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Original Article

Investigating the Relationship between Gingivitis and Level of Vitamin D in Children with Diabetes

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ABSTRACT

The results of some studies have shown that both type 1 (T1DM) and type 2 (T2DM) diabetes can be related to the risk of gingivitis. Inflammatory conditions and a deficiency of vitamin D create a suitable environment for the increase of chronic diseases such as periodontitis and diabetes in children. The current research was done to study the relationship between the gingivitis and level of vitamin D in children with T1DM. This research was a case-control study to investigate the relationship between the gingivitis and level of 25 hydroxyvitamin D (25(OH)D) in 148 children with T1DM. For this purpose, people were divided into two groups, healthy and T1DM, in terms of having gingivitis. In this study, fasting blood sugar, calcium, and level of serum 25(OH)D were evaluated. The findings of the study showed that 25(OH)D in the group with gingivitis was remarkably lower than in the group without gingivitis ($p<0.05$). There was no statistically significant difference in the level of 25(OH)D according to gender between the group with gingivitis and the group without gingivitis ($p>0.05$). In addition, the findings of the chi-square test demonstrated that there was no remarkable difference between the two groups with gingivitis and without gingivitis in terms of gender and age distribution ($p>0.05$). The findings of this study show that vitamin D deficiency is an effective factor in high gingivitis in children with T1DM. Timely monitoring of the level of this vitamin in patients with gingivitis is essential.

Keywords: Diabetes, Children, Vitamin D level, Gingivitis

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Introduction

Diabetes mellitus is the most common endocrine disease and one of the most common causes of blindness, kidney failure, and amputation [1]. According to a study report published in 2020, the prevalence of this disease in the world in 2014 was equal to 8.5%, and it is estimated that the prevalence of this disease will reach from 422 million to 462 million by 2040 [2]. According to the classification of the American Diabetes Association, of the four types of diabetes, two are more common: type 1 diabetes (T1DM), which is the most common form of diabetes in children (also known as juvenile diabetes), and type 2 diabetes (T2DM), which occurs mainly in adults. The findings of some studies revealed that both types of diabetes can be related to the risk of gingivitis [3]. T1DM is a complex metabolic disease. Various environmental, behavioral, and social factors play a role in its occurrence and it causes the disease in people with genetic predisposition [4].

Data on the relationship between periodontitis (PD) or periodontal disease, hyperglycemia, and diabetes have been reported in patients with T2DM. Conversely, information on periodontitis in T1DM is relatively scarce [5]. In this regard, previous studies have shown that teenagers with T1DM have a higher prevalence and severe gingivitis than healthy people of the same age. Metabolic imbalance in tissues may reduce the resistance of people with diabetes to infection and consequently increase the onset, development, and periodontal disease progression in these people [3].

Periodontal inflammatory disease is one of the main chronic inflammatory diseases that can affect any person at any age. The cause of gingivitis is the presence of opportunistic bacteria that naturally exist in the mouth [6]. Gingivitis is a multifactorial disease that is influenced by various factors [7]. Chronic disease risk assessment is important because dental caries and periodontitis are very common in a small group of people who are classified as high-risk [8]. Various factors, including the reduction of the body's immune system and smoking, have been reported as risk factors for gingivitis [9]. In addition, gingivitis can be associated with systemic diseases such as diabetes [10]. In the most recent findings, periodontitis has been accepted as the sixth complication of T1DM [11]. In addition, some studies showed a higher prevalence of gingivitis in adolescents and children with T1DM compared to the healthy population [12]. In addition, more studies have determined that gingivitis also has an effect on worsening the course of diabetes, and in fact, there is a two-way relationship between these two diseases [13].

In a diabetic person, due to the hyperglycemic condition, a large number of proteins and extracellular background molecules are subjected to the enzymatic glycosylation process leading to the production of AGEs (Advanced Glycation End Products). AGE creates cross-links between collagens and reduces the solubility of collagen, ultimately causing disruption in tissue integrity and periodontium and weakness in wound healing. Disorders that diabetes has on the periodontium include the tendency to increase the volume of the gums, gum polyps, abscesses, and periodontitis. The rate of periodontal destruction is similar in non-diabetic and diabetic people before the age of 30, but this value is higher in diabetic people above 30 years of age, and periodontal destruction is more severe in people who have diabetes for more than 10 years [14]. The intensity and progression of periodontal destruction and gingivitis are higher in diabetic people, but the amount of plaque and calculus is not different between the two groups [14, 15]. In terms of the relationship between diabetes and periodontal diseases, uncontrolled or poorly controlled diabetics are more susceptible to periodontal diseases. With increasing age, the probability of periodontitis in diabetics is also higher. Previous research has shown a link between a deficiency of 25-hydroxyvitamin D (25(OH)D) and increased inflammation, such as diabetes and Crohn's disease [16, 17]. Vitamin D (25(OH)D) can affect the occurrence of chronic inflammatory diseases by downregulating NF-kB [18]. In addition, inhibition of TNF-a expression in monocytes in diabetic patients is possible with the help of this substance [19]. Some researchers have shown that 25(OH)D has beneficial impacts on oral and dental diseases and tooth loss, especially due to its anti-inflammatory effects [20]. For example, Li *et al*. provided evidence of the protective effect of 25(OH)D and its clinical significance in the gingivitis treatment caused by diabetes [21]. Wang *et al*. also stated in a study that 25(OH)D deficiency has a strong association with T2DCP and age moderates this association [22]. In addition, abnormal FBG and IL-1B levels should be considered as important risk factors for the development of severe T2DCP.

Therefore, because the inflammatory condition and lack of 25(OH)D create a suitable environment for chronic disease development such as periodontitis and diabetes in children, and also because so far in a study investigating the relationship between the level of 25(OH)D and Gingivitis in diabetic children has not been studied, the current research was done to study the relationship between 25(OH)D level and gingivitis in children with T1DM.

Materials and Methods

This study was a case-control research to study the relationship between vitamin 25(OH)D levels and gingivitis in children with T1DM. For this purpose, people were divided into two groups, healthy and sick, in terms of having gingivitis, and after obtaining written consent, they entered this study. In this consent form, it is stated that participation or non-participation in this study is voluntary and has no effect on the patient's treatment process.

The studied groups included T1DM patients without gingivitis and T1DM patients with gingivitis. The patients of the control group were matched with the patients with gingivitis in terms of age and gender variables. Age, sex, and level of serum 25(OH)D were all recorded in a checklist, and the maximum time interval of these data was 6 months.

The diagnostic criteria for inflammation of the tissues around the teeth were determined according to the 1999 criteria of the American Academy of Periodontology and the definitions of clinical samples provided by the Centers for Disease Control and Prevention. Oral hygiene and gingival condition were evaluated using the Silens and Lowe plaque index (PI) and modified gingival index (MGI). T1DM was defined according to the 2010 standard of care criteria (serum glucose greater than 126 mg/dL after at least 8 hours of fasting). Inferential and Descriptive methods were utilized to analyze the data obtained from the research. In the descriptive part, concentration indices such as median, mean, and dispersion indices including standard deviation and interquartile range were used. In addition, in the section describing demographic characteristics, appropriate tables and graphs were used to describe and identify as much as possible the patients under study and the main variables of the research. To check the analytical assumptions, first, the normality assumption of quantitative research variables was checked by Kolmogorov-Smirnov. Then, in the variables that followed the normal distribution, an independent t-test was utilized to compare the averages of two independent communities, and a one-way analysis of variance (ANOVA) was utilized to compare more than two groups. In addition, Pearson's correlation coefficient was utilized to check the correlation between the two variables. If the variables were not normal, the non-parametric equivalent of the tests, including the Mann-Whitney test, Spearman correlation coefficient, and the Kruskal-Wallis test, were utilized. The level of significance in the present research was considered 5% to examine all the hypotheses, and SPSS version 24 software was utilized to analyze the data. All statistical tests were done at a significance level of 5%. For multiple comparisons, the Benjamin-Hashberg method was utilized at a significant level of 5%.

In this study, fasting blood sugar, calcium, and serum 25-hydroxyvitamin D were evaluated. This form of 25(OH)D is biologically inactive at levels close to 1000 times or greater than circulating levels of 1 and 25-dihydroxy vitamin D. 25(OH) D is the largest storage form of vitamin D in the body, and the half-life of its circulating amount is 2 to 3 weeks. Ideally, 25(OH)D optimal level for general health is equal to or greater than 30 ng/ml, and 20-30 ng/ml means a deficiency of vitamin D. A level < 20 ng/ml is generally considered vitamin D deficiency. In this research, the 25(OH)D levels and other laboratory indicators of children were measured. Also, light electrochemical immunometry was used to measure the 25(OH)D levels in serum. Before estimating the level of 25(OH)D, external and internal quality control was performed. The total duration of the assay was 18 minutes, and the serum was collected and stored at 2 to 8 degrees Celsius. The quantification range was 10–250 ng/mL (defined based on the lowest limit of detection and the maximum of the master curve) [21]. Oral health and gingival condition were evaluated using the Sillens and Lowe plaque index (PI) and the modified gingival index (MGI) of Luben *et al*. A trained investigator undertook the clinical review [21]. In this study, T1DM was defined based on the standard medical care criteria of 2010 (serum glucose greater than 126 mg/dL after at least 8 hours of fasting) [21]. In addition, light electrochemical immunometry was utilized to measure the 25(OH)D levels in serum. It should be noted that all these data were already recorded in the patients' files and these numbers were used as measurement criteria and did not need to be tested again. In addition, a final year dental student under the supervision of a supervisor did the review of patients' files. After obtaining written informed consent, age, gender, level of calcium (mg/dl), and serum 25(OH)D (ng/ml) were all recorded in a checklist, and the maximum time interval for recording these data was 6 months.

Results and Discussion

In this research, 148 children aged 6 to 12 years with T1DM were examined, 74 of whom had gingivitis and 74 of whom did not have gingivitis. In addition, 74 people (50%) of the participants were girls (group with gingivitis: 37 girls, group without gingivitis: 37 girls) and 74 people (50%) were boys (group with gingivitis: 37 boys, group without gingivitis: 37 boys) **(Tables 1-4)**. The average age of all participants was reported as 8.78 ± 1.88 years. The findings of the Chi-square test revealed that the two groups with gingivitis and without gingivitis had no significant difference in age and gender terms distribution **(Table 1)**.

Table 1. Determining and comparing the frequency distribution of demographic characteristics in groups with gingivitis and without gingivitis.

Variable	Group	Gingivitis	Without gingivitis	p-value
Gender	Girl	37 (50%)	37 (50%)	1.000
	Boy	37 (50%)	37 (50%)	

Age	6-7 years	20 (27%)	20 (27%)	1.000
	8-9 years	25 (33.8%)	25 (33.8%)	
	10-12 years	29 (39.2%)	29 (39.2%)	
Total		74 (100%)	74 (100%)	-

The findings of the Kolmogorov-Smirnov test demonstrated that the data did not follow the normal distribution **(Table 2)**, therefore, non-parametric tests were utilized to compare the data.

Table 2. The findings of following the normal distribution of 25(OH)D (ng/ml) and calcium (mg/dl) by Kolmogorov-Smirnov.

Variable	df	p-value
Vitamin D	148	0.002
Calcium	148	0.000

The findings demonstrated that the average of 25(OH)D in the group with gingivitis was 20.72 ± 12.77 and in the group, without gingivitis, it was 29.57 ± 10.72 **(Table 3)**. In the group with gingivitis, a deficiency of 25(OH)D was reported in 24.3% of people, and a sufficient 25(OH)D was reported in 25.7% of people. While in the group without gingivitis, a deficiency of 25(OH)D was reported only in 8.1% of people, and a sufficient level of 25(OH)D was reported in 41.9% of people **(Table 3)**.

Table 3. Determining the mean and frequency distribution of level of 25(OH)D in two groups with gingivitis and without gingivitis.

Variable	Group	Mean ± standard deviation (ng/ml)	25(OH)D levels		
			< 0 (ng/ml) Deficiency	10-30 (ng/ml) Insufficient	> 30 (ng/ml) Sufficient
Vitamin D	Gingivitis	20.72 ± 12.77	18 (24.3%)	37 (50%)	19 (25.7%)
	Without gingivitis	29.57 ± 10.72	6 (8.1%)	37 (50%)	31 (41.9%)

The results revealed that the average calcium in the group with gingivitis was 8.58 ± 0.47 and in the group without gingivitis, it was 9.12 ± 0.47 **(Table 4)**. In the group with gingivitis, calcium deficiency was reported in 27% of people and a sufficient level of calcium in 73% of people; while in the group without gingivitis, calcium deficiency was observed only in 8.1% of people and a sufficient level of calcium in 91.1% of people **(Table 4)**.

Table 4. Determining the mean and frequency distribution of calcium levels in two groups with gingivitis and without gingivitis.

Variable	Group	Mean ± standard deviation (ng/ml)	Values	
			< 8.7 (ng/ml) Deficiency	> 8.7 (ng/ml) Sufficient
Calcium	Gingivitis	8.58 ± 0.47	20 (27%)	54 (73%)
	Without gingivitis	9.12 ± 0.47	6 (8.1%)	68 (91.1%)

The findings of the Kruskal-Wallis test demonstrated that the 25(OH)D level according to age in both the group with gingivitis and the group without gingivitis did not have a statistically significant difference (p = 0.373 and p = 0.741) **(Table 5)**.

Table 5. Determining and comparing the 25(OH)D level according to age in two groups with gingivitis and without gingivitis.

Age / Group	6-7 years	8-9 years	10-12 years	p-value
	Mean ± SD (ng/ml)	Mean ± SD (ng/ml)	Mean ± SD (ng/ml)	
Gingivitis	21.71 ± 10.95	18.79 ± 11.85	21.69 ± 9.26	0.373
Without gingivitis	31.10 ± 14.19	28.87 ± 14.72	29.11 ± 10.02	0.741

The findings of the Mann-Whitney test demonstrated that the level of 25(OH)D by gender was not statistically significant in the group with gingivitis and in the group without gingivitis, respectively (p = 0.673 and p = 0.350) **(Table 6)**.

Table 6. Mean and SD (standard deviation) of 25(OH)D level according to gender in two groups with gingivitis and without gingivitis.

Group \ Gender	Girl	Boy	p-value
	(Mean ± SD) (ng/ml)	**(Mean ± SD) (ng/ml)**	
Gingivitis	20.72 ± 12.77	20.72 ± 12.77	0.673
Without gingivitis	31.57 ± 13.87	27.56 ± 11.44	0.350

The findings of the Spearman correlation coefficient test revealed that there was a significant and positive relationship between the calcium and level of 25(OH)D both in the group with gingivitis and in the group without gingivitis respectively (group with gingivitis: r = 0.862 and p< 0.05; group without gingivitis: p < 0.05 and r = 0.789) **(Table 7)**.

Table 7. Determining the correlation of 25(OH)D level with calcium in two groups with gingivitis and without gingivitis.

Group	Variable	Correlation coefficient	p-value
Gingivitis	Vitamin D	0.862	0.0001
	Calcium		
Without gingivitis	Vitamin D	0.789	0.0001
	Calcium		

This research was done to study the relationship between 25(OH)D level and gingivitis in children with T1DM. In this research, 148 children aged 6 to 12 years with T1DM were examined, 74 of whom had gingivitis and 74 without gingivitis. 50% of the samples were girls. In addition, the average age of all studied subjects was reported to be 88.1±78.8 years. The findings of this study showed that the 25(OH)D level in the group with gingivitis was considerably lower than in the group without gingivitis. Also, in the group with gingivitis, a deficiency of 25(OH)D was reported in 24.3% of people, and a sufficient level of vitamin D was reported in 25.7% of people, while in the group without gingivitis, a deficiency of 25(OH)D was reported in only 8.8% of people and sufficient vitamin D levels was reported in 41.9% of people. According to the findings of the current study, it can be seen that the average serum level of 25(OH)D was insufficient in both study groups, which is consistent with epidemiological studies on the high prevalence of a deficiency of 25(OH)D [23, 24]. So far, research has been done to evaluate the relationship between serum levels of 25(OH)D and T2DM as well as periodontitis [25, 26], however, it should be noted that the relationship between the level of 25(OH)D and gingivitis in T1DM patients has been investigated in few studies.

Aydin *et al.* stated in a study that the levels of bioavailable 25-hydroxyvitamin D, free 25(OH)D, and total 25(OH)D were remarkably lower in the group of periodontitis than in the group of healthy control [27]. Dietrich *et al.* also showed in research that there is a significant and negative correlation between the 25(OH)D level and gingivitis, which may be because of the anti-inflammatory impact of 25(OH)D [28]. Research by Bhargava *et al*. and Abreu *et al*. stated that the 25(OH)D level in people with periodontitis is significantly lower than in healthy people [29, 30]. These results can be considered to some extent in line with the findings obtained from the present research, however, it should be noted that in all the mentioned studies, people were not examined in terms of having diabetes, and for this reason, the mentioned studies are different from the present study.

Agrawal *et al.* who evaluated the serum level of 25(OH)D and calcium in people with healthy periodontal status, chronic gingivitis patients, and chronic periodontitis patients with or without T2DM, showed that the 25(OH)D level decreases with increasing intensity of gingivitis [31]. They also observed that the level of vitamin D in people with chronic gingivitis with type 2 diabetes was lower than those with chronic gingivitis without type 2 diabetes [31]. In addition, the research of Joseph *et al*. and Wang *et al*. revealed lower 25(OH)D levels in T2DM people with chronic periodontitis compared to non-diabetic chronic periodontitis people and higher levels in healthy subjects [22, 32]. In a research done by

Agrawal *et al*. the findings revealed that calcium levels were lower in subjects with chronic gingivitis T2DM compared to subjects with chronic gingivitis without diabetes [31]. In the present study, only people with and without gingivitis, all of whom were suffering from T1DM, were examined, which is different from the aforementioned study and a proper comparison is not possible. In addition, the findings of the present study demonstrated that the 25(OH)D level in terms of age and gender both in the group with gingivitis and in the group without gingivitis had no significant statistical difference.

In a research done by Wang *et al*. the results revealed that a deficiency of 25(OH)D at levels of 15-20 ng/ml was remarkably higher in people aged 50-80 years than in people aged 20-49 years [22]. However, no statistically remarkable difference was found in other levels of 25(OH)D according to age. Finally, the findings of Spearman's correlation coefficient test revealed that there was a remarkable and positive relationship between calcium and 25(OH)D both in the group with gingivitis and in the group without gingivitis respectively; this means that in both studied groups, with the 25(OH)D increase, calcium also increases and with its decrease, calcium decreases.

Correcting a deficiency of vitamin D may have a great impact on the prevalence of chronic diseases, through either supplementation or diet and is considered an effective, safe, and inexpensive way to decrease the prevalence of periodontal disease. However, more studies are required to study to what extent vitamin D plays a role in periodontal tissues protecting against inflammatory degradation. In addition, it is better to specify the optimal dose of vitamin D supplement for each person and evaluate its effect on periodontitis prevention [30].

Conclusion

The findings of the current study demonstrated that the 25(OH)D level in the group with gingivitis was remarkably lower than in the group without gingivitis. In addition, there was no statistically remarkable difference in levels of vitamin D based on age and gender in both groups with and without gingivitis. In addition, a significant and positive correlation was reported between calcium and vitamin D levels in both groups. The findings of this study show that a deficiency of vitamin D is a serious factor in high gingivitis in children with T1DM. Timely monitoring of the level of this vitamin in patients with gingivitis is essential.

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