Influence of Oral Preventive Program on Periodontal and General Health of Type 1 Diabetes (T1D) in Egyptian Children

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Abstract

Background: Some studies show the relationship between the duration of diabetes and severity of periodontitis. On the other hand, it was confirmed that there is a negative effect of periodontitis on blood glucose levels. Human cytomegalovirus was suggested in many studies to have a relationship with both diabetes and periodontitis. Aim of the study: The present study was conducted to assess the bidirectional relationship between T1D and periodontal diseases in Egyptian children. Patients and Methods: This study included 40 children their age ranged from 8 – 13 years and both sexes were presented, the study was done through assessment of gingival health using gingival index (GI), oral cleanliness using plaque index (PI), periodontal health using clinical attachment loss (CAL), as well as Glycosylated hemoglobin (HbA1c %), Human Cytomegalovirus (HCMV) using the real time PCR. Results: all the dental clinical parameters were higher in poorly controlled diabetic group and also had higher levels of HbA1c % than good controlled group which had improvement in both after dental treatment. It was found that (50%) of the studied cases were infected with CMV, and the poor controlled group had a higher prevalence of patient positivity and higher number of CMV than the good controlled group. Thirty five percent of CMV positive results became negative after the period of dental treatment and the rest had very low number of CMV that was considered nearly as negative. Conclusion: Improvements of dental clinical parameters were associated with improvement of HbA1c % and also with the decrease in the number of CMV.

Key Words: Type 1 diabetes, Periodontal diseases, Human cytomegalovirus

Introduction

Type 1 diabetes mellitus (T1D) an autoimmune disease that occurs when T-cells attack and destroy most of the beta cells in the pancreas that are needed to produce insulin so that the pancreas makes too little or no insulin so hyperglycemia is the end result [1]. A periodontal disease is a chronic inflammatory disorder caused by an invasion of anaerobic bacteria into periodontal tissues, including gingival connective tissue, periodontal ligament, and alveolar bone the resulting tooth loss impairs oral functions [2]. Human cytomegalovirus it represents a prototypic pathogenic member of the -subgroup of the herpes virus family. It is not just a DNA virus, but also contains four species of mRNA [3]. There is a strong correlation between CMV genome and islet cell autoantibodies, CMV might be involved in accelerating pancreatic failure to compensate for insulin resistance via at least two possible mechanisms first, it could influence pancreatic cells directly. Secondly, it might act indirectly by influencing the immune system which in turn affects the pancreas [4], Human cytomegalovirus (HCMV) seems to play important roles in the etiopathogenesis of severe types of periodontitis [5,6].

Aim of study

The present study was conducted to assess the bidirectional relationship between T1D and periodontal diseases in Egyptian children.

Patients and Methods

This study included 40 children who were previously diagnosed as T1D patients according to ADA [7]. They were selected from the diabetes outpatient clinic, Maternal and Children Minia University Hospital. Their ages range from 8-13 years and both sexes were presented.

Inclusion criteria

- Age between 8 and 13 years old, diagnosed with (T1D).
- Duration of T1D >6 months.
- Presence of Periodontal disease (periodontitis).
- No periodontal treatment in the last 6 months.
- No suggestive history of any medication that could influence the studied parameters (corticosteroids, antibiotics) in the last 3 months.
- Cooperative patients and caregivers.

Exclusion criteria

- Presence of periapical pathological lesions.
- Presence of other inflammatory diseases.
- Presence of liver or renal impairment.

After fulfillment of inclusion criteria the selected patients were divided into two groups, each group with different degree of periodontal alteration; as regard HbA1c % level, they were divided into good controlled where HbA1c <7% and poorly controlled where HbA1c >7% and classified as:

- Group I: included 20 patients with good controlled-diabetes.
- Group II: included 20 patients with poor controlled diabetes.

Study design

Patient acceptance of treatment procedures was obtained and parent signed an informed consent form prepared by the

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ethical committee of Faculty of Dentistry, Minia University, Egypt, before the start of the treatment.

After the agreement of the patient on the informed consent, all our patients were subjected to:

Thorough history taking

Age, sex, residence, duration of diabetes, presence of any complications of diabetes, history of any dental consultation in the last 6 months.

Clinical examination

Anthropometric measurement: "weight, height, and body-mass index (BMI)", Systematic examination "chest, heart and abdomen".

Intraoral examination: All patients were examined using plane mouth mirror, dental explorer, periodontal probe, and the following clinical parameters were recorded:

- Gingival index (GI) to assess gingival health [8].
- Plaque index (PI) to assess oral cleanliness [8].

Gingival index and Plaque index were measured for permanent and remaining primary teeth, neglected the oral health of those children resulted in loss of most of the primary teeth (extracted).

Clinical attachment loss (CAL) to assess periodontal health. The assessment of CAL was measured for permanent incisors and first permanent molars which were fully erupted at this age (mean age was 10.6 years old) therefore the possibility of presence of pseudo pockets associated with recently erupted teeth is not present. The clinical attachment level (CAL) was measured from CEJ till the base of periodontal pocket two measurements were used to calculate the clinical attachment level: (a) The probing depth. (b) The level of the gingival margin (distance from CEJ to gingival margin).Therefore, the gingival margin may be at the CEJ or apical to the CEJ or cover the CEJ [9].

Special investigations

A venous blood sample was drawn after complete aseptic technique from patients before the treatment program to assess:

- Glycosylated hemoglobin (HbA1c %): -HbA1c % reflects the average plasma glucose over the previous eight to 12 weeks, it was performed at any time of the day and didn't require any special preparation such as fasting [10].
- Human Cytomegalo virus (HCMV): - It was detected by using HCMV real time Polymerized Chain Reaction (PCR) in serum using a kit from Liferiver^{TM}.
- Renal and liver function tests.

Dental treatment program

Dental program involved both curative and preventive parts.

Curative part was carried out to meet all child's treatment needs and included dental prophylaxis and providing restorative care for children.

Restorative care included simple cavity preparation and tooth colored restorations for primary and permanent teeth, pulpotomy and St.St. crown for exposed primary teeth, endodontic treatment for permanent teeth and build up.

Dental prophylaxis which is level 1 periodontal treatment and includes: Scaling with ultrasonic scaler for supra gingival calculus and hand scaling for the sub gingival calculus more than 2 mm. Then polishing was done to make plaque control easier. Curettage to any present gingival pockets, as well as removing the plaque, calculus and necrotic cementum from the root surface, when finished, the goal is to have a clean cementum surface on one side of the periodontal pocket and either fresh bleeding connective tissue or clean bone on the other side. Then healing can take place.

Preventive part included 1-health education (mechanical control):- was done in special room equipped with posters and life size dental models, after referral of the patients to the outpatient clinic pediatric and community department for program implementation.

All patients received health education on plaque control to improve their oral hygiene practice, which included:

Tooth brushing

Patients and their guardians were motivated to take care of oral health and how it will affect positively the function of mastication, speech, aesthetics and so the physical and psychological health of the patient.

Then patients and their parents on life size model tooth brushing technique were demonstrated and explained, Modified Bass method (1948): - It is widely accepted and effective method for plaque control.

Recommendations for brushing frequency: Health education was done with special emphasis on plaque control to inform the patients about tooth brushing techniques and each segment 10 strokes and total brush time of 2-3 minutes with soft or medium tooth brush [11].

Floss technique (the spool method)

Approximately 18 inches of dental floss were wrapped around the middle fingers, leaving about 1/2 to 1-1/2 inches of dental floss stretched firmly between each hand. Index finger and thumb were used to guide the floss between teeth [11]. The dental floss was gently used between teeth, making sure to slide the floss against the sides of each tooth. The floss was curved along the gum line, making a ‘c’ shape around each tooth. The floss was carefully worked under the gums to clean away food debris and plaque.

Chemical control including: topical antimicrobial agent application (oral solution that contains sage oil) in the clinic, and then how to replicate oral solutions three times daily.

Patient's re-evaluation (after 3 months, 6 months and 9 months) for clinical dental parameters: Clinical follow up was carried out weekly during the first month, then after three, six and nine months to assess all tested parameters (GI, PI and CAL).

Laboratory investigations: Glycosylated hemoglobin (HbA1c %) at the beginning, then it was done after three, six and nine months. Human Cytomegalovirus (HCMV) at the beginning, then after nine months.

Statistical methods

- Data were collected, entered and analyzed using the software SPSS 19. Quantitative data were presented as mean and standard deviation, qualitative data was presented as frequency distribution.
- Man-Whitney test was used to compare between good controlled and poor controlled groups regarding quantitative variables.
- Chi square test was used to compare between good controlled and poor controlled groups regarding qualitative variables.
- Friedman test was used to compare between the multiple measurements of quantitative data.
- CMV test was compared between good controlled and poor controlled by Z test.
- Correlation test was used to test association between clinical data and other quantitative variables.
- P value of less than 0.05 was considered as cutoff for significance.
- Graphics by Excel.

Results

Figure 1 shows that group I (good controlled) had a significant lower gingival index (GI) scores than group II (poorly controlled) at the base and at the 3rd month of the study, where (p=0.03) for each. On the other hand, there were insignificant differences between them at 6th months, 9th months of follow up periods where (p>0.05). As regards separate groups, there were significant reductions of GI scores at different periods of follow up on both of them were (p=0.001) for both.

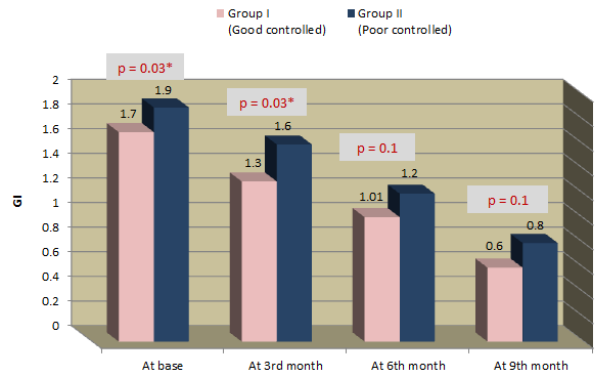

***Figure 1**. Comparison between the studied groups as regard Gingival Index (GI) at different follow up periods.*

According to the plaque index (PI), there were insignificant differences between different groups during the whole study periods, but on the other hand, there were significant improvements in each group in the plaque index through the whole periods of the study until 9thmonth (p>0.001) for each (*Figure 2*).

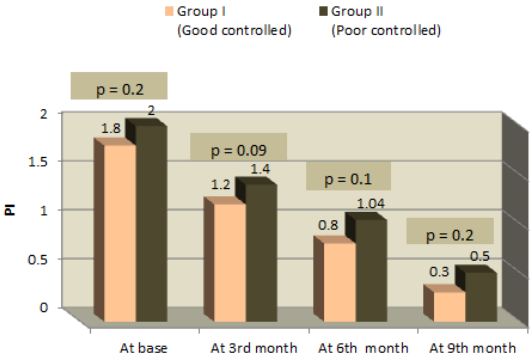

***Figure 2**. Comparison between group I and II as regard Plaque Index (PI) scores at different follow up periods.*

Figure 3 showed that there were insignificant differences in clinical attachment level (CAL) between different groups during the whole study period where (p>0.5).

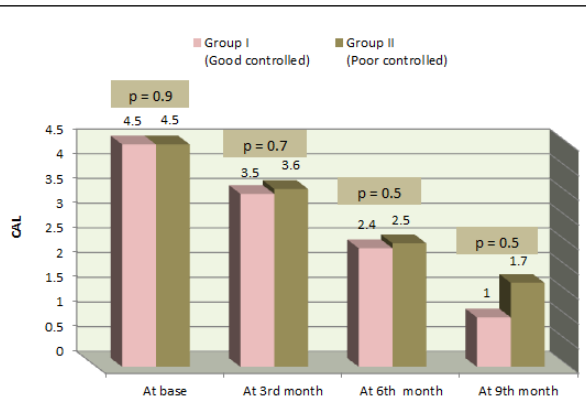

***Figure 3**. Comparison between group I and II as regard Clinical Attachment Level (CAL) scores at different follow up period.*

Table 1 showed that group II (poor controlled group) had significant higher levels of HbA1c % than group I (good controlled group) at different durations of follow up (at the base, at 3rd month, 6th month and 9th month). Moreover, within every group there were significant reduction of HbA1c % levels at different durations of follow up where (p=0.006 and p=0.001) respectively.

Table 2 showed that group II had significant higher positivity of CMV than group I at the base, at 9th months where (p=0. 001) for each.

On the other hand, there was an insignificant difference between groups I, II as regard number of viruses at different durations of follow up. Concerning each group of patients there were significant reductions of the number of viruses at 9th month of follow up compared to the beginning of the study was (p=0.01, 0.005).

Concerning different correlations *Table 3* showed that there was a significant positive moderate correlation between HbA1c % and GI at 6th month of follow up in group I where (r=0.55 and p=0.01). Concerning PI, it had a significant positive weak correlation with HbA1c % at the 3rd month of follow up where (r=0.48 and p=0.03).

Table 1. Comparison between group I and group II regarding HbA1c % at different follow up periods.

P value	Group II		Group I		Follow up periods
	mean ± SD	range	mean ± SD	range	
0.001*	10.4 ± 1.6	8.1-13	7.4 ± 0.4	6.1-7.9	At base
0.001*	10.2 ± 1.6	7.9-14	8.2 ± 1.1	7-11.2	At 3rd month
0.0065	9.2 ± 1.6	7.2-13.9	8.1 ± 0.9	7-10.8	At 6th month
0.01*	8.3 ± 1.6	7.1-13	7.5 ± 0.9	6.5-10.8	At 9th month
	0.001*		0.006*		P value

*p<0.05 is statistically significant

Table 2. Comparison between group I and group II regarding CMV positivity and number at base and 9 months.

CMV	Follow up periods	Group I	Group II	P value
Positivity At base	At base	5 (25%)	15 (75%)	0.001*
	At 9th month	3 (15%)	10 (50%)	0.001*
	P	0.3	0.09	
Number of virus by PCR	At base	$1.5 \times 10^6 \pm 2.9 \times 10^6$	$7.0 \times 10^5 \pm 8.2 \times 10^5$	0.5
	At 9th month	900 ± 210.8	833.3 ± 288.6	0.6
	P	0.005*	0.001*	

Finally, CAL had a highly significant positive, moderate correlation with the HbA1c % at 6th month of follow up where (r=0.58 and p=0.007).

Table 3. Correlations between HbA1c % and dental clinical parameters in group I at different periods of follow.

	HbA1c %			
Dental clinical parameter	At base	At 3rd month	At 6th month	At 9th month
	r(P)	r(P)	r(P)	r(P)
GI	0.009 (0.9)	0.26 (0.2)	0.55 (0.01)*	0.18 (0.4)
PI	0.03 (0.8)	0.48 (0.03)*	0.08 (0.7)	0.04 (0.8)
CAL	0.12 (0.5)	0.36 (0.08)	0.58 (0.007)*	0.32 (0.1)
*p<0.05 is statistically significant				
Grades of correlations: r< 0.24 weak, r=0.25-0.49 fair, r=0.50-0.74 moderate, r≥ 0.75 strong				

Table 4 showed that there were insignificant positive fair, weak correlations between HbA1c % with GI and PI in group II. On the other hand, there was a positive, moderate significant correlation between HbA1c % and CAL at the 3rd month of follow up where (r=0.50, p=0.03).

Table 4. Correlations between HbA1c % and dental clinical parameters in group II at different periods of follow up.

	HbA1c %			
Dental clinical parameter	At base	At 3rd month	At 6th month	At 9th month
	r(P)	r(P)	r(P)	r(P)
GI	0.38 (0.09)	0.34 (0.1)	0.23 (0.3)	0.17 (0.4)
PI	0.21 (0.3)	0.33 (0.3)	0.21 (0.1)	0.25 (0.2)
CAL	0.33 (0.1)	0.50 (0.03)*	0.34 (0.1)	0.11 (0.6)
*p<0.05 is statistically significant				

Table 5 showed that in group I, there were significant positive, strong correlations between number of CMV and gingival index, plaque index at the base of the study. On the other hand, CAL had insignificant positive correlation with the CMV number at the base. At the 9th month of follow up, all the dental parameters had a significant strong correlation with number of CMV.

Table 5. Correlations between number of CMV at base and dental clinical parameters in group I at the base and at 9 months.

Dental clinical parameters	Number of CMV at base		Number of CMV at 9th month	
	r	p	r	p
GI	0.95	0.001*	0.92	0.01*
PI	0.96	0.001*	0.86	0.05*
CAL	0.74	0.1	0.89	0.03*
*p<0.05 is statistically significant				

Table 6 showed that group II had a positive, moderate significant correlation between CMV number and GI at the base of the study.

Table 6. Correlations between number of CMV and dental clinical parameters in group II at different periods of follow up.

Dental clinical parameters	Number of CMV at base	Number of CMV at 9th month

	r	p	r	p
GI	0.65	0.008*	0.68	0.03*
PI	0.25	0.3	0.52	0.03*
CAL	0.4	0.1	0.76	0.02*
*p<0.05 is statistically significant				

At the 9th month of follow up, all the clinical dental parameters had significant moderate to strong correlations with number of CMV.

Discussion

As regards the dental clinical parameters, this study found that the mean values of gingival index scores were significantly higher in poor controlled group than in good controlled one (1.9 ± 0.3 versus 1.7 ± 0.3). This finding was in agreement with Orbak et al. [12] and Jindal et al. [13].

As regards plaque index, the current study revealed that poorly controlled diabetics had significant higher levels than good controlled (2 ± 0.3 versus 1.8 ± 0.3). These scores were similar to those recorded by Jindal et al. [13] and lower than those reported by Joo and Lee [14], who recorded (3.2 ± 1.0) for poorly controlled diabetic patients and (2.8 ± 0.8) for good controlled diabetic children.

As regards the clinical attachment level, the current study revealed high scores in the beginning of the study (4.5 ± 0.6) in both groups. This was in agreement with Tervonen and Oliver [15], who found that 10% of well controlled and 27% of poorly controlled diabetics had loss of attachment >5 mm.

These higher scores of different dental parameters could be explained by in T1D chronic hyperglycemia leads to formation of biologically active glycated proteins and lipids that promote inflammatory responses [13].

Moreover, long-term poor control of T1D patients leads to microvascular damage of the periodontium, alteration in the composition of gingival crevicular fluid, host bacterial flora of the gingiva and impaired healing response of the periodontium. Increased levels of inflammatory markers such as C-reactive protein, tumor necrosis factor-α, interleukin-6 (IL-6), IL-1, prostaglandin E2, and IL-10 observed in patients with diabetes may play a role in periodontal damage [13].

However, significant improvement was recorded in these parameters throughout the follow up period. Application of the dental program to those children improved their glycemic level, which in turn helps in the reduction of the microbial causative agents of the periodontal diseases.

Moreover, the poor controlled group had significantly higher levels of HbA1c % than good controlled group throughout follow up period. Concerning each group, there were significant reductions in HbA1c % levels at different durations of follow up. In the poor controlled group, the mean HbA1c % reduced from 10.4 ± 1.6 to 8.3 ± 1.6 at the end of follow up period.

This reduction was higher than that recorded by Janket et al. [16] in review ten Interventional studies with a combined population of 456 patients; the authors identified a weighted mean reduction in HbA1c of 0.66% as a result of periodontal therapy. Also, a meta-analysis of five studies reported a mean reduction in HbA1c of 0.40% over a follow-up period of 3–9 months after periodontal therapy [17].

In this study, the improvement was higher than results of preshow et al. [9] study. This could be related to the impact of dental health program followed by the participants in the current study and contentious follow up with reassessment of the program that help in reinforcing oral health practices.

Human cytomegalovirus (HCMV) represents a prototypic pathogenic member of the -subgroup of the herpes virus family. There is a direct relation between CMV infections and frailty that may cause immune senescence and cause T1D and high mortality level [18].

Viruses have emerged as putative pathogens in various types of periodontal disease. In particular, human cytomegalovirus (HCMV) seems to play important roles in the etiopathogenesis of severe types of periodontitis [5].

Regarding the level of CMV, there was a higher positivity among group II children, which was triple that in group I (75% versus 25%) respectively, this was in agreement with Kuber et al. [19], who investigated dental plaque samples and found that patients with aggressive periodontits had HCMV (68.8%), versus (0%) in healthy controls. According to Teughels et al. [20], cytomegalovirus can enhance the adherence of bacteria to primary epithelial cells of periodontal pockets. These viruses can alter the function of immune cells, resulting in abnormalities in adherence, chemotaxis and phagoctyosis.

Periodontitis in response to viral infection may be developed stepwise in a series of simultaneous or sequential infectious disease events, including; A high herpes virus load (gingivitis level) in periodontal sites, activation of periodontal herpes viruses, an insufficient antiviral cytotoxic T-lymphocyte response, the presence of specific periodontal pathogenic bacteria, an inadequate antibacterial antibody response [5]. In most individuals, these five suggested pathogenic determinants of periodontitis may be accelerated with suppressed cellular immunity.

Herpes viruses play a major role as activators of the disease process in this model of periodontitis. Indeed, CMV may be a key missing piece of the puzzle that would explain the transition from gingivitis to periodontitis or from stable to progressive periodontitis in pathogenesis of periodontal diseases.

The results of the current study support the theories that CMV may be one of the causative factors of T1D for those children by having a direct effect on pancreatic beta cells. CMV was isolated with another 5 viruses from patients with T1D [21].

The lower results of Abakur et al. [22] in recording CMV may be due to the difference in the method of investigation for the positivity of CMV with ELISA, while in the current study the real time PCR was used which is more precise and accurate in the detecting number of viruses. In the current study, assessment of CMV was more precise and valid so the

results were higher than that which was done using ELISA (50% vs. 37%).

There was a significant reduction in the recorded number of CMV at the end of the follow up period (9 months) than the baseline value, (in both groups). This improvement could be a result of the implemented program and its influence on dental clinical parameters followed by improvement in glycemic control and body immunity, taking into consideration absence of any antiviral medications given to our patients.

Therefore a bidirectional relationship between type I diabetes and periodontal diseases was proved, and supporting studies clarified the increase in the prevalence and severity of periodontal diseases with poor controlled T1D, where diabetes serves as a modifier of the expression of periodontal disease [23,24] and this makes the prevention and control of periodontal diseases in diabetic patients is part of control of diabetes for those children and prevention of any farther dental and health complications. Moreover, the present study emphasis on the role of CMV in this bidirectional relationship.

Conclusion

All the dental clinical parameters were higher in poorly controlled diabetic group, who had higher positivity and number of HCMV than good controlled group. Improvements of dental clinical parameters were associated with improvement of HbA1c % and decrease in the number of HCMV after application of the dental program.

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