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Original Article

The association between Type 1 diabetes mellitus and periodontal diseases

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KEYWORDS
Diabetes;
Type 1 diabetes mellitus (T1DM);
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Cohort study

Background/purpose: Type 1 diabetes mellitus (T1DM) is a chronic autoimmune disease affecting oral health. Evidence shows possible association between T1DM and periodontal diseases (PDs). We conducted a nationwide population-based study in Taiwan, with a 14-year follow-up to investigate the risk of PDs in T1DM patients.
Methods: We used data from the National Health Insurance Research Database in Taiwan. The T1DM cohort was identified with newly diagnosed T1DM from 1998 to 2011. The non-T1DM cohort was frequency matched with the T1DM cohort. Participants comprised 4248 patients in the T1DM cohort and 16992 persons in the non-T1DM cohort.
Results: The T1DM patients showed an increased risk of PDs compared to non-T1DM individuals [adjusted hazard ratio (aHR) = 1.45]. T1DM patients who visited the emergency room more than twice per year had a higher aHR of 13.0 for developing PDs. The aHR for PDs was 13.2 in the T1DM patients who had been hospitalized more than twice per year.
Conclusion: T1DM patients are at higher risk of developing PDs than non-T1DM individuals. Our results further showed that the number of T1DM interventions; that is, annual emergency visits and hospitalizations were associated with increased the risk of developing PDs.

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Introduction

Type 1 diabetes mellitus (T1DM) causes chronic hyperglycemia due to destruction of pancreatic beta cells.[1–3] Alarming rise of T1DM incidence occurs globally, while more recent T1DM cases are diagnosed in adolescence.[4,5] T1DM causes susceptibility to infection, inadequate wound healing while increased mortality and morbidity occurs with disease progression.[5] The comorbidities of T1DM are primarily classified as macrovascular and microvascular diseases.[6] Cardiovascular and cerebrovascular diseases are the most common macrovascular complications,[7] and microvascular complications include retinopathy, nephropathy, and peripheral neuropathy.[8] Periodontal diseases (PDs) have also been identified as a classic complication of diabetes mellitus.[9]

PDs include gingivitis and periodontitis, which gingivitis is caused by the bacterial biofilm that accumulates on teeth adjacent to the gingiva and periodontitis results in loss of connective tissue and bone support.[10] The disease may affect >50% of the world's population.[11] In addition to influencing oral health, periodontal pathogens and their productions (endotoxin and lipopolysaccharide) enter the systemic circulation and elicit systemic inflammatory responses.[12] General contributing factors of PDs include; age, genetics, stress, medications, oral hygiene, and systemic disorders including cardiovascular diseases,[13] diabetes,[14] and low-grade systemic inflammation.[15]

Previously, some studies showed relationship between T1DM and PDs. Patients with T1DM are more susceptible to PDs and tooth loss,[16] and these complications are more prevalent in young T1DM patients.[17] PDs in T1DM usually include gingivitis with bleeding and gingival recession at puberty developing into severe periodontitis.[18] Children with T1DM may develop significantly higher gingival inflammation, plaques, and loss of tooth attachment thus leading to periodontal destruction.[19,20] However, most studies have focused on the associations between Type 2 diabetes mellitus (T2DM) and PDs up to date. Regarding the association between T1DM and PDs, the evidence was scanty. In addition, those studies investigated the association between T1DM and PDs were usually based on a case—control study or cross-sectional study design. The novelty of this study was to employ the nationwide population database and a cohort study design to determine the quantified risk of PDs and the influence of emergency visits and hospitalizations in PD development in T1DM patients.

Materials and methods

Data source

The National Health Research Institutes in Taiwan provided National Health Insurance Research Database (NHIRD) for this study. The NHIRD of Taiwan is a nationwide database covering approximately 99% of Taiwan's 23.74 million residents who are enrolled in the National Health Insurance (NHI) program, which was launched on March 1, 1995. The database was previously used for T1DM and PDs studies.[21–24] We used the scrambled identification of residents to link three data collections, namely the Registry of Catastrophic Illnesses Patient Database (RCIPD), Longitudinal Health Insurance Database 2000 (LHID 2000), and Registry of Beneficiaries. The usage of the database has been detailed previously.[25,26] The NHIRD records the data about the diseases on the basis of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). This study was approved by the Ethics Review Board of China Medical University and Hospital in Taiwan (CMUH-104-REC2-115).

Sampled participants

The T1DM cohort was identified by seeking patients aged <40 years with newly diagnosed T1DM (ICD-9 codes 250.x1 and 250.x3) within the RCIPD from January 1, 1998 to December 31, 2011. We used the T1DM diagnosis date as the index date. We excluded patients with any history of PDs (ICD-9 code 523) before the index date. The non-T1DM cohort comprised identified subjects without T1DM during the period (1998—2011) from the LHID2000 and the exclusion criteria is the same as T1DM cohort. The non-T1DM cohort was frequency matched with the T1DM cohort at a 4:1 ratio for gender and index year.

Outcome and relevant variables

All individuals were followed from the index date to the occurrence of PDs [ICD-9 code, gingivitis (523.0 and 523.1) and periodontitis (523.3 and 523.4)], death, withdrawal from the NHI program or December 31, 2011, whichever came first. Some demographic factors and comorbidities that may be associated with PDs were also identified. These included gender, age, urbanization level (level 1 denoting the most urbanized communities, and level 4 denoting the least urbanized communities), comorbidities, including coronary artery disease (CAD) (ICD-9 codes 410—414), stroke (ICD-9 codes 430—438), asthma (ICD-9 code 493), chronic obstructive pulmonary disease (COPD) (ICD-9 codes 496), obesity (ICD-9 code 278), alcohol-related disease (ICD-9 codes 291, 303, 305, 571.0, 571.1, 571.2, 571.3, 790.3, A215, and V11.3), mental disorders (ICD-9 codes 290—319), and osteoporosis (ICD-9 code 733.0).

Statistical analysis

The distributions of sociodemographic variables and baseline comorbidities between the T1DM cohort and non-T1DM cohort were obtained using a Chi-squared test for categorical variables and a t-test for continuous variables. The cumulative incidences of subsequent PDs in the T1DM and non-T1DM cohorts were estimated using the Kaplan—Meier method, and the significance was determined using a log-rank test. PDs incidence were estimated by dividing the number of PDs cases by the number of person-years in each factor, and then stratifying by gender, age, urbanization level, comorbidity, and follow-up time. Univariable and multivariable Cox proportion hazard regression models were employed to examine the effect of T1DM on the risk of PDs, expressed as hazard ratios (HRs) with 95% confidence intervals (CIs). The multivariate Cox models were adjusted for gender, age, urbanization level, and comorbidities of

CAD, stroke, asthma, COPD, alcohol-related disease, and mental disorders. When the patients had been stratified according to gender, age, urbanization level, comorbidity, and follow-up time, the relative risk of PDs in the T1DM cohort compared with the non-T1DM cohort was analyzed using the Cox models. Additional analysis was performed to assess the effect of the dose response on the risk of developing PDs according to the mean times of annual emergency room (ER) visit and hospitalization for T1DM. Finally, we have divided the outcome of interest, PDs, into 2 specific types: (1) gingivitis and (2) periodontitis and evaluated their risks in the case and control groups. All data processing and statistical analyses were conducted using SAS statistical software (version 9.4 for Windows; SAS Institute, Inc., Cary, NC, USA). Statistical significance was accepted at $p < 0.05$.

Results

Study participants comprised of 4248 T1DM patients and 16992 non-T1DM individuals, with similar gender distributions (Table 1). Of the T1DM patients and non-T1DM individuals, 73.8% and 57.3%, respectively, were aged <20 years. The mean ages in the T1DM cohort and non-T1DM cohort were 15.3 (SD = 9.71) and 19.2 (SD = 10.6) years, respectively. Compared with the non-T1DM individuals, the T1DM patients had a greater tendency to live in urbanized areas (58.6% T1DM patients vs. 56.0% non-T1DM individuals respectively, lived in urbanization level 1 and 2 areas). T1DM patients were more likely to have CAD, stroke, asthma, COPD, obesity, alcohol-related disease, mental disorders, and osteoporosis with significance of ($p < 0.05$) compared to non-T1DM individuals.

Kaplan–Meier analysis for the mean follow-up of T1DM and non-T1DM cohorts for 6.04 and 6.23 years respectively showed a higher cumulative incidence of PDs in T1DM cohort compared to non-T1DM cohort (log-rank test, $p < 0.001$) (Fig. 1). The overall incidence densities of PDs for the cohorts with and without T1DM per 1000 person-years were 50.8 and 34.6 respectively. T1DM cohort exhibited an increased risk of PDs, after adjustment for gender, age, urbanization level, and comorbidities of CAD, stroke, asthma, COPD, alcohol-related disease, and mental disorders compared to that of non-T1DM cohort [adjusted hazard rate (aHR) = 1.45, 95% CI = 1.35–1.56] (Table 2). The aHR of PDs was 1.36-fold higher for women than for men (95% CI = 1.28–1.45). Compared with patients who were 20–40 years old, the risk of PDs was 1.13-fold higher in patients aged <20 years (95% CI = 1.06–1.21). Compared with patients living in areas with the lowest urbanization levels, patients living in areas with the highest (aHR = 1.33, 95% CI = 1.22–1.45), second highest (aHR = 1.24, 95% CI = 1.14–1.35) and third highest (aHR = 1.16, 95% CI = 1.05–1.28) urbanization levels were associated with significantly higher risks for PDs. Patients with CAD, stroke, asthma, or alcohol-related disease had 0.68-, 0.19-, 0.72- and 0.48-fold risk for PDs (95% CI = 0.46–0.98, 0.06–0.60, 0.64–0.81, and 0.48–0.64, respectively).

Table 1 Demographic characteristics and comorbidities in patient with and without T1DM.

	Controls	T1DM	*p*-value
	N = 16992	N = 4248	
	n (%)	n (%)	
Gender			0.99
Women	8504 (50.1)	2126 (50.1)	
Men	8488 (50.0)	2122 (50.0)	
Age			0.001
< 20	9739 (57.3)	3134 (73.8)	
20–40	7253 (42.7)	1114 (26.2)	
Age, mean ± SD [a]	19.2 ± 10.6	15.3 ± 9.71	<0.001
Urbanization level [b]			0.003
1 (highest)	4552 (26.8)	1178 (27.7)	
2	4968 (29.2)	1314 (30.9)	
3	3456 (20.3)	764 (18.0)	
4 (lowest)	4016 (23.6)	992 (23.4)	
Comorbidity			
CAD	117 (0.69)	79 (1.86)	<0.001
Stroke	44 (0.26)	39 (0.92)	<0.001
Asthma	1496 (8.80)	489 (11.5)	<0.001
COPD	272 (1.60)	89 (2.10)	0.03
Obesity	208 (1.22)	124 (2.92)	<0.001
Alcohol-related disease	397 (2.34)	134 (3.15)	0.002
Mental disorders	1590 (9.36)	569 (13.4)	<0.001
Osteoporosis	19 (0.11)	17 (0.40)	<0.001

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; SD, standard deviation; T1DM, type 1 diabetes mellitus.

[a] t-test.

[b] The urbanization level was categorized by the population density of the residential area into 4 levels, with level 1 as the most urbanized and level 4 as the least urbanized.

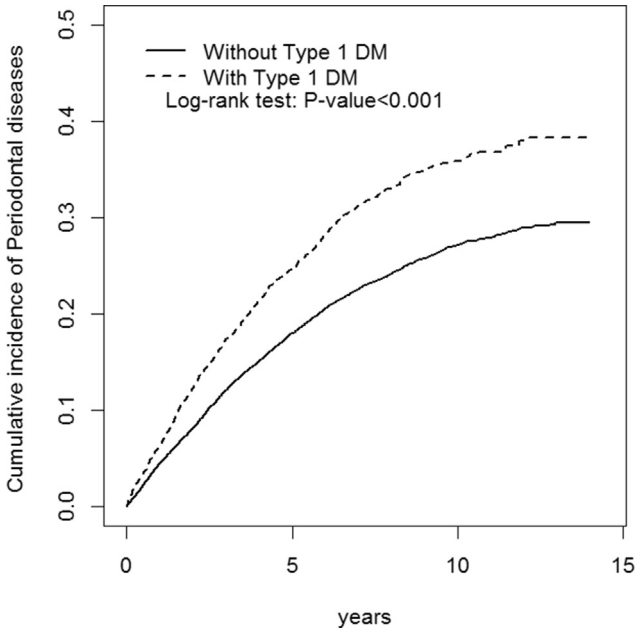

Fig. 1 Cumulative incidence of periodontal diseases (gingivitis and periodontitis) for individuals with (dashed line) and without (solid line) type 1 diabetes mellitus.

Table 2 Incidences and risk factors for periodontal diseases (gingivitis and periodontitis).

Variable	Event	PY	Rate[a]	Crude HR (95% CI)	Adjusted HR (95% CI)[b]
T1DM					
No	3127	90506	34.6	1.00	1.00
Yes	1057	20799	50.8	1.45 (1.35–1.55)***	1.45 (1.35–1.56)***
Gender					
Women	2400	54269	44.2	1.41 (1.32–1.49)***	1.36 (1.28–1.45)***
Men	1784	57037	31.3	1.00	1.00
Age					
< 20	2807	69840	40.2	1.22 (1.14–1.30)***	1.13 (1.06–1.21)***
20–40	1377	41466	33.2	1.00	1.00
Urbanization level [c]					
1 (highest)	1250	29790	42.0	1.33 (1.22–1.45)***	1.33 (1.22–1.45)***
2	1288	32674	39.4	1.25 (1.14–1.36)***	1.24 (1.14–1.35)***
3	804	22178	36.3	1.15 (1.04–1.26)**	1.16 (1.05–1.28)**
4 (lowest)	842	26664	31.6	1.00	1.00
Comorbidity					
CAD					
No	4156	109956	37.8	1.00	1.00
Yes	28	2350	20.7	0.59 (0.41–0.86)**	0.68 (0.46–0.98)*
Stroke					
No	4181	110821	37.7	1.00	1.00
Yes	3	485	6.18	0.17 (0.06–0.53)**	0.19 (0.06–0.60)**
Asthma					
No	3884	100903	38.5	1.00	1.00
Yes	300	10403	28.8	0.74 (0.66–0.84)***	0.72 (0.64–0.81)***
COPD					
No	4132	109221	37.8	1.00	1.00
Yes	52	2085	25.0	0.68 (0.52–0.89)**	0.79 (0.60–1.04)
Obesity					
No	4125	109464	37.7	1.00	1.00
Yes	59	1841	32.0	0.85 (0.66–1.10)	
Alcohol-related disease					
No	4137	107969	38.3	1.00	1.00
Yes	47	3336	14.1	0.38 (0.28–0.51)***	0.48 (0.36–0.64)***
Mental disorders					
No	3785	98805	38.3	1.00	1.00
Yes	399	12501	31.9	0.86 (0.77–0.95)**	0.94 (0.84–1.04)
Osteoporosis					
No	4178	111074	37.6	1.00	1.00
Yes	6	231	25.9	0.73 (0.33–1.62)	

CAD, coronary artery disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; PY, person-years; T1DM, type 1 diabetes mellitus.

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

[a] Incidence rate per 1000 person-years.

[b] Multivariable analysis including gender, age, urbanization level, and comorbidities of CAD, stroke, asthma, COPD, alcohol-related disease, and mental disorders.

[c] The urbanization level was categorized by the population density of the residential area into 4 levels, with level 1 as the most urbanized and level 4 as the least urbanized.

The overall incidence and risk of PDs in T1DM patients were determined using variables, including gender, age, urbanization level, presence or absence of comorbidity, and follow-up period. The risk for PDs in T1DM cohort were determined based on whichever stratification was higher compared to non-T1DM cohort (Table 3). Compared with the non-T1DM cohort, T1DM cohort with more than two ER visits per year for their diabetes had a higher aHR of 13.0 (95% CI = 11.1–15.2) for developing PDs (Table 4). The aHR of PDs was 13.2 (95% CI = 11.5–15.1) in the T1DM patients who had been hospitalized more than twice per year for their diabetes. Furthermore, we have divided the PDs into 2 specific types: (1) gingivitis; (2) periodontitis. We found that T1DM patients have 1.47-fold risk to develop gingivitis (95%

Table 3 Comparison of incidences of periodontal diseases (gingivitis and periodontitis) and hazard ratios between individuals with and without T1DM.

Variables	Controls			T1DM			Crude HR (95% CI)	Adjusted HR (95% CI)[b]
	Event	PY	Rate[a]	Event	PY	Rate[a]		
Gender								
Women	1798	44286	40.6	602	9983	60.3	1.45 (1.32–1.59)***	1.50 (1.37–1.65)***
Men	1329	46220	28.8	455	10817	42.1	1.45 (1.30–1.61)***	1.51 (1.35–1.68)***
Age								
< 20	2007	54363	36.9	800	15476	51.7	1.38 (1.27–1.50)***	1.40 (1.29–1.51)***
20–40	1120	36143	31.0	257	5323	48.3	1.53 (1.34–1.75)***	1.65 (1.44–1.89)***
Urbanization level [c]								
1 (highest)	921	24170	38.1	329	5619	58.6	1.51 (1.33–1.71)***	1.58 (1.39–1.80)***
2	944	26376	35.8	344	6298	54.6	1.49 (1.32–1.69)***	1.54 (1.35–1.74)***
3	616	18353	33.6	188	3825	49.2	1.44 (1.23–1.70)***	1.48 (1.26–1.75)***
4 (lowest)	646	21607	29.9	196	5057	38.8	1.28 (1.09–1.50)**	1.36 (1.16–1.60)***
Comorbidity [d]								
No	2614	70856	36.9	793	14443	54.9	1.46 (1.35–1.58)***	1.48 (1.37–1.61)***
Yes	513	19650	26.1	264	6356	41.5	1.57 (1.35–1.82)***	1.57 (1.35–1.82)***
Follow-up								
< 1 year	715	15773	45.3	259	3923	66.0	1.46 (1.26–1.68)***	1.62 (1.40–1.87)***
2–3 years	1052	25370	41.5	381	6095	62.5	1.51 (1.34–1.70)***	1.64 (1.46–1.85)***
4–5 years	664	18980	35.0	203	4352	46.7	1.33 (1.14–1.56)***	1.34 (1.14–1.57)***
≥ 5 years	696	30383	22.9	214	6429	33.3	1.44 (1.24–1.68)***	1.42 (1.22–1.66)***

CI, confidence interval; HR, hazard ratio; PY, person-years; T1DM, type 1 diabetes mellitus.
**$p < 0.01$, ***$p < 0.001$.
[a] Incidence rate per 1000 person-years.
[b] Multivariable analysis including age, gender, urbanization level, and comorbidities of CAD, stroke, asthma, COPD, alcohol-related disease, and mental disorders.
[c] The urbanization level was categorized by the population density of the residential area into 4 levels, with level 1 as the most urbanized and level 4 as the least urbanized.
[d] Patients with any comorbidity of CAD, stroke, asthma, COPD, obesity, alcohol-related disease, mental disorders, and osteoporosis were classified as the comorbidity group.

CI = 1.36–1.59) and 1.66-fold risk to develop periodontitis (95% CI = 1.41–1.96) compared to non-T1DM individuals (Table 5).

Discussion

To our knowledge, this is the first nationwide population-based cohort study to assess patients with T1DM and their subsequent risk of developing PDs. The study determined that a higher risk for PDs including both gingivitis and periodontitis in T1DM patients compared to non-T1DM individuals. Furthermore, we determined that the increased annual ER visits and hospitalizations for T1DM were proportional to risk of PD development.

Poor periodontal health was prevalent in T1DM.[27] Various factors, including weakened immune response, resistance to infections, diabetic microangiopathy, oral microflora, and impaired collagen metabolism, might involve in PD development in T1DM patients.[18,28] Hyperglycemia elevates oral inflammation by increasing glucose levels in salivary and gingival crevicular fluid, which then directly promote periodontopathic bacteria proliferation and inflammation.[28] Inflammatory cytokines in the gingival crevicular fluid enhance periodontal destruction.[29] Elevated levels of IL-1β and MMP-8 in gingival crevicular fluid were previously observed in T1DM patients.[30] Patients with higher IL-6 levels had poor periodontal healing.[31] Additionally, increased glycoproteins during hyperglycemia line the endothelial cells leading to narrowed and weakened vessels leading to microangiopathy. Thus, the vascular changes in the periodontal tissue lead to PD progression.[28] Hyperglycemia may stimulate the generation of advanced glycation end products (AGE products).[32] The glycosylated products can generate complex molecules, increasing release of the proinflammatory mediator responsible for degrading connective tissues and the bone.[28,33] The interaction of AGE products with macrophages can stimulate cytokine, matrix metalloproteinase and collagenase expressions resulting in connective tissue decomposition.[34] Proinflammatory cytokine expressions are elevated in diabetes,[35,36] which can amplify connective tissue damage and impair wound healing.[29] T1DM group was reported to have altered periodontal pathogens compared with non-T1DM group.[37,38] In addition, spirochetes and motile rods are significantly enriched in the periodontally diseased pockets in the T1DM patients.[39]

The controlled glycemic status of T1DM influences the clinical condition of the PDs. Occurrence of gingivitis were reported to be more common in patients with unsatisfactory glycemic control and high HbA1c levels.[40,41] Metabolic control and duration of the disease is a common factor for

Table 4 Hazard ratios and 95% confidence intervals of periodontal diseases (gingivitis and periodontitis) risk associated with the average number of annual emergency room visits and hospitalizations for T1DM.

	Periodontal diseases		Hazard ratio (95% CI)	
	Event	Rate[a]	Crude	Adjusted[b]
Controls	3127	34.6	1 (Reference)	1 (Reference)
Average number of annual ER visit for T1DM				
<2	877	43.0	1.23 (1.14–1.32)***	1.28 (1.18–1.38)***
≥2	180	469.5	11.8 (10.1–13.8)***	13.0 (11.1–15.2)***
p for trend			<0.001	<0.001
Average number of annual hospitalization for T1DM				
<2	818	40.3	1.15 (1.07–1.24)***	1.20 (1.11–1.30)***
≥2	239	471.2	11.9 (10.4–13.6)***	13.2 (11.5–15.1)***
p for trend			<0.001	<0.001

CI, confidence interval; ER, emergency room; T1DM, type 1 diabetes mellitus.
***$p < 0.001$.
[a] Incidence rate per 1000 person-years.
[b] Multivariable analysis including age, gender, urbanization level, and comorbidities of CAD, stroke, asthma, COPD, alcohol-related disease, and mental disorders.

Table 5 Comparison of incidence densities of gingivitis and periodontitis and hazard ratios between individuals with and without T1DM.

Outcome	Event	Rate[a]	Event	Rate[a]	Crude HR (95% CI)	Adjusted HR (95% CI)[b]
	Controls (Overall)		T1DM (Overall)			
Gingivitis	2534	28.0	856	41.2	1.44 (1.34–1.56)***	1.47 (1.36–1.59)***
Periodontitis	593	6.55	201	9.66	1.45 (1.24–1.71)***	1.66 (1.41–1.96)***
	Controls (Women)		T1DM (Women)			
Gingivitis	1472	33.2	500	50.1	1.47 (1.33–1.63)***	1.49 (1.35–1.65)***
Periodontitis	326	7.36	102	10.2	1.36 (1.09–1.70)**	1.57 (1.25–1.98)***
	Controls (Men)		T1DM (Men)			
Gingivitis	1062	23.0	356	32.9	1.42 (1.26–1.60)***	1.44 (1.28–1.63)***
Periodontitis	267	5.78	99	9.15	1.54 (1.23–1.93)***	1.54 (1.23–1.93)***
	Controls (<20 Y)		T1DM (<20 Y)			
Gingivitis	1708	31.4	680	43.9	1.38 (1.26–1.51)***	1.42 (1.29–1.55)***
Periodontitis	299	5.50	120	7.75	1.40 (1.13–1.73)**	1.42 (1.15–1.76)**
	Controls (20–40 Y)		T1DM (20–40 Y)			
Gingivitis	826	22.9	176	33.1	1.42 (1.21–1.67)***	1.48 (1.25–1.74)***
Periodontitis	294	8.13	81	15.2	1.84 (1.44–2.36)***	2.06 (1.60–2.64)***

CI, confidence interval; HR, hazard ratio; T1DM, type 1 diabetes mellitus.
**$p < 0.01$, ***$p < 0.001$.
[a] Incidence rate per 1000 person-years.
[b] Multivariable analysis including age, gender, urbanization level, and comorbidities of CAD, stroke, asthma, COPD, alcohol-related disease, and mental disorders.

prevalence of T1DM in children and adolescents.[42] Long-term inadequate control of T1DM results in microvascular damage to the periodontium, changed composition of the gingival crevicular fluid and the bacterial flora of the gingiva which altogether impairs healing ability of periodontium.[5] T1DM with unsatisfactory glycemic control has deeper pockets, a higher bleeding index, more dental plaque which exacerbates loss of attachment.[5,41,42] Aggravated marginal loss of alveolar bone was observed in subjects with complicated T1DM.[43,44] In the current study, we have performed an advanced analysis, which demonstrated a dose–response relationship. The hazard of developing PDs increased sharply for T1DM patients with increased annual ER visits and hospitalizations for their diabetes. The confirmed dose–response relationship not only enhances the association between T1DM and the risk of PDs, but also suggests that poor diabetes control is an essential factor associating with the PDs development.

Periodontal therapy plays a vital role in glycemic control and the risk of cardiovascular diseases. Periodontal treatment leads to a reduction in HbA1c levels leading to improved periodontal health in diabetic patients within 3 months.[45,46] Nonsurgical periodontal treatment may have a beneficial effect on glycemic control and HbA1c level in patients with T2DM.[47,48] Metabolic control of T1DM may be achieved by improved insulin sensitivity during periodontal treatment.[49,50] Periodontal treatment instituted in patients with T2DM may ameliorate the inflammatory biomarker

levels and glycemic control.[51] A significant reduction in fasting plasma glucose level and glycated hemoglobin in patients with T2DM and PD was observed with nonsurgical periodontal therapy.[52] Periodontal microbes were not identified as risk factors for cardiovascular disease inT1DM young patients with favorable oral health,[53] thus targeted therapy to maintain oral health might reduce the burden of cardiovascular diseases.[54]

In the present study, we found the overall incidence of PDs (gingivitis and periodontitis) was higher in people with age <20 than people with age 20—40 (Table 2), which was not in accordance with the general concept. In further stratified analysis, we found people with age 20—40 having a higher incidence of periodontitis but a lower incidence of gingivitis than those with age <20 in both case and control groups (Table 5). There is less evidence to compare the incidence of gingivitis between these age groups (20—40 vs. <20). We consider people with age <20 have more chances to check their oral health status; therefore, the incidence of gingivitis was higher in this age group. Nevertheless, the influence should be equal between the case group (T1DM) and the control group (non-TIDM). In addition, the study result showed females could have a higher risk of periodontal diseases than males (Table 2), which was not compatible to some other studies. We consider this is because females with age <40 may be more willing to visit a dentist than males with age <40 do in the real-world practice. In the largest study using the same database, Yu et al. have also reported a higher prevalence of periodontitis in females than in males in similar age groups.[55]

The strength of this study is the use of a nationwide population-based database to retrospectively evaluate the subsequent occurrence of PDs among the T1DM patients. The sampled group (n = 4248) is sufficiently large and the diagnosis of T1DM is reliable because T1DM is categorized as a catastrophic illness in the NHI system. The insurance authority provides catastrophic illness certification issued to all patients diagnosed with T1DM. The certification process requires confirmation from experts specialized in the disease field. The incidence of PDs in the control group in the present study was similar to those of other studies in Taiwan.[24] However, some limitations were identified in the present study. First, the PDs and comorbidities were diagnosed using the ICD format, which relies on the performance of specialist physicians. Checkup is regularly performed to prevent misdiagnoses and negligence. Second, the NHI research center does not hold detailed data on environmental factors, oral hygiene habits, diet, and family history, which are possible confounding factors. Furthermore, pertinent clinical variables, such as serum laboratory data, urinalysis, fundus examination, and detailed dental records were not available in the database.

In conclusion, patients with T1DM have a higher risk of developing PDs than the general population. Our results indicated that the risk of developing PDs is related to the number of annual emergency medical visits and hospitalizations for T1DM.

Conflict of interest

The authors declare that they have no conflict of interest.

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