicarbonate, Na: Sodium

Table 5. Clinical manifestations at presentation according to vitamin D levels in patients with type 1 diabetes compared with controls

Patients with type 1 diabetes						Controls	p
25-OHD (ng/mL)	No Acidosis n / (%)	Mild DKA n / (%)	Moderate DKA n / (%)	Severe DKA n / (%)	Total n / (%)	Total n / (%)	
25-OHD>20	16 / (38.1)	12 / (28.6)	8 / (19.0)	6 / (14.3)	42 / (53)	26 / (86.6)	>0.050
25-OHD 15-20	9 / (52.9)	5 / (29.4)	-	3 / (17.6)	17 / (21)	2 / (6.7)	>0.050
25-OHD<15	7 / (33.3)	8 / (38.1)	2 / (9.5)	4 / (19.0)	21 / (26)	2 / (6.7)	>0.050
Total	32 / (40)	25 / (31)	10 / (12.5)	13 / (16)	80 / (100)	30 / (100)	>0.050

25-OHD: 25-hydroxyvitamin D, DKA: Diabetic ketoacidosis, n: Number

Table 6. Relationships between clinical pictures at presentation and vitamin D, Ca, P, ALP, PTH in patients with type 1 diabetes

DKA status	25-OHD (ng/mL)	Ca (mg/dL)	P (mg/dL)	ALP (U/L)	PTH (pg/mL)
Mild (n=25)	22.86±13.42	9.21±0.52	4.16±0.22	185.32±67	23.38±11.67
Moderate (n=10)	24.90±10.19	9.55±0.64	4.29±0.92	297.30±128.93	25.60±24.03
Severe (n=13)	23.14±15.54	9.49±0.81	3.39±1.43	253.92±141.51	18.53±10.57
No DKA (n=32)	26.03±20.12	9.48±0.54	4.70±0.85	229.92±76.34	28.32±14.18
p	>0.05	>0.05	>0.05	>0.05	>0.05

ALP: Alkaline phosphatase, Ca: Calcium, DKA: Diabetic ketoacidosis, P: Phosphorus, 25-OHD: 25-hydroxyvitamin D, PTH: Parathormone

Pozzilli et al.[14] reported lower 25-OHD levels in 88 newly diagnosed pediatric diabetic patients compared to healthy children. Vitamin D levels were low in both winter and summer in that study, thus the seasonal factors affecting vitamin D levels were ruled out. Littorin et al.[15] observed low 25-OHD levels at the time of diagnosis in newly diagnosed diabetic adolescents in Sweden. In a study from Qatar conducted in 2000, the authors stated that although vitamin D deficiency was frequently seen in children due to lifestyle and nutritional factors, severe deficiency was more common in children with type 1 diabetes[16]. Svoren et al.[17] reported vitamin D insufficiency in 61% and vitamin D deficiency in 15% of 128 patients with newly diagnosed type 1 diabetes. Franchi et al.[18] also stated in their study that vitamin D levels were low at the onset of type 1 diabetes without seasonal variation.

In our study 25-OHD levels were also significantly lower among diabetic patients compared to the control group. However, blood samples were collected throughout the year from the diabetic patient group, but only in summer from the control group, when the synthesis of vitamin D is highest. In order to clarify whether higher vitamin D levels in the control group were seasonal in nature, we compared vitamin D levels between the control group and diabetic patients diagnosed in the same period and the mean vitamin D levels were found to be similar between the two groups in the same season.

Bierschenk et al.[19] analyzed 415 individuals living in Florida, a sunny region of the USA. The participants consisted of 153 controls, 46 newly diagnosed type 1 diabetes patients, 110 patients under follow-up with type 1 diabetes (for ≥5 months from the diagnosis), and 106 first-degree relatives of the diabetic patients. No significant difference was found in 25-OHD levels among the control group, the newly diagnosed diabetic patients, the patients under follow-up for diabetes, and first-degree relatives. The mean 25-OHD level was under 30 ng/mL in all four study groups. Low serum 25-OHD levels were not therefore thought to be associated with type 1 diabetes[19]. A study performed in Kocaeli, a city in Turkey, in 2010, involving 120 patients with type 1 diabetes under follow-up, reported the mean 25-OHD level as 25.6±16.2 (ng/mL) (4.6-101), and the mean time since diagnosis as 3.2±2.3 (0.7-12.8) years. Vitamin D deficiency or insufficiency was present in 36% of the patients[20]. These findings showed that vitamin D levels were low, not only in newly diagnosed patients, but also in patients who had been diagnosed previously. In another study from the same city, which was conducted on 301 obese children in 2006, vitamin D insufficiency/deficiency rate was revealed as 65.1%[21]. One other study, also performed in the same city in 2002, evaluated adolescent girls, and reported vitamin D insufficiency and deficiency in 50% of patients living in rural areas and 57% of those living in urban areas[22]. The participants in our study were living also in Kocaeli city and the rate of vitamin D insufficiency/deficiency was defined as 47%. This rate was a bit higher than the rate detected in 2011 among diabetic patients but lower than the rates in 2002 and 2006 among non-diabetic patients, supporting the idea that vitamin D deficiency/insufficiency is not an additional risk factor for diabetes, its prevalence is high among the children and adolescents in general. Brody et al.[23] stated that vitamin D insufficiency was largely prevalent among Israeli youth with type 1 diabetes mellitus, as is in Israeli youth in general stating that vitamin D level is associated with seasonality, clothing habits[23]. Mäkinen et al.[24] supported the idea in their study that serum vitamin D concentrations were not associated with the development of type 1 diabetes in Finland. Simpson et al.[25] declared that neither vitamin D intake nor 25-OHD levels throughout childhood were associated with the risk of progression to type 1 diabetes in their population.

In terms of the relationship between acidosis and decreased vitamin D levels, acidosis has been shown to affect the physiology of vitamin D. Decreased vitamin D levels reduce insulin secretion or activity and change natural immunity, leading to presentation of patients with DKA[26-28]. Low 25-OHD levels have been associated with acidemia, and usually return to normal once the acidosis has resolved. Devidayal et al.[29] supported this knowledge and stated that metabolic acidosis could alter vitamin D metabolism through different mechanisms, while low vitamin D levels could play a role in presentation of children with acidosis in type 1 diabetes. Franchi et al.[18] reported lower vitamin D levels at DKA than those without acidosis. Al-Zubeidi et al.[30] stated that vitamin D deficiency and insufficiency are common, even in Caucasians, at the onset of type 1 diabetes in pediatrics, worse in those with DKA. In a study from Australia performed by Huynh et al.[5] between July 2006 and December 2007, the relationship between metabolic acidosis and 25-OHD levels at the time of diagnosis in 64 children was investigated. 25-OHD levels were under 50 nmol/L (20 ng/mL) in 14 of these patients. Of these 14 children, 12 had metabolic acidosis, while no metabolic acidosis was present at the time of diagnosis in two, but metabolic acidosis was present in the remaining 50 patients with normal vitamin D levels. 25-OHD levels returned to normal when acidosis resolved in all cases except one. The authors attributed the low vitamin D levels to low exposure to sunlight for religious reasons in this patient[5].

Forty-eight patients were presented with metabolic acidosis in our study, 25 (31%) with mild DKA, 10 (12.5%) with moderate DKA, and 13 (16.5%) with severe DKA. No significant difference was observed between these groups in terms of 25-OHD levels measured at the time of diagnosis. The similar initial mean vitamin D levels thus show that mean vitamin D levels were independent from the form of presentation like the previous study performed by Huynh et al.[5]. It may therefore be

concluded that the presence or absence of acidosis and the degree of acidosis were not associated with vitamin D levels.

The intrauterine period and first years of life have been shown to be important for the development of diabetes. Vitamin D status in infants reflects vitamin D status in mothers during pregnancy[6]. The first year of life is a period in which breastfeeding is predominant, and includes subsequent transition to additional foods, and vitamin D supplementation is important in this period. Comprehensive studies have therefore investigated both periods. In the All Babies in Southeast Sweden (ABIS) study in Sweden, Brekke and Ludvigsson[31] investigated the relationship between the use of vitamin D supplements in infancy and pregnancy and type 1 diabetes in infants aged one year and 2.5 years and the correlation with diabetes-related autoimmunity. That study involved 16,070 infants and was completed with 11,081 patients aged one year, and 8805 aged 2.5 years. At the end of the follow-up period, four of the one-year-old children and 22 of the infants aged 2.5 years developed diabetes. No significant correlation was found in terms of the development of autoantibodies in children aged 1 and 2.5 years among the patients who received 10 mcg (400 IU) vitamin D containing supplements in infancy. However, a decrease was detected in diabetes-related autoimmunity in one-year-old infants whose mothers used vitamin D supplements during pregnancy, with no correlation being observed at 2.5 years of age. The authors were unable to suggest any clear reason why a protective effect was seen at 1 year of age but not at 2.5 years. Granfors et al.[32] declared in their study, as the continued study of ABIS study, that maternal use of vitamin D containing multivitamin supplements during pregnancy was not associated with the risk of developing type 1 diabetes in children before 14-16 years of age in Southeast of Sweden. Hyppönen et al.'s[33] study from Northern Finland in 2001 also investigated the relationship between vitamin D and diabetes. A relationship between the frequency and dosage of vitamin D intake and progression of diabetes was recorded after follow-up of 30 years. The results of that study showed that the incidence of type 1 diabetes was lower in patients receiving vitamin D supplements, independently of dosage and with regular usage. There was no significant difference between the patients with type 1 diabetes whose mothers used vitamin D in pregnancy and the control group[33]. The EURODIAB Substudy 2 Study Group[34] investigated the relationship between vitamin D and diabetes, with the inclusion of 820 diabetic children and 2335 controls. The use of vitamin D during pregnancy and in the first year of life was evaluated. Patients were evaluated after 15-year follow-up. The risk of diabetes was found to decrease by 1/3 in children who received vitamin D during infancy, and the risk of type 1 diabetes was even lower among individuals whose mothers received vitamin D during pregnancy. In our study, the rates of use of vitamin D supplements during pregnancy and during the first year of life were similar between the patient and the control groups, showing that there was no effect on the development of diabetes. These findings were different from the findings mentioned previously but in accordance with the study performed by Thorsen et al.[35]. They completed their study with the suggestion that the role of 25-OHD levels in utero or in early childhood and the later risk for developing type 1 diabetes needed further investigation.

Study Limitations

The principal limitation of the study is that more patients are needed in order to evaluate the relationship between vitamin D and type 1 diabetes more exactly.

CONCLUSION

Vitamin D deficiency/insufficiency had no significant effects on the development of diabetes, or clinical status at presentation such as metabolic acidosis. Metabolic acidosis has no effect on vitamin D, Ca, P, ALP, or PTH levels. Vitamin D intake in infancy and pregnancy exhibited no protective effect against the progression of diabetes. Therefore, it does not seem possible to reach a definitive conclusion concerning the relationship between vitamin D and type 1 diabetes because of the high prevalence of vitamin D deficiency in general and also in diabetic children.

Presented in and Note: The oral presentation titled "The Evaluation of Vitamin D Status and Clinical Presentation Characteristics in Children Diagnosed with Type 1 Diabetes" related to this article was made on September 29-October 2, 2022 at the 2nd Eastern Pediatrics Congress in Diyarbakır. The study conducted in this article was carried out by 1st author as the Child Health and Diseases Speciality Thesis at Kocaeli University Faculty of Medicine with the title of "Vitamin D Status and Its Relationship with Clinical Presentation Characteristics in children with type 1 diabetes".

Ethics

Ethics Committee Approval: The study were approved by the Kocaeli University Faculty of Medicine of Local Ethics Committee [protocol number: 24.02.09-(5/17), date: 21.03.2011-(1/6)].

Informed Consent: Informed consent was obtained from children and their parents.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

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