# Factors Related to Low Salivary Flow in a Group of Thai Diabetes Older Adults

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## Abstract

As the number of older adults with diabetes increases, the number of diabetes-related complications appears to be more common among the older adults with diseases than those without diseases. The oral complication is included as well as hyposalivation. The purpose of this study was to investigate the prevalence of hyposalivation and identify the factors associated with this condition in the older adults with diabetes in the Kaengkhoi district, Saraburi province. Participants and Methods: Three hundred and seventy-seven participants aged 60 years and over who met the eligibility criteria were enrolled in this study. All participants were interviewed about general information and health information. The whole saliva was collected both in resting and stimulating conditions. Medical information and laboratory results were obtained from the hospital's electronic records. Statistical analysis was performed to reveal the association of all factors. Result and Discussion: Among a total number of 377 participants (64.19% female, mean age 68.67±6.33 years old), the prevalence of hyposalivation was 63.40%. The median resting salivary flow rate among male and female participants who had hyposalivation (0.04 and 0.05, respectively) was lower compared to those without hyposalivation (0.17 and 0.19, respectively). The level of glycemic control, determined by HbA1C, and the presence of microalbuminuria were the only two factors associated with hyposalivation in this study. HbA1C level (HbA1C 7-8: OR=2.09; 95%CI: 1.18-3.67; p=0.002 and HbA1C >8: OR=2.39; 95%CI: 1.32-4.31; p=0.004) and presence of microalbuminuria (OR=3.41; 95%CI: 2.11-5.52; p<0.001) associated with hyposalivation. Due to the association between microalbuminuria and duration of disease, glycemic control, and other factors, the association revealed in the present study may therefore be due to changes in salivary gland function caused by poorly controlled and prolonged diabetes. Conclusions: Hyposalivation is a common complication among older adults with diabetes. Objective screening for those conditions and implementing the preventive measurements are beneficial in diabetes older adults, particularly in poorly controlled diseases and those with diabetic-related complications. Although diabetes is a chronic disease, achieving well glycemic control could reduce the various effects, including oral complications.

***Keywords:*** *aged population, diabetes, hyposalivation, glycemic controlled, microalbuminuria*

## 1. Introduction

It is established that the increasing age, the higher risk of developing several diseases. Regarding the Thai public health survey report, the three most common diseases encountered in older adults were hypertension (HT), dyslipidemia, and diabetes mellitus (DM), in descending order (Aekplakorn, 2014). According to the past three decades, the prevalence of DM has risen dramatically in countries of all income levels. In Thailand, among the population aged 15 years and over, 8.3% had DM, which accounted for the fourth largest after China, India, and Japan (Suvi et al., 2020). Prevalence of Type2 DM increased from 2.1% in the 15-29 years to 18.1% in the 60-69 years (Aekplakorn, 2014).

Prolonged high blood glucose can cause abnormalities in the structure and function of several organ systems (Zheng, Ley, & Hu, 2018) as well as the oral cavity. Tooth loss, increased prevalence of periodontal disease, and other soft tissue lesions were reported in diabetes patients (Ravindran et al., 2015; Kaur et al., 2015). Furthermore, decreased salivary flow is more prevalent among diabetic older adults than healthy ones (Lima et al., 2017), which consequently impaired oral function, including speaking, taste perception, chewing, swallowing, and speaking, affecting the quality of life (Nikbin, 2014).


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Hyposalivation is a common oral problem in older adults (Turner & Ship, 2007), which seems to be more serious in older adults who suffer from DM (Lima et al., 2017). Regarding the study conducted in Thailand, the prevalence of hyposalivation, which was assessed by the Modified Schirmer's test among the diabetic group, was 46%, which was a statistically significant difference compared to non-DM subjects (Khovidhunkit et al., 2009). Although there had been studies that reported a decrease in the flow of saliva in diabetic subjects compared with non-diabetics, the higher prevalence of hyposalivation in diabetic patients was inconsistent (López et al., 2016).

The reduction of salivary flow in diabetes patients is affected by several factors such as several classes of medications, increasing age, and degree of neuropathy, as well as patient's feeling of mouth dryness and thirst (Kaur et al., 2015). Diabetic patients with high plasma glucose have a lower stimulated parotid flow rate than those with well-controlled disease and non-DM subjects (Chavez et al., 2000). According to the literature, there are relatively few studies focusing on the factors associated with dry mouth in diabetes older adults. A recent systematic review demonstrated hyposalivation associated with glycemic control and the use of xerogenic medications (Morais et al., 2014). However, the others did not reveal those associations (Chomkhakhai et al., 2009). The other factors such as obesity, which is defined by body mass index (BMI) ≥30 kg/m2 or waist circumference (WC) >88 cm, and dyslipidemia were also reported (Östberg et al., 2012; Narindrarangkura et al., 2019).

Because of several consequences of dry mouth in diabetes patients, particularly in the elderly group, detection of affected patients, proper management of this problem, as well as preventive strategies for oral complications, can be beneficial in improving their quality of life. Therefore, this study aimed to investigate the prevalence of hyposalivation, as well as the potential associated factors of this condition among diabetic older adults in Kaengkhoi district, Saraburi province of Thailand.

## 2. Objectives

1) To investigate the prevalence of hyposalivation in older adults with DM in Kaengkhoi district, Saraburi province

2) To identify the factors associated with hyposalivation in older adults with DM in Kaengkhoi district, Saraburi province

## 3. Materials and Methods

### *3.1 Participants*

The older participants, aged 60 years and over, who had been diagnosed with DM, and received ongoing care at the Kaengkhoi hospital, Saraburi province of Thailand, were enrolled in this cross-sectional study. Participants were excluded from this study if they had other co-existing systemic that resulted in dry mouth conditions; including inflammatory conditions of the salivary gland, previously treated with head and neck radiotherapy or within three months after chemotherapy, received renal replacement therapy, liver cirrhosis, or hepatitis or cancer with liver failure, on an immunosuppressant drug, as well as organ transplant individuals, patients who underwent surgery in the past three months, and individuals who had psychotic disorders including paranoid, confusion, mood disorders, schizophrenia. According to the criteria, 377 voluntary participants were included in the study. The research proposal was approved and reviewed by the ethical committee of the Faculty of Dentistry/Faculty of Pharmacy, Mahidol University, Institutional Review Board (No.MU-DT/PY-IRB 2020/082.2212; December 22, 2020).

### *3.2 Data collection*

The information collected in this study consisted of 3 parts, including the data from interview questions, salivary flow rate measurement, and secondary data from the hospital's medical records.


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*3.3 Demographic and general information*

Participants were interviewed about the general information, health, and behavioral health issues based on a structured questionnaire. General information collecting included educational levels, working and economic status, smoking and alcohol drinking habits, systemic disease, and medication currently used.

*3.4 Assessment of hyposalivation*

A whole salivary flow rate measurement was performed to determine the amount of participants' salivary flow. Participants had been fasting and not performed any oral hygiene at least 2 hours before the saliva collection. Resting salivary flow rate (RSFR) with drainage technique, and stimulated salivary flow rate (SSFR) after 1 minute of chewing 1.5 g of paraffin, were collected. The saliva samples were weighed to obtain their volume. Based on the methods and protocols used in the previous studies (Valdez & Fox, 1993; Navazesh, 2003), a specific gravity of 1.0 to saliva was used to convert weight to volume. The flow rate less than 0.1 mL/min for RSFR or less than 0.7 mL/min for SSFR were considered hyposalivation.

*3.5 Associated factors*

The information on co-existing systemic diseases, prescribed medications, anthropometric measurements, results of laboratory investigations, and the presence of diabetes-related complications were all obtained from the hospital's electronic records. The BMI and WC were recorded from the latest visit. The laboratory tests to be collected included; fasting plasma glucose (FPG), HbA1C level, lipid profile (total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride), glomerular filtration rate (GFR). Diabetes-related complications were obtained from the records of ocular and neurologic examinations and urine microalbuminuria tests, which determine the diabetic retinopathy, neuropathy, and nephropathy, respectively.

*3.6 Statistical analysis*

Statistical analyses were performed with the IBM SPSS Statistics Grad Pack 28.0 Premium software. General information, personal history, and medical information of participants, as well as the prevalence of hyposalivation conditions, were shown with descriptive statistics, including; number, percentage, mean with standard deviation for age, and salivary flow rate. Association between the associated factors and hyposalivation was determined by multiple logistic regression analysis. A p-value of less than 0.05 was statistically significant.

## 4. Results and Discussion

*4.1 Results*

Among the 377 participants, 64.19% were female. The average age of participants was 68.67±6.33 years. Most of them (66.84%) were aged in the early aging group, while only 4.25% were late seniors. Although the study's participants were elderly people, 32.89% were still working, mostly in agriculture. Smoking and alcohol consumption habits revealed that most of the participants had never smoked or drunk alcohol, as shown in Table 1.

When sialometry was conducted, 63.40% had a salivary flow rate classified as hyposalivation. Of those, the reduced RSFR was revealed in 59.95%, and reduced SSFR was 56.76% of participants. In addition, when categorizing the participants into groups; with or without hyposalivation. The median resting salivary flow rate among male and female participants who had hyposalivation (0.04 and 0.05, respectively) was lower compared to those without hyposalivation (0.17 and 0.19, respectively).

Statistical analysis comparing the association between hyposalivation and the general characteristic of participants revealed that the variables associated with hyposalivation, including gender (p=0.011) and smoking habit (p=0.039), are significantly associated with the decreased salivary flow, as shown in Table 1.


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**Table 1** Association between hyposalivation and general characteristics

| Variable | Hyposalivation, n (%) | | *p*-value |
|---|---|---|---|
| | No hyposalivation | Hyposalivation | |
| Gender | | | |
| Male | 61 (44.2) | 74 (31) | 0.011* |
| Female | 77 (55.8) | 165 (69) | |
| Age | | | |
| 60-70 | 99 (71.7) | 153 (64) | |
| 71-80 | 36 (26.1) | 73 (30.6) | 0.168 |
| >80 | 3 (2.2) | 13 (5.4) | |
| Marital status | | | |
| Single | 25 (18.1) | 34 (14.2) | |
| Married | 85 (61.6) | 149 (62.3) | 0.535 |
| Divorce/widow | 28 (20.3) | 56 (23.4) | |
| Educational status | | | |
| Uneducated | 27 (19.6) | 50 (20.9) | |
| Primary school | 93 (67.4) | 170 (71.1) | 0.285 |
| Secondary school or higher | 93 (67.4) | 19 (7.9) | |
| Working status | | | |
| Working | 53 (38.4) | 85 (61.6) | 0.089 |
| Retirement | 85 (61.6) | 168 (70.3) | |
| Monthly income | | | |
| <3,000 baht | 102 (73.9) | 180 (75.3) | |
| 3,000-5,000 baht | 21 (15.2) | 35 (14.6) | 0.951 |
| >5,000 baht | 15 (10.9) | 24 (10) | |
| Smoking habit | | | |
| Non-smoker | 95 (68.8) | 191 (79.9) | |
| Ex-smoker | 40 (29) | 43 (18) | 0.039* |
| Current smoker | 3 (2.2) | 5 (2.1) | |
| Alcohol drinking habit | | | |
| Non-drinker | 86 (62.3) | 167 (69.9) | |
| Ex-drinker | 37 (26.8) | 57 (23.8) | 0.189 |
| Current drinker | 15 (10.9) | 15 (6.3) | |

*p-value from Chi-square test, *Significant at the 0.05 level*

The data of serum lipid profile revealed that most of the participants had normal total cholesterol, LDL, HDL, and triglyceride. On the other hand, evaluating obesity demonstrated that the majority of the participants, which were 46.42% and 67.37%, were obese by the assessment based on the BMI and WC, respectively. For the BMI, only 29.71% had normal BMI, while the remaining two-thirds had an above-normal BMI. In addition to diabetes, hypertension and dyslipidemia were among the two most common comorbidities found to be 89.12% and 83.29%. From the data on the number of medications used, 44.30% used more than five medications, as shown in Table 2.

Among the physical and medical status variables, which focused on the comorbidities of the participants, no medical status variable was found to be associated with hyposalivation, as shown in Table 2 below.

Considering glycemic control regarding FPG measurements, almost 20% of the participants were found to have poor glycemic control, while the evaluation by HbA1C revealed a slightly greater number of poor disease-controlled participants than those assessed by FPG testing, which was 25.20%. In terms of diabetes-related microvascular complications, it revealed that most participants had a GFR greater than or equal to 60 mL/min/1.73m$^2$ and showed no evidence of retinal changes and sensory loss. However, when


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considering microalbuminuria, the earliest sign of diabetic nephropathy, a sample of 255 (67.64%) participants detected microalbumin in their urine, as shown in Table 3.

**Table 2** Association between hyposalivation and physical & medical status

| Variable | Hyposalivation, n (%) | | *p*-value |
|---|---|---|---|
| | No hyposalivation | Hyposalivation | |
| BMI (kg/m$^2$) | | | |
| <23 | 37 (26.8) | 75 (31.4) | |
| 23-24.9 | 41 (29.7) | 49 (20.5) | 0.126 |
| ≥25 | 60 (43.5) | 115 (48.1) | |
| Waist circumference | | | |
| Normal | 42 (30.4) | 81 (33.9) | 0.497 |
| Obesity | 96 (69.6) | 158 (66.1) | |
| Comorbidities | | | |
| HT | 118 (85.5) | 218 (91.2) | 0.121 |
| DLP | 114 (82.6) | 200 (83.7) | 0.886 |
| CKD | 34 (24.6) | 77 (32.2) | 0.129 |
| Numbers of medication | | | |
| 1-5 | 75 (54.3) | 134 (56.3) | |
| 6-10 | 59 (42.8) | 99 (41.6) | 0.847 |
| >10 | 4 (2.9) | 5 (2.1) | |
| Total cholesterol (mg/dL) | | | |
| <200 | 113 (81.9) | 191 (79.9) | |
| 200-239 | 17 (12.3) | 32 (13.4) | 0.896 |
| ≥240 | 8 (5.8) | 16 (6.7) | |
| LDL (mg/dL) | | | |
| <100 | 73 (52.9) | 154 (64.4) | |
| 100-129 | 44 (31.9) | 53 (22.2) | 0.129 |
| 130-159 | 15 (10.9) | 25 (10.5) | |
| ≥160 | 6 (4.3) | 7 (2.9) | |
| HDL | | | |
| High | 90 (65.2) | 48 (34.8) | 0.508 |
| Low | 48 (34.8) | 92 (38.5) | |
| Triglyceride (mg/dL) | | | |
| <150 | 84 (60.9) | 144 (60.3) | |
| 150-199 | 25 (18.1) | 47 (19.7) | 0.932 |
| ≥200 | 29 (21) | 48 (20.1) | |

*p-value from Chi-square test, *Significant at the 0.05 level*

**Table 3** Association between hyposalivation and diabetes status

| Variable | Hyposalivation, n (%) | | *p*-value |
|---|---|---|---|
| | No hyposalivation | Hyposalivation | |
| GFR (ml/min/1.73 m$^2$) | | | |
| ≥60 | 93 (67.4) | 135 (56.5) | |
| 30-59 | 40 (29) | 85 (35.6) | 0.066 |
| <30 | 5 (3.6) | 19 (7.9) | |
| Presence of microalbuminuria | | | |
| Absence | 69 (50) | 53 (22.2) | <0.001* |
| Presence | 69 (50) | 186 (77.8) | |


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| Variable | Hyposalivation, n (%) | | *p*-value |
|---|---|---|---|
| | No hyposalivation | Hyposalivation | |
| Presence of diabetic retinopathy | | | |
| Absence | 129 (93.5) | 219 (91.6) | 0.555 |
| Presence | 9 (6.5) | 20 (8.4) | |
| Presence of diabetic neuropathy | | | |
| Absence | 133 (96.4) | 232 (97.1) | 0.765 |
| Presence | 5 (3.6) | 7 (2.9) | |

*p-value from Chi-square test, *Significant at the 0.05 level*

FPG and HbA1C levels were significantly associated with hyposalivation (p-value of 0.012 and 0.002, respectively). Among the diabetes-related complications, microalbuminuria was the only disorder that demonstrated the association with hyposalivation (*p*-value <0.001), shown in Table 3 below.

Only HbA1C and microalbuminuria demonstrated the association after adjustment for other covariates. The participants who had HbA1C level greater than or equal to 7 were approximately twice as likely to develop hyposalivation compared to participants with HbA1C less than 7 (HbA1C 7-8: OR=2.09; 95%CI: 1.18-3.67; p=0.002 and HbA1C >8: OR=2.39; 95%CI: 1.32-4.31; p=0.004). Besides, participants who were present with microalbuminuria were 3.4 times more likely to have hyposalivation compared to those who were absent (OR=3.41; 95%CI: 2.11-5.52; p<0.001), shown in Table 4.

**Table 4** Univariate and Multiple logistic regression analysis of factors associated with hyposalivation

| Hyposalivation | | Univariable analysis | | Multiple logistic regression | |
|---|---|---|---|---|---|
| | | Crude OR (95% CI) | *p*-value | Adj. OR (95% CI) | *p*-value |
| Gender | Female | 1.77 (1.15, 2.73) | 0.010* | 1.43 (0.84, 2.44) | 0.190 |
| Working status | Working | 0.68 (0.44, 1.05) | 0.084 | 0.65 (0.40, 1.06) | 0.086 |
| Smoking habit | Ex-smoker | 0.54 (0.33, 0.88) | 0.013* | 0.64 (0.35, 1.17) | 0.150 |
| | Current smoker | 0.83 (0.19, 3.54) | 0.800 | 1.38 (0.27, 6.94) | 0.696 |
| FPG (mg/dL) | 100-130 | 0.65 (0.23, 1.86) | 0.423 | - | - |
| | 131-170 | 0.99 (0.35, 2.85) | 0.997 | - | - |
| | >170 | 1.83 (0.59, 5.68) | 0.296 | - | - |
| HbA1C (%) | 7-8 | 1.98 (1.21, 3.23) | 0.006* | 2.35 (1.36, 4.05) | 0.002* |
| | >8 | 2.36 (1.36, 4.10) | 0.002* | 2.39 (1.32, 4.31) | 0.004* |
| GFR | 30-59 | 1.46 (0.93, 2.32) | 0.104 | 1.29 (0.72, 2.30) | 0.485 |
| (mL/min/1.73m$^2$) | <30 | 2.62 (0.94, 7.26) | 0.064 | 2.18 (0.56, 8.48) | 0.396 |
| Microalbuminuria | Presence | 3.51 (2.23, 5.52) | <0.001* | 3.41 (2.11,5.52) | <0.001* |

*Adj. OR was adjusted for gender, working status, smoking habit, FPG, HbA1C, GFR, and microalbuminuria, *Significant at the 0.05 level*

*4.2 Discussion*

The present study aimed to investigate the prevalence of hyposalivation among diabetic older adults, as well as the potential factors related to those conditions. The results showed that 63.40% of the participants had hyposalivation.

From the literature, several studies reported the prevalence of hyposalivation in diabetic patients ranging from 48 to 92.5% (López et al., 2016; Khovidhunkit et al., 2009). Due to the variation in methodology for measuring salivary flow and cut-off value, many studies had presented conflicting results. In comparison to the subjective symptom of dry mouth, the study by Lin et al. (2002) suggested that patients with diabetes who had dry mouth symptoms were more likely to show a reduction in salivary flow. However, several studies had a higher prevalence of hyposalivation than xerostomia. This might imply that measurement of salivary flow rate could be a better way to evaluate dry mouth problems than xerostomia questionnaire in diabetic elders.


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The level of glycemic control, determined by HbA1C, and the presence of microalbuminuria were the only two factors associated with hyposalivation in this study. Although many studies had reported an association between increased age with decreased salivary flow rate (Takeuchi et al., 2015; Islas et al., 2017), as well as the co-existing systemic diseases and polypharmacy (Muñoz et al., 2019; Smidt et al., 2010), those were not exhibited in this present study, which may be due to the majority of participants in this study being an early aging group and only 4% were late seniors. The difference, therefore, was not revealed significantly between the age groups.

Although diabetes increases the risk of complications in many organs, including the oral cavity, the direct contributing factor to those conditions is glycemic control (Verhulst et al., 2019). For that purpose, HbA1C is a widely used test and more accurately reflects glycemic control levels than FPG (Sherwani et al., 2016). Several studies reported the association of HbA1C level with a decrease in salivary flow (Verhulst et al., 2019; Uthayasankar, Jayaraj, & Gayathri, 2020). This study revealed that participants who had HbA1C levels greater than or equal to 7 were approximately twice as likely to develop hyposalivation compared to those with lower HbA1C, which is in accordance with the previous study. Mechanisms that link this relationship were investigated, including dehydration from polyuria, several classes of medication, and autonomic nervous dysfunction (Verhulst et al., 2019). Moreover, changes in the chemical composition of saliva in diabetes patients were also exhibited, such as an increase in salivary amylase and glucose concentration (Pérez et al., 2021). Because of such a relationship, well diabetes control could reduce the hyposalivation condition and decrease subsequent oral problems.

Interestingly, this study reported the high prevalence of microalbuminuria detected in the study participants, as well as the significant association with hyposalivation. The presence of microalbuminuria was associated with a 3.4 times higher risk of hyposalivation when compared to those who were absent with it. Diabetes-related complications such as diabetic retinopathy, neuropathy, and ischemic heart disease were more common among the microalbuminuric group (Ahmad et al., 2017; Maskari, Sadig, & Obineche, 2008). From the literature, many studies evaluated the changes in salivary proteins in diabetic patients, which included salivary albumin. Increased levels of albumin in the saliva of patients with DM were reported (Reena, Indira, & David, 2017; Hasan, Aburahma, & Kazaz, 2017). This could be due to diabetic membranopathy or the change in the integrity of the capillary bed, causing leakage of albumin across the basement membrane into the salivary secretion. This mechanism is similar to the changes that cause microalbuminuria, in which dysfunction of the glomerular filtration barrier, including the basement membrane, was implied (Satchel & Tooke, 2008). Another mechanism underlying the increased salivary albumin is low-grade inflammation of the salivary glands, causing serum proteins to leak into the saliva, which can be commonly found in diabetic patients (Vaziri et al., 2009). However, to the best of our knowledge, there are no studies that demonstrated the relationship of urine albumin to salivary albumin or even to saliva flow rate. Due to the association between microalbuminuria and duration of disease, glycemic control, and other factors, such as age and diastolic blood pressure (Chowta, Pant, & Chowta, 2009; Bhowmick, Kutty, & Shetty, 2007; Ullah et al., 2020), the association revealed in the present study may therefore be due to changes in salivary gland function caused by poorly controlled and prolonged diabetes. Further studies evaluating the relationship between salivary flow rate and microalbuminuria and changes in salivary albumin, as well as the other relevant clinical factors, could provide a better understanding of the relationship between those factors.

## 5. Conclusion

Hyposalivation is a common complication among older adults with diabetes. Objective screening for those conditions and implementing the preventive measurements are beneficial in diabetic older adults, particularly in poorly controlled diseases and those with diabetic-related complications. Although diabetes is a chronic disease, achieving well glycemic control could reduce various effects, including oral complications.

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## 7. References

Aekplakorn, W. (2014). Thai National Health Examination Survey, NHES V. Nonthaburi: The Graphico system co. Ltd.

Ahmad, T., Ulhaq, I., Mawani, M., & Islam, N. (2017). Microalbuminuria in Type-2 Diabetes Mellitus; the tip of iceberg of diabetic complications. *Pakistan journal of medical sciences*, *33*(3), 519.

Al-Maskari, F., El-Sadig, M., & Obineche, E. (2008). Prevalence and determinants of microalbuminuria among diabetic patients in the United Arab Emirates. *BMC nephrology*, *9*(1), 1-8.

Bhowmick, K., Kutty, A. V. M., & Shetty, H. V. (2007). Glycemic control modifies the association between microalbuminuria and c-reactive protein in Type 2 Diabetes Mellitus. *Indian Journal of Clinical Biochemistry*, *22*(2), 53-59.

Chavez, E. M., Taylor, G. W., Borrell, L. N., & Ship, J. A. (2000). Salivary function and glycemic control in older persons with diabetes. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*, *89*(3), 305-311.

Chomkhakhai, U., Thanakun, S., Khovidhunkit, S. O. P., Khovidhunkit, W., & Thaweboon, S. (2009). Oral health in Thai patients with metabolic syndrome. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, *3*(4), 192-197.

Chowta, N. K., Pant, P., & Chowta, M. N. (2009). Microalbuminuria in diabetes mellitus: Association with age, sex, weight, and creatinine clearance. *Indian journal of nephrology*, *19*(2), 53.

Hasan, H. R., Aburahma, N. N. A., & Al-Kazaz, A. K. A. (2017). Proteins Level in Sera and Saliva of Type2 Diabetic Iraqi Patients with and Without Proliferative Diabetic Retinopathy. Oriental *Journal of Chemistry*, *33*(6), 2776.

Islas-Granillo, H., Borges-Yáñez, A., Fernández-Barrera, M. Á., Ávila-Burgos, L., Patiño-Marín, N., Márquez-Corona, M. D. L., Mendoza-Rodríguez, M., & Medina-Solís, C. E. (2017). Relationship of hyposalivation and xerostomia in Mexican elderly with socioeconomic, sociodemographic and dental factors. *Scientific reports*, *7*(1), 1-8.

Kaur, S., Kaur, K., Rai, S., & Khajuria, R. (2015). Oral health management considerations in patients with diabetes mellitus. *Archives of Medicine and Health Sciences*, *3*(1), 72.

Khovidhunkit, S. O. P., Suwantuntula, T., Thaweboon, S., Mitrirattanakul, S., Chomkhakhai, U., & Khovidhunkit, W. (2009). Xerostomia, hyposalivation, and oral microbiota in type 2 diabetic patients: a preliminary study. *J Med Assoc Thai*, *92*(9), 1220-1228. PMID: 19772183.

Lima, D. L. F., Carneiro, S. D. R. M., Barbosa, F. T. D. S., Saintrain, M. V. D. L., Moizan, J. A. H., & Doucet, J. (2017). Salivary flow and xerostomia in older patients with type 2 diabetes mellitus. *PloS one*, *12*(8), e0180891.

Lin, C. C., Sun, S. S., Kao, A., & Lee, C. C. (2002). Impaired salivary function in patients with noninsulin-dependent diabetes mellitus with xerostomia. *Journal of Diabetes and its Complications*, *16*(2), 176-179.

López-Pintor, R. M., Casañas, E., González-Serrano, J., Serrano, J., Ramírez, L., de Arriba, L., & Hernández, G. (2016). Xerostomia, hyposalivation, and salivary flow in diabetes patients. Journal of diabetes research, Article ID 4372852, 1-15. doi.org/10.1155/2016/4372852

Morais, E. F. D., Macedo, R. A. D. P., Lira, J. A. D. S., Lima, K. C. D., & Borges, B. C. D. (2014). Factors related to dry mouth and low salivary flow rates in diabetic elderly: A systematic literature review. *Revista Brasileira de Geriatria e Gerontologia*, *17*, 417-423.

Muñoz, C., Martínez, A., Flores, M., & Catalán, A. (2019). Relationship between xerostomia and hyposalivation in senior Chilean people. *Revista clínica de periodoncia, implantología y rehabilitación oral*, *12*(3), 123-126.


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Narindrarangkura, P., Bosl, W., Rangsin, R., & Hatthachote, P. (2019). Prevalence of dyslipidemia associated with complications in diabetic patients: A nationwide study in Thailand. *Lipids in health and disease, 18*(1), 1-8.

NavazAVAZesh, M. (2003). How can oral health care providers determine if patients have dry mouth?. *The Journal of the American Dental Association, 134*(5), 613-618.

Nikbin, A., Bayani, M., Jenabian, N., & Motallebnejad, M. (2014). Oral health-related quality of life in diabetic patients: comparison of the Persian version of Geriatric Oral Health Assessment Index and Oral Health Impact Profile: A descriptive-analytic study. *Journal of Diabetes & Metabolic Disorders, 13*(1), 1-10.

Östberg, A. L., Bengtsson, C., Lissner, L., & Hakeberg, M. (2012). Oral health and obesity indicators. *BMC oral health, 12*(1), 1-7.

Pérez-Ros, P., Navarro-Flores, E., Julián-Rochina, I., Martínez-Arnau, F. M., & Cauli, O. (2021). Changes in salivary amylase and glucose in diabetes: A scoping review. *Diagnostics, 11*(3), Article ID 453, 1-20.

Ravindran, R., Deepa, M. G., Sruthi, A. K., Kuruvila, C., Priya, S., Sunil, S., ... & Roopesh, G. (2015). Evaluation of Oral Health in Type II Diabetes Mellitus Patients. *Oral & Maxillofacial Pathology Journal, 6*(1), 525-531.

Reena, C. S., Indira, A. P., & David, M. P. (2017). Evaluation of Salivary Albumin in Type II Diabetes Mellitus. *International Journal of Contemporary Medical Research, 4*(6), 1364-1366.

Satchell, S. C., & Tooke, J. E. (2008). What is the mechanism of microalbuminuria in diabetes: A role for the glomerular endothelium?. *Diabetologia, 51*(5), 714-725.

Sherwani, S. I., Khan, H. A., Ekhzaimy, A., Masood, A., & Sakharkar, M. K. (2016). Significance of HbA1c test in diagnosis and prognosis of diabetic patients. *Biomarker insights, 11*, BMI-S38440.

Smidt, D., Torpet, L. A., Nauntofte, B., Heegaard, K. M., & Pedersen, A. M. L. (2010). Associations between labial and whole salivary flow rates, systemic diseases and medications in a sample of older people. *Community dentistry and oral epidemiology, 38*(5), 422-435.

Suvi, K., Belma, M., Pouya, S., Paraskevi, S. (2020). Diabetes in Western Pacific. International Diabetes Federation Diabetes Atlas. 9th ed. IDF. Brussels. Retrieve from https://diabetesatlas.org/idfawp/resource-files/2019/07/IDF_diabetes_atlas_ninth_edition_en.pdf

Takeuchi, K., Furuta, M., Takeshita, T., Shibata, Y., Shimazaki, Y., Akifusa, S., Ninomiya, T., Kiyohara, Y., & Yamashita, Y. (2015). Risk factors for reduced salivary flow rate in a Japanese population: the Hisayama Study. *BioMed research international, 2015*. Article ID 381821, 1-7. doi: 10.1155/2015/381821.

Turner, M. D., & Ship, J. A. (2007). Dry mouth and its effects on the oral health of elderly people. *The Journal of the American Dental Association, 138*, S15-S20.

Ullah, A., Khan, R., Khan, J., Panezai, M. S., Kakar, A. K., & Zarak, M. S. (2020). Microalbuminuria in type 2 diabetes mellitus and glycemic control. *Archives of Nephrology and Urology, 3*(1), 5-16.

Uthayasankar, D., Jayaraj, G., Gayathri, R. (2020). Saliva in diabetes: A review. *European Journal of Molecular & Clinical Medicine, 7*(1), 1395-1403.

Valdez, I. H., & Fox, P. C. (1993). Diagnosis and management of salivary dysfunction. *Critical Reviews in Oral Biology & Medicine, 4*(3), 271-277.

Vaziri, P. B., Vahedi, M. O. H. S. E. N., Abdollahzadeh, S. H., Abdolsamadi, H. R., Hajilooi, M., & Kasraee, S. H. (2009). Evaluation of salivary albumin in diabetic patients. *Iranian journal of public health, 38*(3), 54-59.

Verhulst, M. J., Loos, B. G., Gerdes, V. E., & Teeuw, W. J. (2019). Evaluating all potential oral complications of diabetes mellitus. *Frontiers in endocrinology, 10*, Article ID 56, 1-49. doi: 10.3389/fendo.2019.00056

Zheng, Y., Ley, S. H., & Hu, F. B. (2018). Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nature reviews endocrinology, 14*(2), 88-98.


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