

Original Article

Diabetes type, hemoglobin A1C biomarker and control as predictors for dental treatment needs

Lily A. Hartsock¹, Alexandre R. Vieira^{2⊠}

- 1. Dental Student, Department of Oral Biology, School of Dental Medicine, University of Pittsburgh, Pittsburgh, PA, USA.
- 2. Professor, Department of Oral Biology, School of Dental Medicine, University of Pittsburgh, Pittsburgh, PA, USA.

<u>Corresponding Author</u>: Alexandre R. Vieira, School of Dental Medicine, University of Pittsburgh, Pittsburgh, PA, USA.

Email: arv11@pitt.edu

Tel: +1-412-383-8972

ORCID (0000-0003-3392-6881)

Received: 7 Jun 2020

Accepted: 9 Dec 2020

Abstract

Introduction: The goal of this study was to test the impact of both diabetes type and control via the hemoglobin A1C biomarker on oral health outcomes.

Materials & Methods: In this observational study, data were extracted from the University of Pittsburgh Dental Registry and DNA Repository and analyzed. From 6,026 subjects, 414 ones with a diagnosis of diabetes were matched by sex, age and ethnicity with 414 individuals without diabetes. A number of statistical approaches (chi-square, Fisher's exact, Student's *t*, Wilcox, and Mann Whitney tests) were used and all comparisons were set with an alpha of 0.05.

Results: Patients with type 1 diabetes experienced xerostomia more often compared to non-diabetic matched pairs (p=0.02). Patients with diabetes (n=414) experienced temporomandibular joint (TMJ) discomfort more often than their non-diabetic matched pairs, as did type 1 diabetic patients alone, in comparison to both their matched pairs and type 2 diabetic patients (p=0.01, p=0.004, and p=0.02, respectively). Among patients grouped by diabetic control, all patients reporting control (n=39) experienced xerostomia more often than their non-diabetic matched pairs (p=0.05). Patients in poor diabetic control experienced restoration failure more often than patients in good control (p=0.04). The experience of restoration failure was no different between patients in good diabetic control and their matched controls (p=0.26). The number of restoration failures was higher in patients in poor control, as compared to their matched non-diabetic controls (p=0.03).

Conclusion: Patients with diabetes experienced xerostomia but not necessarily more severe caries experience, and may be protected from TMJ discomfort. Patients in good control of their diabetes were at no greater risk for restoration failure as compared to non-diabetic patients; however, the patients in poor control were at higher risk for failed restorations.

Keywords: Dental caries, Periodontitis, Dental amalgam, Dental restoration failure

Citation for article: Hartsock L A, Vieira A R. Diabetes type, hemoglobin A1C biomarker and control as predictors for dental treatment needs. Caspian J Dent Res 2021; 10:8-18.



نوع دیابت، بیومارکر هموگلوبین A1C و میزان کنترل بعنوان پیش بینی کننده نیازهای درمانی دندانی

لیلی .اً. هار تساک ، الکساندر.اًر. وییرا *

۱. دانشجوی دندانپزشکی، گروه بیولوژی دهان و دندان، دانشکده دندانپزشکی، دانشگاه پیتسبورگ، پیتسبورگ، پنسیلوانیا، ایالات متحده آمریکا.
 ۲. استاد، گروه بیولوژی دهان و دندان، دانشکده دندانپزشکی، دانشگاه پیتسبورگ، پیتسبورگ، پنسیلوانیا، ایالات متحده آمریکا.
 *نویسنده مسئول: الکساندر.آر. وییرا، دانشکده دندانپزشکی، دانشگاه پیتسبورگ، پیتسبورگ، پنسیلوانیا، ایالات متحده آمریکا.
 پست الکترونیکی: arv11@pitt.edu

حكىدە

مقدمه: هدف از این مطالعه بررسی تأثیر نوع و کنترل دیابت از طریق بیومارکر هموگلوبین A1C بر پیامدهای بهداشت دهان بود. مواد و روش ها: این مطالعه مشاهده ای از مرکز تحقیقات ثبت دندانی و مخزن DNA دانشگاه پیتسبورگ استخراج و تحلیل گردید. از ۶٬۰۲۶ مورد ، ۴۱۴ نفر با تشخیص دیابت و ۴۱۴ نفر بدون دیابت از نظر جنس، سن و قومیت با هم همسان شدند.تعدادی از آزمونهای آماری(مجذور کای،اگزکت فیشر،استیودنت-تی،ویلکاس و من ویتنی) استفاده شد. در تمام مقایسه ها آلفا ۰/۰۵ در نظر گرفته شد.

یافته ها: نتایج نشان داد که بیماران مبتلا به دیابت نوع ۱ نسبت به افراد غیردیابتی، خشکی دهان را بیشتر تجربه کردند (p=0.02). بیماران مبتلا به دیابت ملیتوس (۴۱۴ نفر) در مقایسه با جفت های همسان شده غیردیابتی خود ناراحتی مفصل گیجگاهی فکی بیشتری داشتند، همچنین بیماران فقط با دیابت نوع ۱ در مقایسه با غیردیابتیها و دیابتی نوع ۲ ، از این ناراحتی بیشتر رنج میبردند (بترتیب p=0.004،p=0.004،p=0.004، در بین بیمارانی که بر اساس کنترل دیابت گروهبندی شدهاند، همه بیماران گزارش کننده کنترل (p=0.004، بیماران با کنترل ضعیف دیابت نسبت به بیماران با کنترل خوب بیشتر دچار شکست ترمیم شدند (p=0.04). از نظر تجربه عدم شکست در ترمیم، تفاوتی بین بیماران با کنترل خوب دیابت و گروه کنترل وجود نداشت (p=0.04). تعداد شکست ترمیم در بیمارانی که کنترل دیابتی ضعیفی داشتند، بیشتر از گروه غیردیابتی همسان آنها بود (p=0.03).

نتیجه گیری: بیماران مبتلا به دیابت ملیتوس احتمالاً خشکی دهان را تجربه می کنند اما لزوماً پوسیدگی شدیدتری ندارند و ممکن است از ناراحتی مفصل گیجگاهی فکی محافظت شوند. بیمارانی که به خوبی دیابت ملیتوس را کنترل می کنند در مقایسه با بیماران غیردیابتی در معرض خطر بیشتری برای شکست ترمیم نیستند. ولی بیماران با کنترل ضعیف دیابت در معرض خطر بالاتری برای ترمیم ناموفق هستند.

واژگان کلیدی: پوسیدگی دندان ، پریودنتیت ، اَمالگام دندان ، شکست ترمیم دندان

Introduction

Globally, diabetes affects 425 million people with a projection of 629 million affected by the year 2045. Diabetes mellitus is a metabolic disorder characterized by the body's inability to either produce the hormone insulin in the case of insulin dependent diabetes (Type 1) or use endogenous insulin in the case of non-insulin dependent diabetes (Type 2). Both forms of diabetes lead to the dysregulation of blood glucose concentration

and many shared sequelae, despite differing etiologies. Most sequelae associated with diabetes stem from the development of microangiopathy, the thickening of the basement membrane in micro vessels of vascular tissue, caused by chronic hyperglycemia. The thickening of vascular walls reduces both the permeability and diameter of vessels, which can lead to hypertension, hypoxia, delayed wound healing and poor regulation of



inflammation among other concerns.^[3,4] It has been suggested that the risk of developing dental caries is elevated in patients with diabetes due to reduced salivary flow, caused by hyperglycemia.^[2] There are studies that report histological changes to the parotid glands as a result of diabetic complications, leading to xerostomia and reduced salivary flow.^[5] Additionally, during periods of hyperglycemia, the concentration of glucose within the oral cavity may rise and provide an ideal environment to harbor increased counts of Streptococcus mutans.^[2]

Periodontitis which lines the teeth and supportive tissues occurs when bacteria containing biofilm cause an infection so that the body's immune system is unable to control. The association between diabetes and periodontitis has been studied extensively, leading to the generally accepted conclusion that diabetes places patients at a higher risk for periodontitis. It has been suggested that this heightened risk is, due to impaired migration of leukocytes, needed to fight off bacterial infections in patients with diabetes.

In addition to concerns over dental caries and periodontitis, research suggests that diabetes may play a role in the incidence of temporomandibular joint (TMJ) discomfort. Microangiopathy can affect many systems including the capillaries of organs within the mouth. Capillaries allow microcirculation of blood within the articular disc of the temporomandibular joint. As a result of hyperglycemia, diabetic rats displayed significantly thinner articular discs ($16.6 \pm 6.3 \mu m$) compared to non-diabetic rats ($43.4 \pm 22.0 \mu m$, p<0.01). The decreased disc thickness was hypothesized to place diabetic patients at higher risk for TMJ discomfort. [8]

The percent plasma hemoglobin A1C test is the primary clinical measurement for time spent in a hyperglycemic state and a predictive measure of risk for diabetic complications. [9] In non-diabetic persons, hemoglobin A1C comprises 3 to 6 percent of the total hemoglobin, while in diabetic persons this percentage typically falls between 6 to 12 percent. [10] The American Diabetes Association (ADA) recommends that patients with diabetes maintain percent plasma hemoglobin A1C of seven or lower to prevent diabetic complications. [11]

Because of the oral health impact associated with poorly controlled diabetes, our general hypothesis was that patients with diabetes (both type 1 and type 2) would be at a higher risk for all four outcomes (dental caries, periodontitis, xerostomia, and TMJ discomfort), as compared to their matched non-diabetic pairs. The

current study evaluated the hemoglobin A1C biomarker as a marker for dental treatment needs instead of diabetes type. It was hypothesized that patients in poor control of their diabetes would experience poor oral health outcomes more often, compared to patients in good diabetic control. Patients grouped by their last recorded percent hemoglobin A1C were also evaluated for failed amalgam and composite/resin restorations. Restorations are initially placed after the removal of dental caries, to repair tooth fractures, or for aesthetics among other motivations, but may be replaced or restored over time, often due to secondary caries. [12] It was of interest to evaluate if patients with poorly controlled diabetes would be more susceptible to secondary caries and, in turn, restoration failure.

Materials & Methods

Diabetes Patients Grouped by Diabetes Type: Beginning in September of 2006, every individual referred to the University of Pittsburgh School of Dental Medicine for treatment was given the opportunity to be a part of the Dental Registry and DNA Repository project [University of Pittsburgh Institutional Review Board (IRB, code FWA00006790) approval # 0606091]. This study conforms to the STROBE Guidelines.^[13] At the time of this analysis, there were 6,026 subjects in the University of Pittsburgh School of Dental Medicine Dental Registry and DNA Repository project.[14] All individuals that agreed to participate gave written informed consent authorizing the use of information from their dental and medical records. From the total 6,026 individuals participating in the registry, the records of 592 self-reported diabetic patients, type 1 and type 2, were evaluated. Patients reporting prediabetes or insulin dependence with no specification of the type of diabetes were excluded from the ongoing study. Totally, 414 patients, 36 with type 1 diabetes and 378 with type 2 diabetes were selected. Each of the 414 diabetic patients was matched with a non-diabetic patient from the registry in terms of sex, age and ethnicity, to the best of our ability (Table 1).

Disorders were evaluated on categorical yes/no basis, despite potential spectrums of severity. Dental caries was defined based on the decayed, missing due to caries, filled teeth (DMFT) score and caries free individuals separated from individuals with previous caries experience. Xerostomia was defined as the presence of the perception of dry mouth. For



periodontitis, individuals were considered affected if showing signs of at least stage III. [15] TMJ discomfort was defined in anyone with a record of, at least, one symptom in the TMJ discomfort (clicks, sounds or pain). All information was extracted from the dental records and was originally recorded by dental students in training supervised by professionals that are calibrated annually by their supervisors. [14] Chi-square or Fisher's exact tests and odds ratio calculations with respective 95% confidence intervals were used to help interpret differences in frequency between the two comparison groups with an alpha of 0.05. Knowing that the frequency of the conditions tested ranged from 10% to 30%, the sample size needed to detect 10% difference was 356.

Table 1. Demographic characteristics of all cases with diabetes

	Cases (n=414)	Controls (n=414)
Age, y (mean, range)	59.5(15-88)	60.6(15-90)
Sex (n, %)		
Female	204(49.28%)	202(48.79%)
Male	210(50.72%)	212(51.21%)
Self-reported		
Ethnicity (n, %)		
Whites	281(67.87%)	282(68.12%)
African Americans	123(29.71%)	122(29.47%)
Asians	4(0.97%)	4(0.97%)
Other/ Not Available	3(0.72%)	3(0.72%)

Note: diabetic patient cases (n=414) were matched to non-diabetic control patients (n=414) of the same sex and closest age, and ethnicity

Diabetes Patients Grouped by Hemoglobin A1C Marker: There were 414 patients reported to have diabetes among all participants, each of whom was screened for a record of his or her last reported hemoglobin A1C. Of those 414 patients, 50 patients had a record of their hemoglobin A1C and were included in this experiment. Edentulous patients by the time they started treatment at the University of Pittsburgh School of Dental medicine were excluded, leaving a group of 39 patients, three with Type 1 diabetes and 36 with Type 2 diabetes. Each of the remaining 39 patients with diabetes was matched with a non-diabetic patient from the registry for sex, age and ethnicity, to the best of our ability (Table 2).

After the experimental group was defined, each subject was placed into a group of good/fair diabetic

control or poor diabetic control, regardless of diabetes type. Patients with percent plasma hemoglobin A1C recorded at or below seven percent were considered to be in good/fair control and hemoglobin A1C above seven percent qualified as poor control. [11] Eighteen patients qualified as being in good/fair control of his or her diabetes and 21 patients qualified as being in poor control.

Table 2. Demographic characteristics of cases with Hemoglobin A1C information

9	Cases (n=39)			ontrols n=39)
Age, y (mean, range)	60.0	1 (24-80)	60.0	3 (23-80)
Sex (n, %)				
Female	15	(53.43%)	15	(53.43%)
Male	24	(46.57%)	24	(46.57%)
Self-reported				
Ethnicity (n, %)				
Whites	26	(66.67%)	26	(66.67%)
African Americans	11	(28.21%)	11	(28.21%)
Other/ Not Available	2	(5.13%)	2	(5.13%)

Note: diabetic patient cases with plasma hemoglobin AIC levels (n=39) were matched to non-diabetic control patients (n=39) of the same sex and closest age and ethnicity

Patients' records were evaluated using the same diagnostic criteria for dental caries, xerostomia, periodontitis and TMJ discomfort, as stated prior. Chisquare or Fisher's exact tests and odds ratio calculations with respective 95% confidence intervals were used to help interpret differences in frequency between the two comparison groups with an alpha of 0.05. Knowing that the frequency of the conditions tested ranged from 50% to 55%, the sample size needed to detect 30% difference was 36.

Impact of Hemoglobin A1C on Restoration Success:

Patient dental records were screened for a history of restorative dental procedures. The total number of amalgam restorations and composite/resin restorations were counted, regardless of whether the restorations were placed at the University of Pittsburgh School of Dental Medicine. Then, patients' records were screened for repeated amalgam restorations, repeated composite/resin restorations and unsalvaged/extracted due to the recurrent caries. To most accurately report failed restorations, a restoration was only considered repeated/failed if completed at the same site on the same tooth more than once over the span of patient treatment at the



dental school or if otherwise clearly reported as "repeated restoration" or "recurrent caries." Teeth deemed un salvaged/ extracted due to the caries were determined by screening for the following exact four diagnoses: "extracted due to caries," "caries to bone," "significant decay," or "recurrent caries." Teeth extracted after an initial attempt at restoration were considered failed restorations. Matched pairs were evaluated under the same strict screening criteria for failed restorations.

The data obtained were divided into several categories: experience of failed restorations (yes/no), number of failed restorations, repeated amalgam restorations, repeated composite/resin restorations, un salvaged/extracted due to caries, and duration of treatment at the University of Pittsburgh School of Dental Medicine.

Data were analyzed by Fishers exact test, Mann Whitney test for unpaired data, or Wilcoxon test for paired data, depending on the data type. Odds ratios (OR) and 95% confidence intervals (95% C.I.) were used to help interpret differences between the two comparison groups with an alpha of 0.05. All data were corrected using logistic or linear regressions, according to type, to establish that the number of restorative treatments was not directly related to the duration of patient treatment (years), at the University of Pittsburgh School of Dental Medicine.

Results

Diabetes Patients Grouped by Diabetes Type: In a comparison of all patients with diabetes and their controls, patients with diabetes significantly less experience with TMJ discomfort compared to their non-diabetic matched controls (p=0.01, O.R. 0.69, 95% C.I. 0.52-0.92, Table 3). Patients with type 1 diabetes showed significantly less experience with TMJ discomfort, compared to their matched controls (p=0.004, O.R. 0.2, 95% C.I. 0.06-0.63, Table 3). There was a nearly significant difference in the level of experience with TMJ discomfort between type 2 diabetes patients and their matched controls (p=0.07, O.R. 0.76, 95% C.I. 0.56-1.02, Table 3). In the test of type 1 diabetes patients to type 2 diabetes patients, type 1 patients reported significantly less experience with TMJ discomfort (p=0.02, O.R. 0.33, 95% C.I. 0.12-0.87, Table 3).

Type 1 diabetes patients exhibited experience with xerostomia significantly more often compared to their

matched non-diabetic controls (p=0.02, O.R. 5.67, 95% C.I. 1.13 to 28.44, Table 3). Type 2 diabetes patients also exhibited greater experience with xerostomia compared to matched controls; however, the difference was not significant (p=0.23, O.R. 1.25, 95% C.I. 0.87-1.79, Table 3).

Marker: The comparison of all diabetes patients with records of hemoglobin A1C (n=39) and their matched controls revealed that patients with diabetes had significantly more experience with xerostomia (p=0.05, O.R. 3.02, 95% C.I. 0.95-9.63, Table 4). Other comparisons indicated no statistically significant differences (Table 4).

Impact of Hemoglobin A1C on Restoration Success: In the comparison of patients with well-controlled diabetes and poorly controlled diabetes, patients with good/fair control of their diabetes had significantly less restoration failures (experience and number), compared to diabetes patients with poor diabetic control (p=0.04, O.R. 0.25, 95% C.I. 0.07-0.97; Mann Whitney p=0.005, Table 5). Patients with good/fair hemoglobin A1C had significantly less counts of failed restorations (number) and failed composite/resin restorations compared to their matched controls with no significant difference in experience (p=0.007; p=0.04; p=0.09, O.R. 0.32, 95% C.I. 0.08-1.24, Table 5). Patients in poor control of their diabetes had significantly greater counts of failed restorations (number) as compared to their non-diabetic matched controls (p=0.03, Table 5). Patients with good diabetic control had fewer teeth extracted due to the caries compared to both patients with poor diabetic control (hemoglobin A1C > 7) and their matched controls; however, the results were not significant (p=0.1, p=0.17, respectively, Table 5). Patients with poor percent plasma hemoglobin A1C had more teeth extracted due to the caries compared to their matched controls; nevertheless, this result was not statistically significant (p=0.13, Table 5). To correct for the possibility that the duration of patient treatment (years) was a confounding factor with regard to the number of restorations placed at the dental school, all data sets were tested for goodness of fit on a logistic or linear regression. The only trend was noted for amalgam restorations in the comparison of fair/good versus poor control and fair/good control versus matched controls, of which no comparison illustrated no formal significance (p=0.39, p=0.76, respectively, Table 5).



Table 3. Differences in oral health complications in diabetic patients grouped by diabetes type (type 1 and type 2)

Oral Health Outcome		Patients with	Non-Diabetic	p-	Odds	95% Confidence
		Diabetes	Matched Pairs	value	Ratios	Intervals
		(n=414)	(n=414)			
Dental Caries		139	138	1.0	1.01	0.76-1.35
Xerostomia		89	69	0.08	1.37	0.97-1.94
Periodontitis		50	51	1.0	0.98	0.64-1.48
Temporomandibular	joint	129	164	0.01	0.69	0.52-0.92
discomfort						
Oral Health Outcome		Type one Diabetes	Non-Diabetic Matched	p-	Odds	95% Confidence
		Patients	Pairs (n=36)	value	Ratios	Intervals
		(n=36)				
Dental Caries		10	9	0.79	1.15	0.4-3.29
Xerostomia		9	2	0.02	5.67	1.13-28.44
Periodontitis		5	3	0.45	1.77	0.39-8.05
Temporomandibular	joint	5	16	0.004	0.2	0.06-0.64
discomfort						
Oral Health Outcome		Type two Diabetes	Non-Diabetic Matched	p-	Odds	95% Confidence
		Patients	Pairs	value	Ratios	Intervals
		(n=378)	(n=378)			
Dental Caries		129	129	1	1	0.74-1.35
Xerostomia		80	67	0.23	1.25	0.87-1.79
Periodontitis		45	48	0.74	0.93	0.6-1.43
Temporomandibular	joint	124	148	0.07	0.76	0.56-1.02
discomfort						_
Oral Health Outcome		Type one Diabetes	Type two Diabetes	p-	Odds	95% Confidence
		Patients	Patients	value	Ratios	Intervals
		(n=36)	(n=378)			
Dental Caries		10	129	0.44	0.74	0.35-1.59
Xerostomia		9	80	0.59	1.24	1.56-2.75
Periodontitis		5	45	0.73	1.19	0.44-3.23
Temporomandibular	joint	5	124	0.02	0.33	0.12-0.87
discomfort						

Note: Chi-square and Fischer's exact tests were used with an alpha equal to 0.05

GDR

Table 4. Differences in oral health outcomes in diabetes patients (both types included) grouped by percent plasma hemoglobin A1C. Chi-square and Fischer's exact tests were used with an alpha equal to 0.05

Oral Health Outcome	All Diabetes Patients	Non-Diabetic	p-	Odds	95% Confidence
	with Reported	Matched Pairs	value	Ratios	Intervals
	HbA1C	(n=39)			
	(n=39)				
Dental Caries	34	32	0.53	1.49	0.43-5.17
Xerostomia	12	5	0.05	3.02	0.95-9.63
Periodontitis	9	8	0.78	1.16	0.4-3.41
Temporomandibular joint	10	15	0.22	0.55	0.21-1.45
discomfort					
Oral Health Outcome	Patients with Good	Patients with Poor	p-	Odds	95% Confidence
	HbA1C Control	HbA1C Control	value	Ratios	Intervals
	(n=18)	(n=21)			
Dental Caries	15	19	0.51	0.53	0.08-3.56
Xerostomia	7	5	0.31	2.04	0.51-8.1
Periodontitis	2	7	0.1	0.25	0.04-1.41
Temporomandibular joint	5	5	0.78	1.23	0.29-5.19
discomfort					
Oral Health Outcome	Patients with Good	Non-Diabetic	p-	Odds	95% Confidence
	HbA1C Control	Matched Pairs (n=18)	value	Ratios	Intervals
	(n=18)				
Dental Caries	15	15	1	1	0.17-5.77
Xerostomia	7	3	0.14	3.18	0.67-15.15
Periodontitis	2	3	0.63	0.62	0.09-4.27
Temporomandibular joint	5	6	0.72	0.77	0.18-3.19
discomfort	_				
Oral Health Outcome	Patients with Poor	Non-Diabetic	p-	Odds	95% Confidence
	HbA1C Control	Matched Pairs	value	Ratios	Intervals
	(n=21)	(n=21)			
Dental Caries	19	17	0.38	2.23	0.36-13.78
Xerostomia	5	2	0.21	2.97	0.51-17.42
Periodontitis	7	5	0.49	1.6	0.41-6.19
Temporomandibular joint	5	9	0.19	0.42	0.11-1.57
discomfort					



Table 5. Failed amalgam and composite restorations due to caries in diabetic (both types included) patients grouped according to percent plasma hemoglobin A1C. Patient experience with restorative failures and teeth extracted due to caries are displayed

Restorative Conditions	All Diabetes Patients with Reported HbA1C (n=39)	Non-Diabetic Matched Pairs (n=39)	p-values, Odds Ratios (OR) and 95% Confidence Intervals (95% C.I.)
←Experience of Failed Restorations (Yes/No)*	22	23	p=0.82 O.R.=0.9 95% C.I =0.37-2.21
Number of Failed Restorations**	72	74	0.82
Repeated Amalgam Restorations**	22	21	0.68
Repeated Composite/Resin Restorations**	20	30	0.53
Teeth Extracted Due to Caries**	67	76	0.73
Restorative Conditions	Patients with Good	Patients with Poor	p-values,
	HbA1C Control	HbA1C Control	Odds Ratios (OR) and 95%
	(n=18)	(n=21)	Confidence Intervals (95% C.I.)
Experience of Failed Restorations	7	15	p=0.04
(Yes/No)*			O.R.=0.25
			95% C.I =0.07-0.97
Number of Failed Restorations***	13	59	0.005
Repeated Amalgam Restorations***	8	14	0.39
Repeated Composite/Resin	4	16	0.19
Restorations***			
Teeth Extracted Due to Caries***	7	60	0.1
Restorative Conditions	Patients with Good HbA1C Control (n=18)	Non-Diabetic Matched Pairs (n=18)	p-values, Odds Ratios (OR) and 95% Confidence Intervals (95% C.I.)
Experience of Failed Restorations (Yes/No)*	7	12	p=0.09 O.R.=0.32 95% C.I =0.08-1.24
Number of Failed Restorations**	13	49	0.007
Repeated Amalgam Restorations**	8	12	0.76
Repeated Composite/Resin Restorations**	4	23	0.04
Teeth Extracted Due to Caries**	7	38	0.17
Restorative Conditions	Patients with Poor	Non-Diabetic Matched	p-values,
	HbA1C Control	Pairs	Odds Ratios (OR) and 95%
	(n=21)	(n=21)	Confidence Intervals (95% C.I.)
Experience of Failed Restorations (Yes/No)*	15	11	p=0.2 O.R.=2.27 95% C.I =0.63-8.15
Number of Failed Restorations**	59	25	93% C.1=0.03-8.13 0.03
Repeated Amalgam Restorations**	14	9	0.03
Repeated Composite/Resin	16	7	0.41
Restorations** Teeth Extracted Due to Caries**	60	38	0.13

Notes: Different statistical tests can be distinguished by the presence of asterisks: *Chi squared test, **Wilcox for paired data, and ***Mann Whitney test for unpaired



Discussion

To our knowledge, this is the first study to consider diabetes type and diabetes control via the hemoglobin A1C biomarker when describing dental treatment needs. We aimed to determine if type 1 diabetes and type 2 diabetes patients would differ in the incidence of four oral health disorders; dental caries, xerostomia, periodontitis, and TMJ discomfort, as well as in comparison to their matched non-diabetic controls. We tested these same four conditions using the hemoglobin A1C biomarker as a metric instead of diabetes type, as it is arguably a better predictor for complications resulting from diabetes. Finally, we hoped to determine if diabetic control, qualified by the hemoglobin A1C biomarker, was an indicator for restoration success.

Xerostomia is considered one of the signs of oral health complication due to the diabetes.^[5] Thus, it was hypothesized that xerostomia would be more prevalent in diabetic patients compared to non-diabetic controls. Several comparisons within our study revealed significant or nearly significant differences in counts of xerostomia, suggesting that diabetes is associated with higher experience with the disorder (Table 3 and Table 4). These results concur with studies that have found significant prevalence of xerostomia in populations of patients with diabetes. [16,17] Earlier post-mortem investigations of the basement membrane of parotid glands in 15 patients with a history of diabetes found abnormalities in all subjects.^[18] This displays that the cause of xerostomia in patients with diabetes may be a result of microangiopathy of the parotid gland due to the prolonged hyperglycemia.

It had been expected that dental caries experience would be significantly different in one or more comparisons, as diabetes has been associated with higher risk of dental caries. [19,20] The results of our study did not provide a statistically significant difference in dental caries, in any grouping. However, in our comparison of restoration failures in patients with wellcontrolled versus poorly controlled diabetes, patients with poorly controlled diabetes exhibited greater experience with and counts of restorative failure (Table 5). Patients with good/fair control of their diabetes were at no higher risk for experience with restoration failure than their matched controls; however, the overall number of failed restorations in patients with wellcontrolled diabetes was less as compared to their matched controls (Table 5). We have concluded that when diabetes is well controlled, patients are expected incur the same level or risk for restorative complications as compared to non-diabetic patients. Poor control of diabetes; however, places patients at a higher risk for secondary caries experience and resultant restoration failure.

Our study on (TMJ) discomfort revealed multiple surprising results. First, while several studies indicated association between periodontitis and diabetes, our comparisons did not demonstrate a significant difference between patients with diabetes and their nondiabetic matched controls. [21-23] Additionally, patients with diabetes (n=414) presented with significantly less TMJ discomfort as compared to matched non-diabetic controls (Table 3). Type 1 diabetes patients also represented significantly less TMJ discomfort compared to matched controls and type 2 diabetes patients (Table 3). Based on these results alone, one may consider that diabetes protects patients from TMJ discomfort by some mechanism. However, results of a study conducted in rats revealed that rats with type 2 diabetes were at higher risk for TMJ discomfort, resulting from decreased blood flow to the capillary tissue surrounding the TMJ as a result of microangiopathy. [8] Therefore, we looked to our hemoglobin A1C group, to see if the results aligned with our initial comparison. If TMJ discomfort was a result of microangiopathy, patients in poor diabetic control would be expected to show more experience with TMJ discomfort. In the comparisons of diabetic patients who had provided hemoglobin A1C percentages, no significant difference was found with regard to TMJ discomfort in any comparative group.

We predict that the results surrounding periodontitis and TMJ discomfort are a product of the overall oral health status of the population studied. Patients studied along the Appalachian strip had overall worse oral health and higher susceptibility to oral health complications. Metropolitan areas are typically healthier than more rural areas in the strip, but pockets of extremely impoverished people with very poor oral health skew the statewide reports of oral health.^[24] The population of studied patients in the current study may be at higher risk for poor oral health outcomes due to the socioeconomic status of many patients seen in our clinic. This, in turn, causes patients with diabetes to look as healthy or healthier than their matched non-diabetic controls.

There were several limitations of this study. In patients with diabetes, diabetes was self-reported and



sample size for some of the comparisons were small. The TMJ dysfunction could not be defined according to international standards; therefore' patients symptoms were described as having temporomandibular "discomfort." Procedures completed at the school of dental medicine were performed by many different professionals and reported in different ways. Patients' records were screened for a strict set of key words and phrases, in an effort to most accurately report patient conditions. Based on the results of our study, it is concluded that xerostomia is of clinical concern in patients with diabetes and should be regularly screened by dental practitioners. In addition, in the present study, when the hemoglobin A1C was kept at or below 7%, patients with diabetes incurred no higher risk of oral health complications as compared to non-diabetic patients. Patients with poorly controlled diabetes; however, are placed at a higher risk for secondary caries related restoration failures.

In conclusion herefore, it is revealed that more thorough preventative and educational measures should be initiated to limit experience with poor oral health outcomes in patients with poorly controlled diabetes. Because diabetes type does not dictate the percent plasma hemoglobin A1C, the best indicator of future complications due to the diabetes, it is represented that the hemoglobin A1C can be used as an indicator of oral health complications, not diabetes type.

Acknowledgements

Data reported, here, were obtained from the Dental Registry and DNA Repository project, which is supported by the University of Pittsburgh School of Dental Medicine.

Funding: Financial support disclosure for this project was provided to L.A.H. by the University of Pittsburgh School of Dental Medicine's Dean's Summer Research Scholarship.

Conflict of interest disclosure: The authors have no conflicts of interest to disclose.

Author Contributions

L.A.H. contributed to conception, design, data acquisition, interpretation, statistical analysis, drafted and critically revised the manuscript.

A.R.V. contributed to conception, design, data acquisition, interpretation, statistical analysis, and critically revised the manuscript.

Both authors have read and approved the submitted version of the manuscript.

References

- 1. Cho NH, Kirigia J, Mbanya JC, Ogurstova K, Guariguata L, Rathmann Q,et al, editors. IDF 8th Diabetes Atlas[Online]. ed. Brussels, Belgium:International Diabetes Federation; 2017 [2019]. Available cited July 11, https://www.idf.org/e-library/epidemiologyresearch/diabetes-atlas/134-idf-diabetes-atlas-8thedition.html
- Latti BR, Kalburge JV, Birajdar SB, Latti RG. Evaluation of relationship between dental caries, diabetes mellitus and oral microbiota in diabetics. J Oral Maxillofac Pathol 2018; 22:282.
- Chawla A, Chawla R, Jaggi S. Microvascular and macrovascular complications in diabetes mellitus: distinct or continuum? Indian J Endocrinol Metab 2016; 20:546-51.
- Huang S, Dang H, Huynh W, Sambrook PJ, Goss AN. The healing of dental extraction sockets in patients with type 2 diabetes on oral hypoglycaemics: a prospective cohort. Aust Dent J 2013; 58:89-93.
- 5. Sousa MGC, Costa Ade L, Roncalli AG. Clinical study of the oral manifestations and related factors in type 2 diabetics patients. Braz J Otorhinolaryngol 2011; 77:145-52. [Article In English, Portuguese]
- Ramírez JH, Parra B, Gutierrez S, Arce RM, Jaramillo A, Ariza Y, et al. Biomarkers of cardiovascular disease are increased in untreated chronic periodontitis: a case control study. Aust Dent J 2014; 59:29-36.
- 7. Loe H. Periodontal Disease: The sixth complication of diabetes mellitus. Diabetes Care 1993; 16:329-34.
- 8. Uemura M, Toda I, Kawashima W, Yoshimoto G, Fang YR, Xu YJ, et al. Morphological study of the articular disc and capillary of the retrodiscal tissue in a type 2 spontaneous diabetes mellitus rat model. Okajimas Folia Anat Jpn 2016; 92:53-9.
- Saleh J. Glycated hemoglobin and its spinoffs: Cardiovascular disease markers or risk factors? World J Cardiol 2015; 7:449-53.

- **GDR**
 - Trivelli LA, Ranney HM, Lai HT. Hemoglobin components in patients with diabetes mellitus. N Engl J Med 1971; 284:353-7.
 - 11. American Diabetes Association® deeply concerned about new guidance from American College of Physicians regarding blood glucose targets for people with type 2 diabetes [Online]. American Diabetes Association; 2018 [cited 2019 July 1]. Available
 - from:http://www.diabetes.org/newsroom/press-releases/2018/ada-acp-guidance-response.html
 - 12. Collares K, Opdam NJM, Laske M, Bronkhorst EM, Demarco FF, Correa MB, et al. Longevity of anterior composite restorations in a general dental practice-based network. J Dent Res 2017; 96:1092-9.
 - von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol 2008;

 61:344-9.

 Vieira AR, Silva MB, Souza KKA, Filho AVA, Rosenblatt A, Modesto A. A pragmatic study shows failure of dental composite fillings is genetically determined: A contribution to the discussion on dental amalgams. Front Med (Lausanne) 2017;
 - 15. Graziani F, Greenwell H, Herrera D, Kao RT, Kebschull M, Kinane DF, et al. Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. J Periodontol 2018; 89 Suppl:S173-82.
 - Hoseini A, Mirzapour A, Bijani A, Shirzad A. Salivary flow rate and xerostomia in patients with type I and II diabetes mellitus. Electron Physician 2017; 9:5244-9.
 - 17. Carramolino-Cuéllar E, Lauritano D, Silvestre FJ, Carinci F, Lucchese A, Silvestre-Rangil J. Salivary

- flow and xerostomia in patients with type 2 diabetes. J Oral Pathol Med 2018; 47:526-30.
- Murrah VA, Crosson JT, Sauk JJ. Parotid gland basement membrane variation in diabetes mellitus. J Oral Pathol 1985; 14:236-46.
- 19. Suzuki S, Yoshino K, Takayanagi A, Ishizuka Y, Satou R, Nara N, et al. Relationship between blood HbA1c level and decayed teeth in patients with type 2 diabetes: A cross-sectional study. Bull Tokyo Dent Coll 2019; 60:89-96.
- 20. Majbauddin A, Tanimura C, Aoto H, Otani S, Parrenas MCE, Kobayashi N, et al. Association between dental caries indicators and serum glycated hemoglobin-levels among patients with type 2 diabetes mellitus. J Oral Sci 2019; 61:335-42.
- Tervonen T, Oliver RC. Long-term control of diabetes mellitus and periodontitis. J Clin Periodontol 1993; 20:431-5.
- Sandberg GE, Sundberg HE, Fjellstrom CA, Wikblad KF. Type 2 diabetes and oral health: A comparison between diabetic and non-diabetic subjects. Diabetes Res Clin Pract 2000; 50:27-34.
- 23. Ajita M, Karan P, Vivek G, S MA, Anuj M. Periodontal disease and type 1 diabetes mellitus: Associations with glycemic control and complications: An Indian perspective. Diabetes Metab Syndr. 2013; 7:61-3.
- Krause DD, Cossman JS, May WL. Oral health in Appalachia: regional, state, sub-state, and national comparisons. J Appalach Stud 2016; 22: 80-102.

4:186.