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Association between diabetes and oral health in non-smokers

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ASSOCIATION BETWEEN DIABETES AND ORAL HEALTH IN NON-SMOKERS

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DEDICATION

I would like to dedicate this work to my patient family, including my wonderful parents and my brother who have been there for me every step of the way.

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ASSOCIATION BETWEEN DIABETES AND

ORAL HEALTH IN NON-SMOKERS

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ABSTRACT

Background: There is a dearth of studies on the association between diabetes mellitus (DM) and the risk of developing oral health complications in nonsmokers. Recent studies have presented a strong link between smoking and increased risk of periodontal disease in patients with T2DM. This study attempts to look at the risk of developing caries and poor oral health in nonsmokers who also have DM. Male and female subjects from the cross-sectional National Health and Nutrition Examination Survey (NHANES) 2017-2018 study who were 21+ years at the time of entering the study were included. The exposures are DM and smoking, and the outcome is oral health.

Hypothesis: DM-IFG will increase the risk of developing dental caries and tooth loss, thus lowering the quality of oral health in smokers compared to nonsmokers.

Methods: DM was defined as either the self-report of a doctor's diagnosis of DM or a fasting glucose level of 126mg/dL or higher, or both. IFG was defined as a level of fasting glucose between 100mg/dL and 126mg/dL, as well as being informed by a medical doctor about having borderline DM. Subjects with IFG or DM were further combined into a DM-IFG group. Each subject's status was classified on the basis of both DM-IFG status and smoking status, yielding four exposure groups: (1) no DM-IFG/non-smokers, (2) no DM-IFG/smokers, (3) DM-IFG/non-smokers, and (4) DM-IFG/smokers.

Oral health outcomes were defined as a percent of missing teeth (due to dental health issues), percent of teeth with dental caries, and percent of teeth either missing or with caries. The primary statistical analysis for association between DM-IFG and smoking exposures and oral health outcomes was multivariable logistic regression. Adjusted models controlled for covariates such age, gender, Body Mass Index (BMI), education level, minutes of sedentary activity, race, HR, and percent of calories from fat intake.

Results: Overall, the prevalence of having 25% or more of teeth with dental caries was similar in those with and without DM-IFG (50.9% vs. 49.9%, respectively) and, surprisingly, was with higher among non-smokers than smokers (51.9% vs. 42.1%, respectively. Those with DM-IFG had a prevalence of missing teeth due to dental causes ($\geq$ 15% missing) of 43.2% compared with a prevalence of 28.6% among those without DM-IFG. Since the majority of missing teeth were likely to be due to caries as well, the final outcome for these analyses consists of participants with either missing teeth or carious remaining teeth. Here, we found that 55.8% of those with DM-IFG had 40% of more of teeth missing vs. 44.8% of those without DM-IFG ($p<0.0001$). Similarly, 52.1% of smokers vs. 48.8% of non-smokers had more missing or carious teeth ($p=0.1587$). In the multivariable models, adjusting for age, race, HR, and percent of calories from fat, these analyses showed that DM-IFG alone (among non-smokers) was associated with a 1.42-fold increased risk of missing teeth while smoking along was associated with a 2.86-fold increased risk. The combined effects of the two factors were even stronger. Those who smoked cigarettes and who had DM-IFG (compared with those who did not smoke and had no DM-IFG) had a 3.88-fold increased risk of have 15% or more of their teeth

missing due to dental health issues. Lastly, I examined these same effects on the risk of having either missing teeth or dental caries. In these analyses, smokers without DM-IFG had a 67% higher risk (95% CI: 1.27-2.19) of have 40% or more of their teeth missing or with caries while non-smokers with DM-IFG had no excess risk. Finally, those with DM-IFG who also smoked cigarettes had a 52% increased risk (95% CI: 1.08-2.14) of have 40% or more of their teeth missing or with caries compared with non-smokers who did not have DM-IFG.

Conclusion: These results suggest that smoking was a more important risk factor for having missing teeth or dental caries than was DM or IFG.

Key Words: Diabetes Mellitus, Hyperglycemia, Type 2 Diabetes Mellitus, Impaired Fasting Glucose, Glycohemoglobin, Periodontal Disease, Tooth Loss, Smoking, Chronic Inflammation, Caries.

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LIST OF ABBREVIATIONS

BMI	BODY MASS INDEX
CDC	CENTERS FOR DISEASE CONTROL AND PREVENTION
DM	DIABETES MELLITUS
DMD	DOCTOR OF DENTAL MEDICINE
DM-IFG	DIABETES MELLITUS OR IMPAIRED FASTING GLUCOSE
HR	HEART RATE
IFG	IMPAIRED FASTING GLUCOSE
MEC	MOBILE EXAMINATION CENTER
NHANES	NATIONAL HEALTH & NUTRITION EXAMINATION SURVEY
PD	PERIODONTAL DISEASE
SAS	STATISTICAL ANALYSIS SOFTWARE
T2DM	TYPE 2 DIABETES MELLITUSX

INTRODUCTION

Background and Rationale

Diabetes Mellitus (DM) is a common morbidity characterized by elevated blood glucose, or hyperglycemia, and/or abnormalities of carbohydrate, fat, and protein metabolism (Lamster et al., 2008). DM results from impaired insulin secretion, abnormal insulin action or a combination of the two mechanisms (Bascones-Martínez et al., 2015). The Centers for Disease Control and Prevention (CDC) reports 463 million people have DM worldwide. In the US up to 10.5 percent of the US population have DM, with American Indians/Alaskan Natives making up the highest percent (14.7%) nationally. Up to 26.8 percent of Americans are seniors of age 65 and older. (Centers for Disease Control and Prevention, 2020) DM can be further classified into three types: Type 1, Type 2, and Gestational Diabetes, of which Type 2 (T2DM) is most common nationally and globally. There are six main complications of DM, which include microangiopathy (disease of the capillaries), nephropathy (kidney disease), neuropathy (disease of the peripheral nerves), macrovascular disease, and delayed wound healing. Periodontitis, or periodontal disease (PD) has been accepted as the sixth complication of DM. (Grover & Luthra, 2013)

PD is an advanced stage of gum disease that stems from a bacterial infection that reaches and causes inflammation of the bone below the gums which supports the teeth. Gingivitis is an early stage of PD and is characterized by inflammation of the gingival tissue with no loss of attachment or bone. According to the American Dental Association (ADA), 42 percent, or nearly 65 million adults of 30 years or older have at least one

permanent tooth with PD between 2009 and 2014 (Eke et al., 2018). Of these, 9 percent with mild gum disease, 30 percent with moderate disease and 8.5 percent with severe disease. This report also highlights that adults who are 65 years or older, as well as Mexican Americans, non-Hispanic blacks, and smokers had the highest prevalence of severe PD (Eke et al., 2018). If PD is left untreated, this comorbidity can damage the bone that supports the tooth and eventually leads to tooth loss. Periodontal inflammation is worse in smokers than in nonsmokers (Javed et al., 2015), yet there is improvement in the PD status of people who stop smoking (Fiorini et al., 2014). Also, PD increases with age and with decreasing income status, according to a 2020 global study of the prevalence of PD (Nazir et al., 2020). A study in Hispanic Americans with type 2 diabetes mellitus (T2DM) further suggested that DM and smoking increase the risk and severity of PD (Novak et al., 2008).

Much of the evidence linking DM with PD stem from case control studies (Loe, 1993). One case-control study found that smoking increased the likelihood of PD, especially when combined with the condition of DM. Other case-control studies have reported that smoking while also having DM is strongly associated with edentulism – or tooth loss (Battancs et al., 2020). Recent studies on PD and DM reported that there was a bidirectional relationship between the two. In other words, patients with PD have missing or falling teeth that forces them to eat a soft-food diet, and thus interferes with the blood sugar levels. On the other hand, people with DM are more likely to experience complications that increase their risk of developing PD.

The two-way relationship between DM with oral health is of interest. Systemic inflammation affects blood glucose levels, leading to an imbalance in sugar levels. (Borgnakke 2019) A case control study which is the first study on the bidirectional relationship between PD and T2DM in Jazan, Saudi Arabia confirms previous studies on this topic (Quadri et al., 2020). However, epidemiologic studies with regards to the association between PD and DM are conflicting, as multiple ways have been reported for assessment of the two conditions. At least one study concluded that there is no association between PD and pre-DM/DM (Joshipura et al., 2018). In contrast, Wu et al reviewed 53 observational studies and arrived at a conclusion that T2DM could elevate the risk of developing PD (Wu et al., 2020). Additionally, a 2010 longitudinal study of 362 subjects showed an 11-fold risk of alveolar bone loss for Indians with DM compared to non-DM controls (Deshpande et al., 2010).

Salivary gland function can be impeded in subjects with DM (Negrato & Tarzia, 2010). Saliva is important to maintain a pH which is slightly basic within the oral cavity; when the salivary gland becomes nonfunctional, then it can influence oral health (Leite et al., 2013). Lack of oral care affects quality of life in subjects with DM. Furthermore, it contributes to unhealthy nutrition choice (Azogui-Lévy et al., 2018). The presence of DM tends to increase the risk of PD and vice versa (Zhou et al., 2014). Moreover, patients with DM tend to overlook their oral health and this leads to an increased risk of developing oral health problems, such as edentulism and dental caries (Poudel et al., 2018).

In the past, medical doctors and dentists focused specifically on their field of specialization, while disregarding the other conditions that their patients might have had (Taiyeb-Ali et al., 2000). Today, awareness of the connection between oral health and systemic health has increasingly become more common. However, medical professionals do not have hard or soft tissue of the oral cavity included in their medical school curriculum (Borgnakke, 2019). It is crucial to emphasize the importance of acknowledging the bidirectional relationship between PD and DM (Mauri-Obradors et al., 2017). Doctors' and dentists' awareness on this topic can help with identifying the symptoms of DM and making accurate and early diagnoses of these two morbidities. In turn, medical professionals will be able to educate their patients with regards to the attention necessary for maintaining their patients' oral health and blood sugar in check. This could also help to take preventive measures towards the PD and DM complications, especially since it disproportionately affects adults from health centers (Aldukhail et al., 2021).

Smoking is a risk factor of developing both DM and PD. A recent cross-sectional study of 154,404 participants found that there is an increase in the odds of reporting pre-DM as a result of smoking e-cigarettes (Atuegwu et al., 2019). Apical PD is independently linked with T2DM and with uncontrolled glycemia in patients (Yip et al., 2021). Another risk factor for tooth loss and PD is due to nocturnal eating (Lundgren et al., 2010). Systemic conditions are associated with indicators of PD (Özçaka et al., 2014). To prevent PD, dentists need to identify and treat gum disease in its early stages (gingivitis). Furthermore, both dental and medical doctors should learn to recognize the

signs and symptoms associated with PD and DM. In doing so they could inform their patients about ways to control inflammation and subsequently aid in preventing further complications. Essentially, identifying factors associated with higher risk of PD could help health professionals to determine which patients should be screened, and this is very important especially for patients with a higher risk such as those who smoke or have DM.

Impaired fasting glucose (IFG) has been defined as levels of glucose in fasting patients between 100 and 125 mg per dL (Rao et al., 2004). This cross-sectional study examines the question of whether DM or IFG is associated with dental caries and edentulism in smokers compared to non-smokers, after controlling for confounding by other demographic and lifestyle factors.

MATERIALS AND METHODS

Study Population and Exclusion Criteria

The study population consists of multiracial groups of survey participants in the National Health and Nutrition Examination Survey (NHANES). Survey sampling was performed in stages throughout the 2017-2018 period. In the first stage there was cluster sampling of select counties throughout the nation. Within each county, segments of the population were selected, from which the households and subsequently the individuals within each household were selected into the survey. A complex, multistage probability design was used for data collection in which the sample is representative of the US population. For these analyses we selected adults ages 21 and over for both sexes. Out of 9254 participants in the 2017-2018 surveys, 5493 subjects were 21 years or older at the

time of survey, and they all had data on their DM/IFG status and smoking status. Of those, 3421 completed at least one 24-hour recall and had an average daily energy intake between 800kcal and 4000kcal per day. Further, we excluded those missing data on physical activity as well as those reporting more than 1080 minutes/day of sedentary activity (per NHANES guidelines), leaving 3399 subjects. From that group, five people lacked data on education status, and this left a group of 3394 subjects with data with a complete oral health examination as part of the study.

Assessment of Oral Health

All oral health data in this study were collected in the oral health examination rooms of the mobile examination center (MEC) where dental exams were conducted. Data for oral health conditions were collected by a health technician, who worked together with the licensed dentists and entered the examiner observations into a computerized data collection system. The oral health examinations were performed with the study participant in a recumbent position with the D.D.S./D.M.D. seating behind the study participant, and this position is typical of the regular examinations in the MEC. In this study, oral health was assessed according to markers such as percent of teeth with dental caries, percent of missing teeth due to dental diseases, and percent of teeth either with caries or missing due to dental diseases. Each patient had data on status of dental caries and missing teeth for each individual tooth in the NHANES 2017-2018 dataset. These data were combined for teeth 2 through 30 to create a complete profile of the patient. A healthy individual has a full mouth of 28 teeth, excluding wisdom teeth.

Wisdom teeth were excluded from the dataset because their presence or absence does not usually reflect oral health status.

Assessment of Diabetes and Impaired Fasting Glucose

The DM status was determined with the help of a categorical variable— doctors told participants that they have DM—and a continuous variable—measured fasting glucose levels. The participants were divided into three DM groups: DM, IFG, and non-DM. Subjects were placed into the DM group if they were either told by their doctor that they had DM and/or had a fasting glucose above 126mg/dL. The IFG category consists of subjects who were told by their doctor that they are borderline DM as well as those subjects who had fasting glucose levels between 100 mg/dL and 126 mg/dL. The non-DM group is made of subjects who were told that they do not have DM as well as those who had fasting glucose less than 100 mg/dL. The subjects with DM or IFG were further combined to form the binary variable for DM-IFG.

Assessment of Potential Confounders

Potential confounders included in this study were smoking status (smoking at least one cigarette in the past five days), age in years at screening, race, gender, education level, percent daily fat intake, minutes of sedentary activity, heart rate (HR), and body mass index (BMI). The participants who had at least one cigarette in the past five days were considered as smokers. Participants were classified into Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, non-Hispanic Asian, and other races including multi-racial. For education levels, there were participants who completed less than 9^{th} grade, 9-11^{th} grade, high school graduate/ GED or equivalent, some college or

AA degree, and college graduate or above. Data for dietary intake came from a two-day average of total nutrients intake per day, and the percent consumption of fats (gm) was calculated. Sedentary activity was assessed according to the NHANES 2017-2018 survey on physical activity. Minutes of sedentary activity include sitting at school or at home, getting to and from places, time spent with friends, time spent sitting at a desk, traveling in a car or bus, reading, playing cards, watching television, or using a computer. These activities are considered for one 24-hour day, and do not include time spent sleeping. HR has also been associated with DM and is thus assessed for confounding (Hillis et al., 2012).

Statistical Analysis

The statistical analysis software (SAS) on demand version 15.2 was used in the analysis of the data acquired from the NHANES study. For producing the descriptive characteristics data in Figure 1, the frequency and analysis of variance (ANOVA) procedures in SAS were implemented. Participants were stratified by smoking status (currently smokers vs. nonsmokers) to eliminate confounding by smoking. Subjects were also stratified according to DM-IFG status.

Smoking status is represented as a categorical variable, which is comprised of two other categorical variables, namely the number of days that the participants smoked cigarettes in the last 5 days combined with the number of cigarettes smoked per day. The two specific variables for smoking were merged from the survey data collected and posted into the Smoking - Recent Tobacco Use dataset from NHANES (CDC). The data contained a category for those who smoked at least 1 cigarette in the past 5 days

(N=915), with 1 person not knowing if they smoked in the past 5 days. The subject in the "don't know" category was placed in the smoking category. The rest of the subjects who did not report cigarettes smoked in the past 5 days were classified as nonsmokers (n=5485). Smokers make up 14 percent in this sample, which is consistent with recently reported national statistics on smoking from 2019 (Centers for Disease Control [CDC], 2020).

First, the separate effects of DM/IFG on the oral health variables of interest and the effects of smoking status on oral health was examined using the Univariate Procedure as well as the Multivariable Logistic Regression analyses in SAS. We then examined the combined effects of these two factors by categorizing all subjects into one of four groups as follows: (1) individuals who have DM or IFG and who smoked cigarettes (DM-IFG/Smoker), (2) individuals without DM or IFG and smoke cigarettes (No DM-IFG/Smoker), individuals who have DM or have IFG and do not smoke (DM-IFG/Non-Smoker), and (4) individuals who do not have DM and do not smoke (No DM-IFG/Non-Smoker). The latter group serves as the reference group for these analyses.

The statistical tests used in this study for analysis of the results were the Univariate Procedure, Chi Square Test of Independence, Wilcoxon Rank Sums Test, and Multivariable Logistic Regression analyses. Chi Square test was used for statistical analysis of dichotomous DM and smoking exposures, and categorical oral health outcome variables, with a significance level set at α=0.05. Wilcoxon Rank Sums Test assessed the effects of DM and smoking on the number of teeth with caries or the number of missing teeth (due to poor dental health). Logistic regression analyses were used to estimate the

risk of having more dental caries or missing teeth due to poor dental health. Confounding was assessed using multivariable logistic regression. Factors that changed the primary effect estimates by 10 percent or more were considered as confounders. Logistic regression analysis was done individually for each dichotomous outcome – <25% vs. ≥25% of teeth with caries, <15% vs. ≥15% of teeth missing due to dental disease, and <40% vs. ≥40% of teeth missing or with caries. Seven different models were used in logistic regression analysis: Model 1 – unadjusted; Model 2 –adjusting for gender; Model 3 –adjusting for gender and BMI; Model 4 – adjusting for gender, BMI, and education; Model 5 – adjusting for gender, BMI, education, and sedentary activity; Model 6 – adjusting for age and race; Model 7 – adjusting for age, race, HR, and percent calories from fat.

RESULTS

Characteristics of both male and female non-smokers who were 21 years of age and older, classified according to prevalent DM-IFG and smoking status, are shown in Table 1. Male subjects make up the majority in both the DM (52.9%) and current smoking (56.8%) groups. Subjects classified as having DM-IFG show a higher average BMI (31.5 kg/m^2) compared with non-diabetic subjects (29.2 kg/m^2), while non-smokers had a higher BMI (30.2 kg/m^2) than smokers (29.7 kg/m^2). Fewer adults with DM-IFG had a college and/or higher education (51.0% vs. 63.0% of those without DM-IFG). Non-smokers had higher levels of education than smokers (63.6% with college or higher vs. 49.2%, respectively).

Table 1. Characteristics of subjects according to DM status and smoking status among adults in NHANES 2017-2018

	Diabetes or IFG				Current Smoker			
	Yes		No		Yes		No	
Subject Characteristics	n=1409		n=1990		n=537		n=2862	
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Age	**57.2**	15.6	**48.7**	17.3	**48.6**	15.4	**52.9**	17.3
BMI (kg/m^2)	**31.5**	7.7	29.20	7.00	**29.7**	7.7	**30.2**	7.3
Dietary Fats (% intake)	**36.5**	7.4	**35.9**	7.6	**35.4**	7.4	**36.2**	7.5
Gender (column %, male)		52.9		43.0		56.8		45.3
Heart Rate (bpm)	**70.9**	11.4	71.5	11.4	**71.8**	11.8	**71.1**	11.3
Minutes Sedentary Activity (min)	**349.6**	204.0	335.0	193.4	**330.7**	202.1	**343.0**	197.1
Education (column %, college or higher)		51.0		63.0		49.2		63.6
Race (column %)								
Mexican American		11.5		14.0		7.8		13.5
Other Hispanic		8.9		8.5		5.0		9.4
Non-Hispanic White		37.0		36.8		41.1		36.0
Non-Hispanic Black		24.7		23.0		31.7		22.5
Non-Hispanic Asian		13.4		12.9		5.4		14.6
Other race		4.6		4.8		8.0		4.0
Current smokers (column %)		14.4		16.9		100.0		0.00

Table 2. Oral health variables according to the status of diabetes mellitus (DM)/impaired fasting glucose (IFG) and smoking status among adults in NHANES 2017-2018

	Diabetes or IFG					
Subject Characteristics	**Yes (N=1406)**			**No (N=1988)**		
	Median	*Min-Max*	*25%-75%*	***Median***	*Min-Max*	*25%-75%*
Number permanent teeth	**24**	0-28	15-27	**26**	0-28	21-28
Number with caries	**5**	0-28	1-9	**5**	**0-26**	1-10
Number healthy teeth	**14**	0-28	7-21	**17**	**0-28**	10-23
Number missing teeth (from dental issues)	**3**	0-28	0-10	**1**	**0-28**	0-5.5
	Current Smoker					
Subject Characteristics	**Yes (N=537)**			**No (N=2857)**		
	Median	*Min-Max*	*25%-75%*	***Median***	*Min-Max*	*25%-75%*
Number permanent teeth	**23**	0-28	12-27	**25**	**0-28**	19-28
Number with caries	**4**	0-26	0-8	**6**	**0-26**	1-10
Number healthy teeth	**15**	0-28	7-22	**16**	**0-28**	9-22
Number missing teeth (from dental issues)	**4**	0-28	0-12	**2**	**0-28**	0-7

As presented in Table 2, subjects with DM-IFG had fewer healthy teeth (Median (M) = 14, IQR = 7-21 vs. M=17, IQR=10-23, respectively) than those without DM-IFG. For subjects with DM-IFG the average number of permanent teeth (M = 24; IQR = 15-27) is lower compared to subjects without DM-IFG (M = 26, IQR = 21-28). Conversely, missing teeth due to dental diseases tends to be higher in subjects with DM-IFG (M = 3, IQR = 0-10) compared to non-DIFG subjects (M = 1, IQR = 0-5.5). There is a similar trend for current smokers compared to non-smokers. Specifically, on average, the current smokers tended to have fewer remaining teeth (M = 23, IQR = 12-27) compared to nonsmokers (M = 25, IQR = 19-28), while they also had more missing teeth (M = 4, IQR = 0-12) compared to non-smokers (M = 2, IQR = 0-7).

Table 3. Percent of teeth missing or with caries according to DM-IFG status or smoking status

	Diabetes or IFG					
Subject Characteristics	**Yes (N=1371)**			**No (N=1945)**		
	Median	*Min-Max*	*25%-75%*	***Median***	*Min-Max*	*25%-75%*
Remaining teeth with caries (% of total)	**29.2**	0.0 - 100.0	12.5 - 46.4	**25.9**	0.0 - 100.0	10.7 - 44.4
Missing teeth due to dental causes (% of total)	**11.5**	0.0 - 100.0	0.0 - 39.3	**3.7**	0.0 - 100.0	0.0 - 21.4
Caries or missing due to dental problems (% of total)	**46.4**	0.0 - 100.0	25.0 - 71.4	**35.7**	0.0 - 100.0	15.4 - 60.7
	Current Smoker					
	Yes (N=527)			**No (N=2789)**		
	Median	*Min-Max*	*25%-75%*	***Median***	*Min-Max*	*25%-75%*
Remaining teeth with caries (% of total)	**22.5**	0.0 - 100.0	7.7 - 40.0	**28.6**	**0.0 - 100.0**	11.1 - 46.2
Missing teeth due to dental causes (% of total	**14.3**	0.0 - 100.0	0.0 - 50.0	**7.1**	**0.0 - 100.0**	0.0 - 25.0
Caries or missing due to dental problems (% of total)	**44.0**	0.0 - 100.0	21.4 - 71.4	**40.0**	**0.0 - 100.0**	20.8 - 64.3

A similar trend can be observed in percent of teeth missing or with caries according to the DM-IFG or smoking status (Table 3). Overall, 46.4% of the teeth of

subjects with DM-IFG were missing or had caries compared with 35.7% of teeth in those without DM-IFG. Among smokers 44.0% of teeth were missing or had varies compared with 40.0% of non-smokers. Of note, smokers had twice as many missing teeth as non-smokers and those with DM-IFG had three times as many missing teeth as those without DM-IFG.

We further examined these oral health outcomes according to the combined categories of DM-IFG status and smoking status (Table 4). A greater percent of teeth were missing in smokers who have DM-IFG (M = 21.4%, IQR = 3.6-75.0) compared with any of the other three groups, especially the group with no DM-IFG who were non-smokers who had only 3.6% of teeth missing (IQR = 0.0-17.9). Interestingly, subjects with either DM-IFG or who smoked cigarettes were missing 10.7% of their teeth. For percent of teeth with caries, there was no apparent adverse association with smoking or DM-IFG in this table. Finally, both groups of subjects with DM-IFG, regardless of smoking status had more than 46% of their teeth that were missing or with caries compared with about 40% of teeth among smokers alone (without DM-IFG). The lowest % of total teeth missing or with caries was observed in those without DM-IFG who did not smoke cigarettes.

Table 4. Percent of teeth missing or with caries according to DM-IFG status or smoking status

Subject Characteristics	No DM or IFG Non-Smoker	No DM or IFG Smoker	DM or IFG Non-Smoker	DM or IFG Smoker
	Median (25%-75%)	*Median (25%-75%)*	*Median (25%-75%)*	*Median (25%-75%)*
Remaining teeth with caries (% of total)	26.9 (10.7 - 45.8)	25.0 (8.5 - 41.0)	29.8 (14.3 - 48.1)	22.0 (7.1 - 38.1)
Missing teeth due to dental causes (% of total)	3.6 (0.0 - 17.9)	10.7 (0.0 - 40.7)	10.7 (0.0 - 35.7)	21.4 (3.6 - 75.0)
Caries or missing due to dental problems (% of total)	35.7 (14.3 - 57.1)	40.7 (18.5 - 67.9)	46.4 (25.0 - 71.4)	46.4 (25.0 - 85.7)

Table 5 shows the Wilcoxon Rank Sum Test for assessing the null hypotheses that there is no difference in the percent of teeth with caries or missing between different exposure groups (DM-IFG/no DM-IFG or smokers/non-smokers). Here, we found the opposite. There was a strong positive (adverse) association between percent teeth with caries and DM-IFG status ($Z = 3.29$, $p = 0.001$), but a strong negative (favorable) association between percent teeth with caries and current smoking status ($Z = -3.48$, $p = 0.0005$). The percent teeth missing was adversely associated with DM-IFG status ($Z = 10.35$, $p < .0001$) and with smoking status ($Z = 7.08$, $p < .0001$). This adverse association also manifests itself in the final outcome category (percent caries or missing), ($Z = 8.69$, $p < .0001$ for DM-IFG) and ($Z = 2.38$, $p = 0.0172$ for smoking status).

Table 5. Wilcoxon Rank Sum testing the effects of DM status and smoking status on dental outcomes

	% of Teeth with Caries		% of Teeth Missing		% Caries or Missing	
	Z-score	p-value	Z-score	p-value	Z-score	p-value
Diabetes/IFG (yes vs. no)	3.29	0.001	10.35	<.0001	8.69	<.0001
Current smoker (yes vs. no)	-3.48	0.0005	7.08	<.0001	2.38	0.0172

Table 6 shows the chi square test of association between oral health conditions and DM-IFG, smoking, and the combined effect of DM-IFG and smoking. For these analyses, we classified each subject according to the percent of teeth missing, or with caries, or both. Specifically, subjects were classified into the following three categories: (1) <25% vs. ≥25% of teeth with caries, (2) <15% vs. ≥15% of teeth missing, and (3) <40% vs. ≥40% of teeth missing or with caries.

First of all, there was no association between DM-IFG status and the likelihood of having more than 25 percent of teeth with caries ($p = 0.557$). Among current smokers ($N = 537$), 42.1 percent of subjects have more than 25 percent teeth with caries ($p < .0001$) compared with 51.9% in non-smokers. When looking at the combined effect, the percent of subjects who have more than 25 percent caries increases in the following order: DM-IFG/smokers (37.1 %), followed by non-DM-IFG/smokers (45.1 %), then non-DM-IFG/nonsmokers (50.9%), and, finally, DM-IFG/non-smokers (53.2 %) ($p < .0001$).

Subjects with DM-IFG who had more than 15 percent of teeth missing due to dental causes made up 43.2% of subjects compared with 28.6% of those without DM-IFG ($p < .0001$). Further, 46.2% current smokers had more than 15 percent teeth missing

compared with 32.5% of non-smokers ($p < .0001$). In our combined effect categories, subjects with both exposures (DM-IFG) had the highest percent of subjects (55.0%) with at least 15 percent of teeth missing. In contrast, non-DM-IFG/non-smokers had 26.1 % with high levels of missing teeth while smokers who had no, non-DM-IFG/smokers had 40.9% with more missing teeth and, finally, those with DM-IFG alone (non-smokers) had 41.2% of subjects with higher levels of missing teeth ($p < .0001$). For the combined outcome category of more than 40 percent teeth with caries or missing, there are 55.8% participants with DM-IFG ($p < .0001$), 52.1% current smokers ($p = 0.1587$), 43.7% in the non-DM-IFG non-smoker group ($p < .0001$), 50.2% in the non-DM-IFG smoker group ($p < .0001$), 55.9% in the DM-IFG non-smoker group ($p < .0001$), and 55.5% in the DM-IFG smoker group ($p < .0001$).

Table 6. Prevalence of oral health outcomes associated with the independent and combined effects of DM or IFG (DM-IFG) and smoking. Showing percent

	Caries (<25% vs. ≥25%)		Missing Teeth (<15% vs. ≥15%)		Caries or Missing (<40% vs. ≥40%)	
	Total N	# Cases (row %)	Total N	# Cases (row %)	Total N	# Cases (row %)
DIABETES STATUS						
No DM or IFG	1984	990 (49.9)	1984	567 (28.6)	1984	888 (44.8)
DM or IFG	1410	718 (50.9)	1410	609 (43.2)	1410	787 (55.8)
*p-value**	**0.557**		**<.0001**		**<.0001**	
SMOKING STATUS						
current smoker	537	226 (42.1)	537	248 (46.2)	537	280 (52.1)
non-smoker	2857	1482 (51.9)	2857	928 (32.5)	2857	1395 (48.8)
*p-value**	**<.0001**		**<.0001**		**0.1587**	
COMBINED EFFECTS						
No DM or IFG / Non-smoker	1649	839 (50.9)	1649	430 (26.1)	1649	720 (43.7)
No DM or IFG / Smoker	335	151 (45.1)	335	137 (40.9)	335	168 (50.2)
DM or IFG / Non-smoker	1208	643 (53.2)	1208	498 (41.2)	1208	675 (55.9)
DM or IFG / Smoker	202	75 (37.1)	202	111 (55.0)	202	112 (55.5)
p-value	**<.0001**		**<.0001**		**<.0001**	

Table 7 shows the adjusted OR and 95% confidence interval (95% CI) for having at least 25 percent dental caries compared to having less, according to independent or

combined exposures of DM-IFG and smoking. The association between DM-IFG and percent caries after adjusting for gender, BMI and education shows 1.10 increased relative odds compared to the non-DM-IFG group (95% CI: 0.96-1.26). In the model controlling for age, race, HR, and percent calories from fat, those with DM-IFG had 0.86 times the odds of having dental caries compared to those without DM-IFG (95% CI, 0.74-0.99). After adjusting for various confounding variables, smokers compared with non-smokers had 26-33% lower risks of having more dental caries ($p<0.05$ for all models). In the final model, after adjusting for age, race, HR, and percent of calories from fat, the odds ratio is 0.73 in smokers compared to nonsmokers (95%CI, 0.60-0.88). Among subjects without DM-IFG but who were current smokers (vs. those with no-DM-IFG who were non-smokers) had a 20% lower risk of having more dental caries. In contrast, subjects with DM-IFG who were non-smokers had 1.14 increased odds of developing dental caries compared to non-DM-IFG/non-smoker controls. Finally, combined exposure to DM-IFG and smoking was associated with a statistically significant reduction in risk of dental caries ($p <0.5$ for all models).

Table 8 shows the adjusted OR and 95% CI for having 15 percent or more teeth missing due to dental disease compared to less than 15 percent missing. The unadjusted association shows 1.90-fold increased odds (95% CI, 1.65-2.19) of having 15 percent or more teeth missing due to dental disease in patients with DM-IFG (vs. those without). In these analyses, race was a strong confounder and in the final models (with age, race, HR, and percent calories from fat), the odds ratio is 1.37 (95% CI, 1.16-1.61). The unadjusted model for the association between smoking and the oral health outcome of missing 15

percent or more of teeth due to dental disease is 1.78 (95% CI, 1.49-2.15). After adjusting for sex, BMI, and education, the OR was attenuated (OR=1.59 (95% CI, 1.31-1.93). However, after adjusting for age, race, HR, and percent calories from fat, we found a 2.77-fold increased risk of missing teeth (95% CI, 2.21-3.48) associated with cigarette smoking.

Lasty in Table 3, we examined the combined effects of DM-IFG and smoking on risk of have 15% or more of teeth missing. After adjusting for sex, BMI, and education, smokers with no DM-IFG had 1.70 higher odds of missing 15 percent or more teeth compared to non-smokers with no DM-IFG (95%CI, 1.33-2.19), while non-smokers with DM-IFG and smokers with DM-IFG have 1.93 (95% CI, 1.63-2.27) and 3.16 (95% CI, 2.32-4.29) higher odds, respectively, of missing 15 percent or more teeth compared to non-smokers with no DM-IFG. After adjusting for age, race, HR, and percent of calories from fat, smokers with no DM-IFG had 2.86-fold higher odds of missing 15 percent or more teeth compared to non-smokers without DM-IFG (95% CI, 2.15-3.81); non-smokers with DM-IFG and smokers with DM-IFG had 1.41 (95% CI, 1.18-1.69) and 3.88 (95% CI, 2.73-5.50) higher odds, respectively, compared to non-smokers with no DM-IFG. The risk of missing 15 percent or more teeth due to dental diseases among smokers with DM-IFG was increased approximately four-fold.

Table 7. Relative odds for having 25% or more of remaining teeth with dental caries associated with independent and combined effects of prevalent DM or IFG and smoking status

		Odds Ratios for Dental Caries showing ⩾25% (vs. <25%)													
		Model 1		Model 2		Model 3		Model 4		Model 5		Model 6		Model 7	
	Events/N	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
No diabetes or IFG	990	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref
Diabetes or IFG	718	**1.04**	0.91-1.19	**1.07**	0.93-1.23	**1.08**	0.94-1.25	**1.10**	0.96-1.27	**1.09**	0.94-1.25	**0.86**	0.75-1.00	**0.86**	0.74-0.99
No smoking	1482	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref
Current smoking	226	**0.67**	0.56-0.81	**0.69**	0.57-0.83	**0.68**	0.57-0.82	**0.72**	0.59-0.87	**0.68**	0.57-0.83	**0.74**	0.61-0.89	**0.73**	0.60-0.88
No DM or IFG / No smoking	839	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref
No DM or IFG / Current smoking	151	**0.79**	0.63-1.00	**0.82**	0.65-1.04	**0.80**	0.63-1.02	**0.86**	0.68-1.09	**0.80**	0.63-1.02	**0.83**	0.65-1.06	**0.81**	0.63-1.03
DM or IFG / No smoking	643	**1.10**	0.95-1.28	**1.13**	0.97-1.31	**1.14**	0.98-1.33	**1.17**	1.00-1.36	**1.14**	0.98-1.33	**0.90**	0.77-1.05	**0.89**	0.76-1.04
DM or IFG / Current smoking	75	**0.57**	0.42-0.77	**0.59**	0.44-0.80	**0.60**	0.45-0.82	**0.63**	0.46-0.86	**0.61**	0.45-0.82	**0.54**	0.39-0.73	**0.54**	0.39-0.73

Using logistic regression, we adjusted
Model 1 (Unadjusted)
Model 2 adjusts for gender
Model 3 adjusts for gender and BMI
Model 4 adjusts for gender, BMI and education
Model 5 adjusts for gender, BMI, education, and sedentary activity
Model 6 adjusts for age and race
Model 7 adjusts for age, race, HR, and percent of calories from fat

Finally, I examined the relative odds for having 40 percent or more teeth missing due to dental disease or with dental caries compared according to the individual or combined DM-IFG and smoking exposures in Table 9. First, I observed that subjects with DM-IFG had 1.56-fold increased odds (95% CI, 1.36-1.79) of having 40 percent or more missing or carious teeth compared to those without DM-IFG. These effects were eliminated after controlling for race. Next, in the final adjusted model, smokers (vs. non-smokers) had a 57% increased risk of having 40 percent or more missing or carious teeth (OR = 1.57 and 95% CI, 1.27-1.95) after adjusting for age, race, HR, and percent calories from fat. Lastly, I once again looked at the combined exposure groups and found in the final model that current smokers without DM-IFG had 1.67 times increased odds of having 40 percent or more missing or carious teeth compared to those non-DM-IFG/non-smoker controls (95% CI, 1.27-2.19). In that same model, non-smokers with DM-IFG and smokers with DM-IFG had a 1.06 (95% CI, 0.89-1.27) and 1.52 (95% CI, 1.08-2.14) times higher odds compared with non-DM-IFG/non-smoking controls.

Table 8. Relative odds for having 15% or more of teeth missing associated with independent and combined effects of prevalent DM or IFG and smoking status

		Odds Ratios for Missing Teeth shoowing ⩾15% (vs. <15%)													
		Model 1		Model 2		Model 3		Model 4		Model 5		Model 6		Model 7	
	Events/N	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
No diabetes or IFG	567	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref
Diabetes or IFG	609	**1.90**	1.65-2.19	**1.88**	1.63-2.17	**1.89**	1.64-2.19	**1.87**	1.61-2.17	**1.89**	1.63-2.19	**1.39**	1.18-1.62	**1.37**	1.16-1.61
No smoking	928	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref
Current smoking	248	**1.78**	1.49-2.15	**1.76**	1.46-2.12	**1.78**	1.48-2.15	**1.59**	1.31-1.93	**1.77**	1.47-2.14	**2.76**	2.20-3.45	**2.77**	2.21-3.48
No DM or IFG / No smoking	430	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref
No DM or IFG / Current smoking	137	**1.96**	1.54-2.50	**1.94**	1.52-2.48	**1.99**	1.55-2.54	**1.70**	1.33-2.19	**1.99**	1.56-2.54	**2.79**	2.10-3.72	**2.86**	2.15-3.81
DM or IFG / No smoking	498	**1.99**	1.70-2.33	**1.97**	1.68-2.31	**2.00**	1.70-2.35	**1.93**	1.63-2.27	**2.00**	1.70-2.35	**1.42**	1.19-1.70	**1.41**	1.18-1.69
DM or IFG / Current smoking	111	**3.46**	2.57-4.66	**3.41**	2.53-4.60	**3.42**	2.53-4.63	**3.16**	2.32-4.29	**3.39**	2.50-4.58	**4.01**	2.83-5.67	**3.88**	2.73-5.50

Using logistic regression, we adjusted
Model 1 (Unadjusted)
Model 2 adjusts for gender
Model 3 adjusts for gender and BMI
Model 4 adjusts for gender, BMI, and education
Model 5 adjusts for gender, BMI, education, and sedentary activity
Model 6 adjusts for age and race
Model 7 adjusts for age, race, HR, and percent of calories from fat

Table 9. Relative odds for more dental caries or missing teeth (≥40% of total teeth) associated with independent and combined effects of prevalent DM or IFG and smoking status.

		Odds Ratios for Dental Caries or Missing Teeth showing ⩾40% (vs. <40%)													
		Model 1		Model 2		Model 3		Model 4		Model 5		Model 6		Model 7	
	Events/N	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
No diabetes or IFG	888	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref
Diabetes or IFG	787	**1.56**	1.36-1.79	**1.58**	1.37-1.81	**1.60**	1.39-1.84	**1.58**	1.37-1.82	**1.60**	1.39-1.85	**1.04**	0.89-1.22	**1.03**	0.88-1.21
No smoking	1395	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref
Current smoking	280	**1.14**	0.95-1.37	**1.15**	0.96-1.38	**1.154**	0.96-1.39	**1.09**	0.90-1.31	**1.16**	0.96-1.39	**1.579**	1.27-1.96	**1.57**	1.27-1.95
No DM or IFG / No smoking	720	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref	**1.00**	Ref
No DM or IFG / Current smoking	168	**1.30**	1.03-1.64	**1.32**	1.04-1.67	**1.335**	1.05-1.69	**1.24**	0.97-1.57	**1.33**	1.05-1.69	**1.67**	1.27-2.19	**1.67**	1.27-2.19
DM or IFG / No smoking	675	**1.63**	1.41-1.90	**1.66**	1.43-1.93	**1.689**	1.45-1.97	**1.65**	1.42-1.93	**1.69**	1.45-1.97	**1.07**	0.90-1.27	**1.06**	0.89-1.27
DM or IFG / Current smoking	112	**1.61**	1.20-2.16	**1.64**	1.22-1.10	**1.65**	1.23-2.23	**1.57**	1.17-2.12	**1.67**	1.24-2.25	**1.55**	1.10-2.17	**1.52**	1.08-2.14

Using logistic regression, we adjusted
Model 1 (Unadjusted)
Model 2 adjusts for gender
Model 3 adjusts for gender and BMI
Model 4 adjusts for gender, BMI and education
Model 5 adjusts for gender, BMI, education, and sedentary activity
Model 6 adjusts for age and race
Model 7 adjusts for age, race, HR, and percent of calories from fat

DISCUSSION

Oral diseases such as dental caries and PD can contribute to conditions such as cardiovascular disease (Dietrich et al., 2017). PD is a disease of the mouth that affects the periodontium and leads to detachment and tooth loss. PD and dental caries occur in the presence of risk factors such as advanced age, gender, BMI, race, education, and smoking (Genco & Borgnakke, 2013). Uncontrolled DM can affect the health of the periodontium as well as increase dental caries (Teshome & Yitayeh, 2017). The link between oral diseases and DM is guided by inflammation which results from prolonged elevated blood glucose (Tsalamandris et al., 2019). Based on this hypothesis it has been speculated that PD increases the risk of tooth loss and dental caries in smokers.

This study looked at the association between DM and oral health conditions – dental caries and tooth loss due to dental disease. Both conditions indicate dental disease or symptoms of dental disease. After stratifying subjects into combined categories of exposure based on smoking status and DM-IFG status, effects on three oral health outcomes were examined. A total of 3,394 adults over the age of 21 years were included in the analysis, of which the majority were non-smokers and without DM or IFG (Table1-2). There are more male subjects than female subjects in the DM-IFG and smoker groups than in the no DM-IFG and non-smoker groups, respectively. This pattern indicates that there is a gender difference in the exposure of DM and smoking habits.

In the current study, adults with DM or IFG had a lower risk of having teeth with dental caries as those without DM or IFG. Further, current smokers also had fewer carious teeth than non-smoker controls. This pattern is also observed in the combined

exposure groups. Study participants who were smokers alone (without DM-IFG) as well those with DM-IFG (who were not smokers had a lower risk of having more teeth with dental caries. In addition, those with DM-IFG who were also smokers had the lowest risk of having a lot of teeth with caries. This is opposite to the report of other research articles, which state that cigarette smoking increases the likelihood of developing dental caries, and there might be a dose-dependent effect (Wu & Huang, 2019; Goto et al., 2019). It is possible that the results of the current study are actually a product of underestimation of the carious teeth due to their advanced pathology to the point where they needed to be extracted. That lead to an elevated number of extracted/missing teeth due to dental diseases and a smaller number of carious teeth. Since many subjects with missing teeth will be missing those teeth due to dental caries, we may be under-counting subjects with dental caries in this category. Further, subjects with DM-IFG or who smoke cigarettes may have more severe caries or periodontal health issues leading to tooth loss, which may also lead to under-counting dental caries in those categories.

The percent missing teeth due to dental disease was higher in subjects with DM-IFG (compared with those without DM-IFG) and higher in smokers compared with non-smokers. Likewise, subjects who smoked and had DM-IFG tended to have fewer teeth than other groups of subjects. Subjects with DM or IFG had almost a 40% increased risk of having 15 percent or more of their teeth missing due to dental disease compared to without DM or IFG. On the other hand, smokers had a much greater risk, with a 2.77-fold increased risk of having at least 15% of their teeth missing. Those with DM or IFG who also smoked had even greater risk than those with either of these risk factors alone.

Finally, we explored the risk of having either missing teeth or teeth with caries. In these analyses, the effects of smoking in particular were associated with the highest risks of having missing or carious teeth.

In previous research, subjects with DM have been reported to experience reduced salivary secretion, which leads to dry mouth - a condition called xerostomia which is present in 40-80% of diabetic patients (Sreebny et al., 1992). Reduced salivary flow rate has been shown to contribute to increased risk of dental caries and infections from bacteria (Rohani, 2019). The final results of the current study suggest that both DM-IFG and smoking are associated with missing teeth but of the two exposure variables, smoking seems to have the stronger effects on these oral health outcomes (Gupta et al., 2016; Şentürk et al., 2018).

This study has a number of strengths and limitations. First, it is a large sample with detailed oral health exams. Further, data on a number of important potential confounders were available. The most important limitation of the study is its cross-sectional design. However, these objective exposure variables (DM-IFG status and smoking status) are likely to reflect long-term exposures and are unlikely to lead to reverse causality. Another limitation was the fact that we had too few subjects to run separate analyses for males and females or to separately explore their different smoking habits. To do that a larger study population would be necessary, and that could be achieved by combining data across multiple survey years. Additionally, a small pool of covariates was used either due to missing information or because the variables may be

causally related to oral health conditions among people with DM-IFG. Thus, these variables could not be considered for confounding and were excluded from analysis.

CONCLUSION

In the present study, we concluded that both DM-IFG and smoking were independently associated with a higher percentage of missing teeth due to dental diseases. Non-smokers with DM-IFG had no increased risk of having more total teeth with dental caries or that were missing. Overall, smoking was a stronger risk factor than DM for the negative oral health outcomes observed in this study.

BIBLIOGRAPHY

AlDukhail, S., Alhazmi, H., Riedy, C., Barrow, J. R., & Chamut, S. (2021). Oral health outcomes among adults with diabetes served at HRSA-funded health centers. *Journal Of Diabetes And Its Complications*, 107979. Advance online publication. https://doi.org/10.1016/j.jdiacomp.2021.107979

Aslam, M., Mishra, B. K., Goyal, S., Siddiqui, A. A., & Madhu, S. V. (2021). Family history of diabetes determines the association of HOMA-IR with fasting and postprandial triglycerides in individuals with normal glucose tolerance. *Journal Of Clinical Lipidology*, *15*(1), 227–234. https://doi.org/10.1016/j.jacl.2020.11.002

Atuegwu, N. C., Perez, M. F., Oncken, C., Mead, E. L., Maheshwari, N., & Mortensen, E. M. (2019). E-cigarette use is associated with a self-reported diagnosis of prediabetes in never cigarette smokers: Results from the behavioral risk factor surveillance system survey. *Drug And Alcohol Dependence*, *205*, 107692. https://doi.org/10.1016/j.drugalcdep.2019.107692

Azogui-Lévy, S., Dray-Spira, R., Attal, S., Hartemann, A., Anagnostou, F., & Azerad, J. (2018). Factors associated with oral health-related quality of life in patients with diabetes. *Australian Dental Journal*, 63(2), 163–169. https://doi.org/10.1111/adj.12577

Bascones-Martínez A, Muñoz-Corcuera M, Bascones-Ilundain J. [Diabetes and periodontitis: A bidirectional relationship]. *Medicina Clinica.* 2015 Jul;145(1):31-35. DOI: 10.1016/j.medcli.2014.07.019. PMID: 25192582.

Battancs, E., Gheorghita, D., Nyiraty, S. *et al.* Periodontal Disease in Diabetes Mellitus: A Case–Control Study in Smokers and Non-Smokers. *Diabetes Therapy Journal* 11, 2715–2728 (2020). https://doi.org/10.1007/s13300-020-00933-8

Borgnakke W. S. (2019). IDF Diabetes Atlas: Diabetes and oral health - A two-way relationship of clinical importance. *Diabetes Research And Clinical Practice*, *157*, 107839. https://doi.org/10.1016/j.diabres.2019.107839

Centers for Disease Control and Prevention. (2020, August 28). *National Diabetes Statistics Report, 2020*. Centers for Disease Control and Prevention. https://www.cdc.gov/diabetes/data/statistics-report/index.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fdiabetes%2Fdata%2Fstatistics%2Fstatistics-report.html.

Centers for Disease Control and Prevention. (2020, December 10). *Current cigarette smoking among adults in the United States*. Centers for Disease Control and Prevention.

https://www.cdc.gov/tobacco/data_statistics/fact_sheets/adult_data/cig_smoking/index.htm#nation.

Deshpande, K., Jain, A., Sharma, R., Prashar, S., & Jain, R. (2010). Diabetes and periodontitis. *Journal Of Indian Society Of Periodontology*, *14*(4), 207–212. https://doi.org/10.4103/0972-124X.76917

Dietrich, T., Webb, I., Stenhouse, L. *et al.* Evidence summary: the relationship between oral and cardiovascular disease. *British Dental Journal* **222,** 381–385 (2017). https://doi.org/10.1038/sj.bdj.2017.224

Eke, P. I., Thornton-Evans, G. O., Wei, L., Borgnakke, W. S., Dye, B. A., & Genco, R. J. (2018). Periodontitis in US Adults. *The Journal Of The American Dental Association*, *149*(7). https://doi.org/10.1016/j.adaj.2018.04.023

Fiorini, T., Musskopf, M. L., Oppermann, R. V., & Susin, C. (2014). Is there a positive effect of smoking cessation on periodontal health? A systematic review. *Journal Of Periodontology*, *85*(1), 83–91. https://doi.org/10.1902/jop.2013.130047

Goto, Y., Wada, K., Konishi, K. *et al.* Association between exposure to household smoking and dental caries in preschool children: a cross-sectional study. *Environmental Health And Preventive Medicine* **24,** 9 (2019). https://doi.org/10.1186/s12199-019-0764-1

Grover, H. S., & Luthra, S. (2013). Molecular mechanisms involved in the bidirectional relationship between diabetes mellitus and periodontal disease. *Journal Of Indian Society Of Periodontology*, *17*(3), 292–301. https://doi.org/10.4103/0972-124X.115642

Gupta, N., Gupta, N. D., Garg, S., Goyal, L., Gupta, A., Khan, S., & Moin, S. (2016). The effect of type 2 diabetes mellitus and smoking on periodontal parameters and salivary matrix metalloproteinase-8 levels. *Journal Of Oral Science*, *58*(1), 1–6. https://doi.org/10.2334/josnusd.58.1

Hillis, G. S., Woodward, M., Rodgers, A., Chow, C. K., Li, Q., Zoungas, S., Patel, A., Webster, R., Batty, G. D., Ninomiya, T., Mancia, G., Poulter, N. R., & Chalmers, J. (2012). Resting heart rate and the risk of death and cardiovascular complications in patients with type 2 diabetes mellitus. *Diabetologia*, *55*(5), 1283–1290. https://doi.org/10.1007/s00125-012-2471-y

Javed F, Al-Kheraif AA, Salazar-Lazo K, Yanez-Fontenla V, Aldosary KM, Alshehri M, Malmstrom H, Romanos GE. Periodontal Inflammatory Conditions Among Smokers and Never-Smokers With and Without Type 2 Diabetes Mellitus. *Journal Of Periodontology*. 2015 Jul; 86(7): 839-46. doi: 10.1902/jop.2015.150120. Epub 2015 Apr 16. PMID: 25879874.

Lamster IB, Lalla E, Borgnakke WS, Taylor GW. The relationship between oral health and diabetes mellitus. *Journal Of American Dental Association.* 2008 Oct;139 Suppl:19S-24S. doi: 10.14219/jada.archive.2008.0363. PMID: 18809650.

Leite, R. S., Marlow, N. M., Fernandes, J. K., & Hermayer, K. (2013). Oral health and type 2 diabetes. *The American Journal Of The Medical Sciences*, *345*(4), 271–273. https://doi.org/10.1097/MAJ.0b013e31828bdedf

Loe H. Periodontal disease. The sixth complication of diabetes mellitus. *Diabetes Care.* 1993;16(1):329–34.

Mauri-Obradors, E., Estrugo-Devesa, A., Jané-Salas, E., Viñas, M., & López-López, J. (2017). Oral manifestations of Diabetes Mellitus. A systematic review. *Medicina Oral, Patologia Oral Y Cirugia Bucal*, *22*(5), e586–e594. https://doi.org/10.4317/medoral.21655

Nazir M, Al-Ansari A, Al-Khalifa K, Alhareky M, Gaffar B, Almas K. Global Prevalence of Periodontal Disease and Lack of Its Surveillance. *Scientific World Journal.* 2020 May 28;2020:2146160. doi: 10.1155/2020/2146160. PMID: 32549797; PMCID: PMC7275199.

Negrato, C. A., & Tarzia, O. (2010). Buccal alterations in diabetes mellitus. *Diabetology & Metabolic Syndrome*, *2*, 3. https://doi.org/10.1186/1758-5996-2-3

Novak, M. J., Potter, R. M., Blodgett, J., & Ebersole, J. L. (2008). Periodontal disease in Hispanic Americans with type 2 diabetes. *Journal Of Periodontology*, *79*(4), 629–636. https://doi.org/10.1902/jop.2008.070442

Özçaka, Ö., Becerik, S., Bıçakcı, N., & Kiyak, A. H. (2014). Periodontal disease and systemic diseases in an older population. *Archives Of Gerontology And Geriatrics*, *59*(2), 474–479. https://doi.org/10.1016/j.archger.2014.05.011

Poudel, P., Griffiths, R., Wong, V. W., Arora, A., Flack, J. R., Khoo, C. L., & George, A. (2018). Oral health knowledge, attitudes and care practices of people with diabetes: a systematic review. *BMC Public Health*, 18(1), 577. https://doi.org/10.1186/s12889-018-5485-7

Quadri, M., Fageeh, H. I., Ibraheem, W., & Jessani, A. (2020). A Case-Control Study of Type 2 Diabetes Mellitus and Periodontitis in Saudi Arabian Adults. *Journal Of Multidisciplinary Healthcare*, *13*, 1741–1748. https://doi.org/10.2147/JMDH.S288681

Rao, S. S., Disraeli, P., & McGregor, T. (2004). Impaired glucose tolerance and impaired fasting glucose. *American Family Physician*, *69*(8), 1961–1968.

Rohani B. (2019). Oral manifestations in patients with diabetes mellitus. *World Journal Of Diabetes*, 10(9), 485–489. https://doi.org/10.4239/wjd.v10.i9.485

Şentürk, R. A., Sezgin, Y., Bulut, Ş., & Özdemir, B. H. (2018). The effects of smoking on the expression of gelatinases in chronic periodontitis: a cross-sectional study. *Brazilian Oral Research*, 32, e114. https://doi.org/10.1590/1807-3107bor-2018.vol32.0114

Sreebny, L. M., Yu, A., Green, A., & Valdini, A. (1992). Xerostomia in diabetes mellitus. *Diabetes Care*, *15*(7), 900–904. https://doi.org/10.2337/diacare.15.7.900

Taiyeb-Ali, T. B., Raman, R. P., & Vaithilingam, R. D. (2011). Relationship between periodontal disease and diabetes mellitus: an Asian perspective. *Periodontology 2000*, *56*(1), 258–268. https://doi.org/10.1111/j.1600-0757.2010.00370.x

Teshome, A., Yitayeh, A. The effect of periodontal therapy on glycemic control and fasting plasma glucose level in type 2 diabetic patients: systematic review and meta-analysis. *BMC Oral Health* **17,** 31 (2017). https://doi.org/10.1186/s12903-016-0249-1

Tsalamandris, S., Antonopoulos, A. S., Oikonomou, E., Papamikroulis, G. A., Vogiatzi, G., Papaioannou, S., Deftereos, S., & Tousoulis, D. (2019). The Role of Inflammation in Diabetes: Current Concepts and Future Perspectives. *European Cardiology*, *14*(1), 50–59. https://doi.org/10.15420/ecr.2018.33.1

Wu, J., Li, M., & Huang, R. (2019). The effect of smoking on caries-related microorganisms. *Tobacco Induced Diseases*, *17*, 32. https://doi.org/10.18332/tid/105913

Wu, Cz., Yuan, Yh., Liu, Hh. *et al.* Epidemiologic relationship between periodontitis and type 2 diabetes mellitus. *BMC Oral Health* 20, 204 (2020). https://doi.org/10.1186/s12903-020-01180-w

Yip, N., Liu, C., Wu, D., & Fouad, A. F. (2021). The association of apical periodontitis and type 2 diabetes mellitus: A large hospital network cross-sectional case-controlled study. *Journal Of The American Dental Association (1939)*, *152*(6), 434–443. https://doi.org/10.1016/j.adaj.2021.01.005

Zhou, X., Zhang, W., Liu, X., Zhang, W., & Li, Y. (2015). Interrelationship between diabetes and periodontitis: role of hyperlipidemia. *Archives Of Oral Biology*, *60*(4), 667–674. https://doi.org/10.1016/j.archoralbio.2014.11.008

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