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Xerostomia and Salivary Dysfunction in Patients With Diabetes Mellitus. A Cross-Sectional Study

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ABSTRACT

Background: Diabetes mellitus (DM) has been associated with salivary disorders such as xerostomia and hyposalivation. The aim of this study was to determine the prevalence of these disorders and their risk factors in DM patients.

Methods: DM patients from two health centers were included. Epidemiological and DM control-related variables were collected. Xerostomia Inventory was filled out by the patients and unstimulated whole salivary flow was collected. Logistic regression tests were performed.

Results: A total of 168 patients were included (46.4% men, 53.6% women, mean age 72.54 [SD 11.03 years]). Thirteen patients had Type 1 DM and 155 had Type 2 DM. 52.4% experienced xerostomia and 41.1% had unstimulated whole salivary flow hyposalivation. Women were more likely to suffer hyposalivation than men (OR 2.5, 95% CI 1.32–4.73; $p = 0.005$). Patients with T2DM were less likely to suffer UWS hyposalivation than T1DM patients (OR 0.28, 95% CI 0.08–0.95; $p = 0.04$). Glycemic control was not significantly worse in patients with xerostomia and hyposalivation. The drugs for the treatment of DM were not associated with salivary disorders. However, some drugs to treat other comorbidities such hypertension and neurological diseases were associated with xerostomia and hyposalivation.

Conclusions: The prevalence of xerostomia and unstimulated whole salivary flow hyposalivation in patients with DM is high. Female sex, T1DM, and the use of certain non-antidiabetic drugs increased the risk of suffering these disorders. The possible association between DM, xerostomia, and/or hyposalivation is complex and may be influenced by multiple factors. Therefore, further studies are needed to evaluate whether DM influences these salivary disorders.

1 | Introduction

Diabetes mellitus (DM) is a frequent endocrine disease characterized by disturbance in the assimilation, metabolism, and balance of glucose concentration in the blood. DM is due to a deficit in the production of insulin by the pancreas or to a progressive resistance of the cells to the insulin action. The three main types of DM are: Type 1 DM (T1DM), Type 2 DM (T2DM), and gestational DM [1].

In 2021, there were 529 million people living with DM worldwide, with a global age-standardized prevalence of 6.1% [2]. This accounts for 10.5% of the population aged 20–79 years. It is projected that this percentage will rise to 12.2% by the year 2045 [3], and by 2050, more than 1.31 billion people are expected to have DM [2]. DM is also a highly prevalent disease in the elderly population. More than a quarter of people over 65 years old have DM [4, 5]. The prevalence is higher in urban areas (10.8%)

than in rural areas (7.2%), and higher in high-income countries (10.4%) than in low-income countries (4%) [6].

DM may be diagnosed based on plasma glucose criteria, which include either a fasting plasma glucose (FPG) value ≥ 126 mg/dL or a 2-h plasma glucose (2-h PG) value ≥ 200 mg/dL during a 75 g oral glucose tolerance test, or a glycosilated hemoglobin (HbA1c) value ≥ 6.5%. Based on the recommendations from the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD), a good DM control is considered when HbA1c is less than 7% (53–58 mmol/mol) [7].

Xerostomia is the subjective complain of dry mouth, while salivary disfunction or hyposalivation is the objective decrease in salivary flow. Unstimulated whole salivary (UWS) flow values of less than 0.1 mL/min are considered hyposalivation. Previous studies have shown that DM patients are more prone to suffer from xerostomia and hyposalivation [8, 9]. Some studies have shown that DM patients with uncontrolled glycemia had significantly lower salivary flow values than DM patients with good glycemic control [9, 10]. But other studies did not show these results [11].

Salivary disorders in DM patients may be due to damage to the glandular parenchyma, polyuria, neuropathies, alterations in the microcirculation of the salivary glands, dehydration, and alterations in the glycemic control [8, 12]. But, there are other risk factors such as advanced age, other systemic diseases and the intake of multiple drugs [12]. It should be noted that many of the previous studies in DM patients assessing salivary disorders did not consider these other risk factors.

On the other hand, glycemic control values have changed recently. Some previous studies about salivary disorders in patients with DM considered a poor glycemic control when HbA1c values were greater than 8% [13, 14]. Recently, ADA and EASD have agreed that older adults in good overall health should have glycemic goals with an (HbA1c level of < 7.0%–7.5% [53–58 mmol/mol]) [7]. The values for diagnosing DM have also changed. Diagnostic criteria for DM changed from 140 mg/dL (7.8 mmol/L) to 126 mg/dL (7 mmol/L) of fasting glucose levels [1]. For these reasons, we believe that it is necessary to conduct studies that follow the current diagnostic criteria for DM, as well as for glycemic control.

Therefore, the main objective of this study is to determine the prevalence of xerostomia and hyposalivation in a group of patients with DM diagnosed according to current DM criteria. Also, we want to evaluate whether these salivary disorders are associated with DM control, as well as other systemic and local factors.

2 | Materials and Methods

2.1 | Study Design

The present study is an observational cross-sectional study. The study protocol was approved by the Ethics Committee of the Hospital San Carlos of Madrid (IEC no. 17.067-E) and by the Central Research Commission of the Primary Care Management of the Community of Madrid. Consecutive DM patients who attended their medical consultation at two health centers (Adelfas and Canal de Panama Health-Care Centers) in Community of Madrid (Spain) were included. Due to the COVID-19 pandemic, 85% of patients were collected between September 2019 and 10 January 2020 and the remaining 15% were collected from January 2021 to May 2021. These latter DM patients were tested for COVID prior to data and saliva collection. None of the included patients were COVID positive. The present study followed the principles of the Helsinki Declaration and its subsequent updates, and the guidelines established by the Strobe Statement (http://www.strobe-statement.org/). All patients received and signed an informed consent form explaining the objective of the study and the tests to be performed.

2.2 | Participants

Patients had to meet the following inclusion criteria: (1) Patients diagnosed with DM according to current diagnostic criteria GBP ≥ 126 mg/dL or a 2-h PG value ≥ 200 mg/dL during a 75 g oral glucose tolerance test [1]; (2) Patients suffering from DM who wanted to participate in the study had to be competent to fill in the questionnaires and perform the required tests; (3) If the patient was under 18 years of age, he/she had to have the consent of his/her father, mother, or guardian legal.

The exclusion criteria were: (1) Patients with Sjögren's Syndrome; (2) Patients with a history of head and neck radiation therapy; and (3) Patients on current chemotherapy treatment or who have received this treatment in the last year.

2.3 | Data Collection

At the first appointment, the primary care doctor invited DM patients to participate in a study during routine consultations. Patients were given comprehensive information and if interested, signed informed consent forms. Descriptive variables were collected by the patient's physician. The following variables were collected: gender, age, type of DM, time since DM diagnosis, level of HbA1c during the last 3 months, smoking habit, dose of tobacco (cigarettes/day), alcohol habit, dose of alcohol (units/day), presence of dentures, type of diseases, and number and type of drugs taken by the patient. The drugs the patient was taking were classified according to the Anatomical, Therapeutic, Chemical Classification (ATC) System instituted by WHO, which categorizes drugs into five levels, depending on the receptor system or organ and the pharmacological effect [15]. Patient's diseases were classified according to the International Classification of Diseases (ICD-11) [16]. HbA1c values were also categorized into uncontrolled diabetes when the values of HbA1c were ≥ 7%, or controlled diabetes if the values were < 7% [7].

2.4 | Saliva Collection

Saliva collection was carried out first thing in the morning (8–11 am) to avoid variations in saliva flow rate due to the circadian rhythm [17]. On the day of saliva collection, patients were

required to come to the center without brushing their teeth, eating, drinking, or smoking 90 min before the test. UWS flow was collected. The patient had to drop the saliva produced in their mouth for 15 min into a sterile container. Patients were in a place where they could be relaxed, seated, with his/her chin slightly down to help the collection of saliva [18]. Saliva collection was recorded in mL/min by two dentists specialized in oral medicine. Hyposalivation was considered when the patient presented an UWS flow ≤ 0.1 mL/min [19–21]. Saliva was discarded after its quantification.

2.5 | Xerostomia Questionnaires

Prior to saliva collection the patient filled out questionnaires regarding xerostomia. First the patient was asked the following question "Does your mouth usually feel dry?" If the answer was affirmative, we considered that the patient suffered from xerostomia [22].

Patients also filled out the Xerostomia Inventory questionnaire to assess the degree of xerostomia, which was translated and validated in Spanish [23]. This tool consists of 11 questions about dry mouth, skin, eyes, and nose. Answers follows a Lickert scale from 1 to 5 (never: value 1; rarely: value 2; occasionally: value 3; quite frequent: value 4; very frequently: value 5) [24]. The patients completed the questionnaires using paper booklets, which were collected after completion.

2.6 | Sample Size

We considered that the main outcome was the percentage of DM patients suffering from xerostomia. To calculate the sample size, we considered the previous study on the prevalence of xerostomia in patients with DM realized by Vasconcelos et al. in 2010 [25]. The prevalence of xerostomia in this study was 12.5%. To calculate the sample size, we applied the corresponding formula to estimate a proportion when the population size is unknown. Using an $\alpha = 0.05$ and a statistical power of 95%, 168 patients were needed.

2.7 | Statistical Analysis

The data were analyzed using the SPSS version 29.0 software (IBM, Armonk, New York, USA). Descriptive statistics, including means, standard deviations (SD), and percentages were calculated. The prevalence of xerostomia and hyposalivation was calculated by extracting the proportions (patients with xerostomia or hyposalivation as numerator/patients with DM as denominator) given as a percentage and their respective 95% confidence intervals (CI) were calculated. Kolmogorov Smirnov test was used to establish the goodness of fit to normality of the numerical variables. Chi-squared test or Fisher's exact test were used to study the association between two qualitative variables. Mann–Whitney *U* test was used to assess the association between categorical and numerical variables. Spearman's rank correlation (r) coefficient was used to correlate two continuous variables. Univariate and multivariate logistic regressions (force entry method) were conducted to identify significant associations between xerostomia or UWS hyposalivation and risk factors. Independent variables showing a $p \leq 0.20$ in univariate analyses were incorporated into the multivariate models. ATC drugs with < 5 observations and variables that showed multicollinearity (such as drugs from higher levels of the ATC classification that were represented in lower levels) were removed. Odds ratios (ORs) with 95% CI were reported together with two-tailed *p* values derived from Wald test. Adjustment for age was also performed. Statistically significant results were considered when $p < 0.05$.

3 | Results

Patient characteristics are shown in Table 1. A total of 168 patients with DM were included of which 78 were men (46.4%) and 90 women (53.6%). The mean age of DM patients was 72.54 (11.03). Thirteen patients presented T1DM (7.7%) and 155 T2DM (92.3%). The mean HbA1c was 6.84 (1.27). Regarding habits, 22 patients were smokers (13.1%) and 29 patients (17.3%) consumed alcohol. The mean number of drugs taken by the DM patients was 7.21 (3.7) and patients suffered a mean of 4.11 (3.26) diseases. The mean total score obtained in the Xerostomy Inventory questionnaire was 21.96 (8.78).

The specific treatments for DM that patients were taking are shown in Appendix S1. The most frequent antidiabetic drugs taken by patients were oral hypoglycemic agents (A10B = 73.8%), and within them metformin (A10BA02 = 38.7%) was the most frequently prescribed. A 12.5% of the patients controlled their DM with insulin and its analogs (A10A).

Seventy-nine patients (42.3%; 95% CI 35–50) presented with oral lesions, with several of them having multiple oral lesions (Appendix S2). The presence of oral lesions was not higher in patients with xerostomia (OR = 0.98, CI 0.53-1.8; $p = 0.95$) or hyposalivation (OR = 0.89, CI 0.48-1.66; $p = 0.71$). Appendix S3 and S4 also show the oral lesions observed in patients with and without xerostomia or hyposalivation.

3.1 | Xerostomia

Eighty-eight patients suffered from xerostomia. The xerostomia prevalence was 52.4% (95% CI 59.8–44.8). Regarding the XI questionnaire, the results for each item and the total scores are shown in Appendix S5. Patients with xerostomia were found to score significantly higher on 9 of the 11 items and on the total score than those without xerostomia.

The results of the univariate analysis between xerostomia and the different variables collected is shown in Table 2. Xerostomia was more frequent in women than in men, but not significantly (OR 1.76, 95% CI 0.95–3.2; $p = 0.71$). When categorizing the number of cigarettes, it could be observed that in the group of patients with xerostomia there were fewer smokers of up to 10 cigarettes and more smokers of more than 10 cigarettes. Xerostomia patients were observed to be 2.71 times more likely to have UWS hyposalivation (OR 2.71, 95% CI 1.4–5.15; $p = 0.002$) than patients without xerostomia. No significant association was observed between xerostomia and the rest of the variables studied. The correlation between XI

TABLE 1 | Demographic characteristics of diabetes patients included.

Variable	Patients ($n=168$)
Gender	
Male	78 (46.4%)
Female	90 (53.6%)
Age (years)	
Overall	72.54 (11.03)
45–54	11 (6.5%)
55–64	29 (17.3%)
65–74	48 (28.6%)
75–84	57 (33.9%)
>85	23 (13.7%)
Tobacco	
Active smokers	22 (13.1%)
Number cigarettes/day	
Overall	1.63 (4.98)
Non-smoker	145 (86.3%)
≤10 cigarettes/day	14 (8.3%)
>10 cigarettes/day	9 (5.4%)
Alcohol	
Alcohol-consuming patients	29 (17.3%)
Alcohol units	
Overall	0.23 (0.56)
Non-alcohol drinker	139 (82.7%)
≤2 units/day	28 (16.7%)
>2 units/day	1 (0.6%)
Patients with dentures	65 (38.7%)
Type of diabetes	
T1DM	13 (7.7%)
T2DM	155 (92.3%)
Time from diabetes diagnosis (months)	121.40 (89.13)
HbA1c (%)	6.8 (1.27)
Patients with xerostomia	88 (52.4%)
Patients with UWS hyposalivation	69 (41.1%)
Number of systemic diseases	
Overall	4.11 (3.26)
1–3 diseases	88 (52.4%)
4–6 diseases	49 (29.2%)
7–9 diseases	21 (12.5%)
>10 diseases	10 (6%)
Number of drugs received	
Overall	7.21 (3.7)
1–3 drugs	21 (12.5%)
4–6 drugs	64 (38.1%)
7–9 drugs	47 (28%)
>10 drugs	36 (21.4%)
Patients undergoing antidiabetic treatment	127 (75.6%)
Xerostomy inventory score	21.96 (8.78)
Uncontrolled diabetes (HbA1C ≥ 7%)	55 (33.1%)

Abbreviations: HbA1C, hemoglobin A1c;T1DM, diabetes mellitus Type 1; T2DM, diabetes mellitus Type 2; UWS, unstimulated whole saliva.

results and glycemic control (HbA1c%) was practically null ($r=0.03$; $p=0.68$).

All medications taken by DM patients can be found in Appendix S6. Table 2 shows the results for drugs and diseases that showed a significance ≤0.20. The intake of the following drugs was associated with xerostomia: drugs for acid related disorders (OR 1.94, 95% CI 1.05–3.59; $p=0.03$), drugs for gastro-esophageal reflux disease (OR 1.94, 95% CI 1.05–3.59; $p=0.03$), proton pump inhibitors (OR 1.95, 95% CI 1.05–3.6; $p=0.03$), angiotensin-converting enzyme (ACE) inhibitors combinations (OR 4.05, 95% CI 1.10–14.93; $p=0.03$), ACE inhibitors and diuretics (OR 5.57, 95% CI 1.19–25.97; $p=0.03$), psycholeptics (OR 2.12, 95% CI 1.06–4.22; $p=0.03$), psychoanaleptics (OR 2.63, 95% CI 1.13–6.12; $p=0.02$), and antidepressants (OR 3.48, 95% CI 1.39–8.66; $p=0.008$).

The diseases suffered by DM patients with and without xerostomia can be found in Appendix S7. A significant association was observed between suffering from xerostomia and having depressive disorders (OR 4.22, 95% CI 1.34–13.23; $p=0.013$).

The results of the multivariate logistic regression analysis for xerostomia (Table 3) showed that patients taking Angiotensin II receptor blockers (other combinations) were more likely to suffer from xerostomia (OR 10.65, 95% CI 1.48–76.35; $p=0.02$). It was also observed that patients using ramipril (OR 0.06, 95% CI 0.005–0.91; $p=0.04$), an ACE inhibitor, and lipid modifiying agents combinations (OR 0.19, 95% CI 0.04–0.77; $p=0.02$) were less likely to suffer from xerostomia. The results of the age-adjusted model followed the same trend (Table 3).

3.2 | Salivary Hypofunction

Sixty-nine patients had a reduced salivary flow. The UWS hyposalivation prevalence was 41.1% (95% CI 48.6–33.8). Regarding the XI questionnaire, the results for each item and the total

TABLE 2 | Associations between xerostomia and the different variables collected. Only diseases according to ICD-11 classification and drugs according to ATC classification with a significance ≤ 0.20 are shown. Crude ORs and their 95% confidence interval are also available.

	No xerostomia ($n = 80$)	Xerostomia ($n = 88$)	p	Crude OR (95% CI)	p
Gender					
Male	43 (53.8%)	35 (39.8%)	0.07	1	
Female	37 (46.3%)	53 (60.2%)		1.76 (0.95–3.2)	0.71
Age (years)					
Overall	72.26 (10.85)	72.78 (11.25)	0.76	1.004 (0.98–1.03)	0.76
45–54	5 (6.3%)	6 (6.8%)	0.63	1	
55–64	16 (20%)	13 (14.8)		0.68 (0.17–2.73)	0.58
65–74	20 (25%)	28 (31.8%)		1.17 (0.31–4.36)	0.82
75–84	30 (37.5%)	27 (30.7%)		0.75 (0.20–2.74)	0.66
> 85	9 (11.3)	14 (15.9%)		1.29 (0.30–5.54)	0.73
Tobacco					
Active smokers	12 (15%)	11 (12.5%)	0.64	0.81 (0.34–1.95)	0.64
Number cigarettes/day					
Overall	1.29 (3.55)	1.94 (6.01)	0.4		
Non-smoker	68 (85%)	77 (87.5%)	0.006	1	
≤ 10 cigarettes/day	11 (13.8%)	3 (3.4%)		0.24 (0.64–0.90)	0.03
> 10 cigarettes/day	1 (1.3%)	8 (9.1%)		7.06 (0.86–57.94)	0.07
Alcohol					
Alcohol-consuming patients	14 (17.5%)	14 (15.9%)	0.78	0.89 (0.4–2.01)	0.78
Alcohol units					
Overall	0.28 (0.67)	0.18 (0.44)	0.4	1.03 (0.96–1.09)	0.41
Non-alcohol drinker	65 (81.3%)	74 (84.1%)	0.5	1	
≤ 2 units/day	14 (17.5%)	14 (15.9%)		0.88 (0.39–1.98)	0.75
> 2 units/day	1 (1.3%)	0		0	1
Patients with dentures	32 (40%)	33 (37.5%)	0.74	0.90 (0.48–1.67)	0.74
Type of diabetes					
T1DM	5 (6.3%)	8 (9.1%)	0.49	1	
T2DM	75 (93.8%)	80 (90.9%)		0.71 (0.37–1.35)	0.29
Time from diabetes diagnosis	123 (86.66)	119.84 (91.99)	0.82	1 (0.99–1.003)	0.82
HbA1c (%)	6.7 (1.4)	6.8 (1)	0.66	1.01 (0.81–1.27)	0.92
Poorly controlled diabetes (> 7%)	23 (29.1%)	32 (36.8%)	0.3	0.71 (0.37–1.35)	0.29
UWS flow rate (ml/min)	0.25 (0.26)	0.15 (0.18)	0.001	0.11 (0.021–0.56)	0.008
UWS hyposalivation	23 (28.7%)	46 (52.3%)	0.002	2.71 (1.4–5.15)	0.002
Number systemic diseases					
Overall	3.81 (3.08)	4.38 (3.42)	0.22	1.05 (0.95–1.15)	0.33
1–3 diseases	47 (58.8%)	46.6%)	0.14	1	
4–6 diseases	18 (22.5%)	31 (35.2%)		1.97 (0.96–4.04)	0.06

(Continues)

TABLE 2 | (Continued)

	No xerostomia ($n=80$)	Xerostomia ($n=88$)	p	Crude OR (95% CI)	p
7–9 diseases	12 (15%)	9 (10.2%)		0.86 (0.33–2.25)	0.76
> 10 diseases	3 (3.8%)	7 (8%)		2.67 (0.65–11.02)	0.17
Number of drugs					
Overall	6.95 (3.81)	7.44 (3.60)	0.39	1.04 (0.95–1.13)	0.39
1–3 drugs	13 (16.3%)	8 (9.1%)	0.57	1	
4–6 drugs	29 (36.3%)	35 (39.8%)		1.96 (0.71–5.38)	0.19
7–9 drugs	22 (27.5%)	25 (28.4%)		1.84 (0.65–5.28)	0.25
> 10 drugs	16 (20%)	20 (22.7%)		2.03 (0.67–6.1)	0.21
A02 drugs for acid related disorders	37 (45.7%)	55 (63.2%)	0.02	1.94 (1.05–3.59)	0.03
A02B GORD	37 (45.7%)	55 (63.2%)	0.02	1.94 (1.05–3.59)	0.03
A02BC proton pump inhibitors	35 (43.2%)	53 (60.9%)	0.02	1.95 (1.05–3.6)	0.03
A02BC01 omeprazole	28 (34.6%)	40 (46%)	0.13	1.55 (0.83–2.88)	0.17
A12A calcium	4 (5%)	10 (11.4%)	0.14	2.44 (0.73–8.1)	0.15
A12AX calcium, combinations with vitamin D and/or other drugs	3 (3.8%)	8 (9.1%)	0.16	2.57 (0.66–10.03)	0.17
B03BA01 cyanocobalamin	4 (4.9%)	9 (10.3%)	0.19	2.16 (0.64–7.33)	0.21
C02CA alpha-adrenoreceptor antagonists	6 (7.5%)	2 (2.3%)	0.15	0.29 (0.056–1.46)	0.13
C03 diuretics	8 (9.9%)	16 (18.4%)	0.11	2 (0.81–4.97)	0.13
C07 beta blocking agents	11 (13.6%)	20 (23%)	0.12	1.84 (0.82–4.14)	0.14
C07A beta blocking agents	10 (12.5%)	20 (22.7%)	0.08	2.06 (0.9–4.72)	0.09
C07AB beta blocking agents, selective	6 (7.5%)	13 (4.8%)	0.14	2.14 (0.77–5.93)	0.14
C08CA13 lercadipine	4 (5%)	1 (1.1%)	0.19	0.22 (0.02–1.99)	0.18
C09 agents acting on the renin-angiotensin system	52 (64.2%)	46 (52.9%)	0.14	0.68 (0.37–1.27)	0.23
C09AA05 ACE inhibitors monodrugs. Ramipril	6 (7.5%)	1 (1.1%)	0.05	0.14 (0.017–1.20)	0.074
C09B ACE inhibitors combinations	3 (3.8%)	12 (13.6%)	0.03	4.05 (1.10–14.93)	0.03
C09BA ACE inhibitors + diuretics	2 (2.5%)	11 (12.5%)	0.02	5.57 (1.19–25.97)	0.03
C09DA ARBs and diuretics	9 (11.3%)	3 (3.4%)	0.05	0.28 (0.07–1.07)	0.06
C09DB ARBs and calcium channel blockers	4 (5%)	1 (1.1%)	0.19	0.22 (0.02–1.99)	0.18
C09DX arbs, other combinations	2 (2.5%)	9 (10.2%)	0.04	4.44 (0.93–21.2)	0.06
C10B lipid modifying agents, combinations	12 (14.8%)	6 (6.9%)	0.09	0.41 (0.15–1.16)	0.09

(Continues)

TABLE 2 | (Continued)

	No xerostomia ($n=80$)	Xerostomia ($n=88$)	p	Crude OR (95% CI)	p
C10BA combinations of various lipid modifying agents	11 (13.6%)	6 (6.9%)	0.15	0.46 (0.16–1.30)	0.14
C10BA05 atorvastatin and ezetimibe	8 (9.9%)	4 (4.6%)	0.18	0.43 (012–1.48)	0.18
G genito urinary system and sex hormones	12 (14.8%)	21 (24.1%)	0.13	1.78 (0.81–3.9)	0.15
H02 corticosteroids for systemic use	1 (1.3%)	7 (8%)	0.06	6.83 (0.82–56.77)	0.75
N nervous System	45 (55.6%)	59 (67.8%)	0.1	1.66 (0.89–3.11)	0.11
N02 analgesics	32 (40%)	44 (50%)	0.19	1.5 (0.81–2.77)	0.19
N05 psycholeptics	17 (21%)	32 (36.8%)	0.02	2.12 (1.06–4.22)	0.03
N05B anxiolytics	16 (19.8%)	27 (31%)	0.09	1.77 (0.87–3.60)	0.11
N05BA benzodiazepine derivatives	15 (18.5%)	27 (31%)	0.06	1.92 (0.93–3.95)	0.77
N05C hypnotics and sedatives	1 (1.2%)	8 (9.2%)	0.03	7.9 (0.97–64.64)	0.05
N06 psychoanaleptics	10 (12.3%)	22 (25.3%)	0.03	2.63 (1.13–6.12)	0.02
N06A antidepressants	7 (8.8%)	22 (25%)	0.005	3.48 (1.39–8.66)	0.008
N06AB SSRIS antidepressant	5 (6.3%)	14 (15.9%)	0.05	2.84 (0.97–8.28)	0.06
6: Mental, behavioral or neurodevelopmental disorders	8 (10%)	17 (19.3%)	0.09	2.15 (0.87–5.31)	0.95
6A7Z Depressive disorders, unspecified	4 (5%)	16 (18.2%)	0.008	4.22 (1.34–13.23)	0.013
9B10 cataract	8 (10%)	4 (4.5%)	0.17	0.43 (0.12–1.48)	0.18

Note: Chi-squared test or Fisher's exact test were used for categorical variables and Mann–Whitney *U* test for numerical variables.
Abbreviations: ACE, angiotensin-converting enzyme; ARBs, angiotensin II receptor blockers; GORD, gastro-oesophageal reflux disease drugs; HbA1C, hemoglobin A1c; SSRIs, selective serotonin reuptake inhibitors; T1DM, diabetes Mellitus Type 1; T2DM, diabetes Mellitus Type 2; UWS, unstimulated whole saliva.

scores in patients with and without hyposalivation are shown in Appendix S8. Patients with hyposalivation were found to score significantly higher on 7 of the 11 items and on the total score than those without hyposalivation.

The results of the univariate analysis between hyposalivation and the different variables collected is shown in Table 4. UWS hyposalivation was significantly higher in women than in men (OR 2.5, 95% CI 1.32–4.73; $p=0.005$). Patients with T2DM were less likely to suffer UWS hyposalivation than T1DM patients (OR 0.28, 95% CI 0.08–0.95; $p=0.04$). The correlation between UWS flow and glycemic control (HbA1c%) was negative but practically null ($r=-0.03$; $p=0.68$).

Drugs taken by DM patients with and without UWS hyposalivation can be found in Appendix S9. Table 4 shows the results for drugs and diseases that showed a significance ≤ 0.20. Patients taking the following drugs were more likely to suffer xerostomia: calcium combinations with vitamin D (OR 4.20, 95% CI 1.07–16.44; $p=0.04$), combinations of angiotensin II receptor blockers (ARBs) (OR 2.91, 95% CI 1.24–6.83; $p=0.01$), psycholeptics (OR 2, 95% CI 1.02–3.9; $p=0.04$), hypnotics and sedatives (OR 5.48, 95% CI 1.10–27.22; $p=0.04$), glucocorticoids (OR 11.06, 95% CI 1.3–92.11; $p=0.03$), psychoanaleptics (OR 2.33, 95% CI 1.06–5.16; $p=0.04$), antidepressants (OR 2.37, 95% CI 1.05–5.35; $p=0.04$), and antidepressants selective serotonin reuptake inhibitors (OR 2.77, 95% CI 1.03–7.44; $p=0.04$). On the contrary, patients taking lipid-modifying agents were less likely to suffer UWS hyposalivation (OR 0.25, 95% CI 0.07–0.92; $p=0.04$), and among them, atorvastatin and ezetimibe (OR 0.12, 95% CI 0.01–0.93; $p=0.04$).

The diseases suffered by DM patients with and without UWS hyposalivation can be found in Appendix S10. Patients with vitamin D deficiency were less likely to suffer hyposalivation (OR 0.17, 95% CI 0.04–0.76; $p=0.02$).

The results of multivariate logistic regression analysis (Table 5) showed that women were more likely to suffer from hyposalivation (OR 2.47, 95% CI 0.98–6.23; $p=0.05$), as were patients taking combinations of ACE inhibitors combinations (OR 4.3, 95% CI 0.99–18.68; $p=0.05$), and angiotensin II receptor blocker combinations (OR 4.6, 95% CI 1.54–13.83; $p=0.006$). However, patients taking 4–6 drugs (OR 0.08, 95% CI 0.02–0.32; $p=0.02$) and 7–9 drugs (OR 0.09, 95% CI 0.2–0.41; $p=0.002$), as well as patients with vitamin D deficiency (OR 0.08, 95% CI 0.01–0.5; $p=0.007$), were less likely to suffer from hyposalivation. The results of the age-adjusted model followed the same trend (Table 5).

TABLE 3 | Multivariate logistic regression analysis of factors associated with xerostomia in DM patients.

	Multivariate analysis Crude model (95% CI)	*p*	Multivariate analysis Adjusted model (95% CI)	*p*
Gender (Female)	2.27 (0.88–5.82)	0.09	2.26 (0.88–5.80)	0.09
Number cigarettes/day				
Non-smoker	1		1	
≤10 cigarettes/day	0.14 (0.02–1.07)	0.06	0.14 (0.02–1.05)	0.06
>10 cigarettes/day	5.85 (0.61–56.55)	0.13	5.47 (0.54–55.31)	0.15
Number systemic diseases				
1–3 diseases	1		1	
4–6 diseases	2.07 (0.82–5.23)	0.12	2.06 (0.81–5.21)	0.13
7–9 diseases	0.85 (0.24–2.99)	0.80	0.84 (0.24–2.97)	0.79
>10 diseases	0.71 (0.09–5.46)	0.74	0.69 (0.08–5.3)	0.72
A02 Drugs for acid related disorders	1.38 (0.6–3.15)	0.45	1.39 (0.61–3.18)	0.44
A12A calcium	1.26 (0.27–5.82)	0.76	1.27 (0.27–5.83)	0.76
B03BA01 cyanocobalamin	1.85 (0.37–9.14)	0.45	1.81 (0.37–8.96)	0.46
C02CA alpha-adrenoreceptor antagonists	0.26 (0.03–2.6)	0.25	0.27 (0.03–2.65)	0.26
C03 diuretics	2.71 (0.75–9.86)	0.13	2.76 (0.76–10.07)	0.12
C07 beta blocking agents	1.92 (0.61–6.02)	0.26	1.94 (0.62–6.12)	0.26
C08CA13 lercadipine	1.55 (0.11–21.35)	0.74	1.6 (0.11–22.22)	0.73
C09AA05 ACE inhibitors monodrugs. Ramipril	0.06 (0.005–0.91)	0.04	0.06 (0.004–0.91)	0.04
C09B ACE inhibitors combinations	3.79 (0.82–17.61)	0.09	3.92 (0.83–18.53)	0.08
C09DA ARBs and diuretics	0.2 (0.03–1.19)	0.08	0.21 (0.04–1.24)	0.08
C09DB ARBs and calcium channel blockers	0.09 (0.004–2.23)	0.14	0.09 (0.004–2.3)	0.15
C09DX arbs, other combinations	10.65 (1.48–76.35)	0.02	10.54 (1.45–76.38)	0.02
C10B lipid modifying agents, combinations	0.19 (0.04–0.77)	0.02	0.19 (0.04–0.78)	0.02
G genito urinary system and sex hormones	2.92 (0.89–9.64)	0.08	2.99 (0.9–9.97)	0.07
H02 corticosteroids for systemic use	2.82 (0.17–47.15)	0.47	2.87 (0.17–48.07)	0.47
N02 analgesics	1.48 (0.6–3.63)	0.39	1.5 (0.61–3.68)	0.38
N05 psycholeptics	1.31 (0.49–3.48)	0.59	1.33 (0.5–3.55)	0.57
N06 psychoanaleptics	2.17 (0.49–9.43)	0.3	2.16 (0.5–9.44)	0.3
6A7Z depressive disorders, unspecified	2.82 (0.44–18.08)	0.27	2.86 (0.44–18.35)	0.27
9B10 cataract	0.84 (0.16–4.47)	0.84	0.87 (0.16–4.69)	0.87

Note: Model I: crude model, no adjustment. Model II: adjusted for age.
Abbreviations: ACE, angiotensin-converting enzyme; ARBs, angiotensin II receptor blockers; SSRIs, selective serotonin reuptake inhibitors.

4 | Discussion

The aim of this study was to determine the prevalence of xerostomia and hyposalivation in a group of patients diagnosed with DM according to current criteria, as well as to evaluate the related risk factors. The results of this study revealed a high prevalence of xerostomia (52.4%) and hyposalivation (41.1%). These conditions were not found to be associated with glycemic control or the use of drugs for treating DM. However, they were associated with the presence of other diseases and/or the use of medications for treating other comorbidities.

Previous studies have reported a wide range in the prevalence of xerostomia among DM patients, varying from 12.5% to 76.4%

TABLE 4 | Associations between the presence of hyposalivation and the different variables collected. Only diseases according to ICD-11 classification and drugs according to ATC classification with a significance ≤ 0.20 are shown. Crude ORs and their 95% confidence interval are also available.

	No UWS hyposalivation ($n = 99$)	UWS hyposalivation ($n = 69$)	p	Crude OR (95% CI)	p
Gender					
Male	55 (55.6%)	23 (33.3%)	0.004	1	
Female	44 (44.4%)	46 (66.7%)		2.5 (1.32–4.73)	0.005
Age (years)					
Overall	72.62 (10.72)	72.42 (11.53)	0.91	0.99 (0.97–1.03)	0.91
45–54	6 (6.1%)	5 (7.2%)	0.59	1	
55–64	17 (17.2%)	12 (17.4%)		0.85 (0.21–3.43)	0.82
65–74	27 (27.3%)	21 (30.4%)		0.93 (0.25–3.48)	0.92
75–84	38 (38.4%)	19 (27.5%)		0.60 (0.16–2.22)	0.44
> 85	11 (11.1%)	12 (17.4%)		1.31 (0.31–5.53)	0.71
Tobacco					
Active smokers	16 (16.2%)	7 (10.1%)	0.26	0.59 (0.23–1.51)	0.27
Number cigarettes/day					
Overall	1.89 (5.21)	1.26 (4.64)	0.42	0.97 (0.91–1.04)	0.44
Non-smoker	83 (83.8%)	62 (89.9%)	0.52	1	
≤ 10 cigarettes/day	10 (10.1%)	4 (5.8%)		0.53 (0.16–1.79)	0.31
> 10 cigarettes/day	6 (6.1%)	3 (4.3%)		0.67 (0.16–2.78)	0.58
Alcohol					
Alcohol-consuming patients	21 (21.2%)	7 (10.1%)	0.06	0.42 (0.17–1.05)	0.06
Alcohol units					
Overall	0.3 (0.66)	0.12 (0.36)	0.03	0.47 (0.22–0.98)	0.04
Non-alcohol drinker	77 (77.8%)	62 (89.9%)	0.11	1	
≤ 2 units/day	21 (21.2%)	7 (10.1%)		0.41 (0.16–1.04)	0.06
> 2 units/day	1 (1%)	0		0	1
Patients with dentures	39 (39.4%)	26 (37.7%)	0.82	0.93 (0.49–1.75)	0.82
Type of diabetes					
T1DM	4 (30.77%)	9 (69.23%)	0.03	1	
T2DM	95 (61.29%)	60 (38.71%)		0.28 (0.08–0.95)	0.04
Time from diabetes diagnosis	114.16 (74.72)	132.08 (106.67)	0.21	1.002 (0.99–1)	0.22
HbA1c (%)	6.71 (0.91)	7.03 (1.65)	0.11	1.14 (0.89–1.44)	0.29
Poorly controlled diabetes (> 7%)	28 (28.3%)	27 (40.3%)	0.11	0.58 (0.30–1.12)	0.11
Number systemic diseases					
Overall	4.25 (3.39)	3.90 (3.09)	0.61	0.97 (0.88–1.06)	0.49
1–3 diseases	50 (50.5%)	38 (55.1%)	0.85	1	
4–6 diseases	30 (30.3%)	19 (27.5%)		0.83 (0.41–1.70)	0.62

(Continues)

TABLE 4 | (Continued)

	No UWS hyposalivation ($n=99$)	UWS hyposalivation ($n=69$)	p	Crude OR (95% CI)	p
7–9 diseases	12 (12.1%)	9 (13%)		0.99 (0.38–2.58)	0.98
> 10 diseases	7 (7.1%)	3 (4.3%)		0.56 (0.14–2.32)	0.43
Number of drugs					
Overall	6.93 (3.45)	7.61 (4.01)	0.24	1.05 (0.97–1.14)	0.24
1–3 drugs	9 (9.1%)	12 (17.4%)	0.01	1	
4–6 drugs	46 (46.5%)	18 (26.1%)		0.29 (0.11–0.81)	0.02
7–9 drugs	29 (29.3%)	18 (26.1%)		0.47 (0.16–1.32)	0.15
> 10 drugs	15 (15.2%)	21 (30.4%)		1.05 (0.35–3.12)	0.93
A12AX calcium combined with vitamin D	3 (3%)	8 (11.6%)	0.05	4.20 (1.07–16.44)	0.04
A12AXP1 calcium carbonate and, colecalciferol	3 (3%)	7 (10.1%)	0.09	3.61 (0.90–14.50)	0.07
C07AB03 atenolol	1 (1%)	5 (7.2%)	0.04	7.66 (0.87–67.06)	0.07
C09B ACE inhibitors combinations	6 (6.1%)	9 (13%)	0.11	2.32 (0.79–6.86)	0.13
C09BA ACE inhibitors and diuretics	5 (5.1%)	8 (11.6%)	0.11	2.47 (0.77–7.88)	0.13
C09BA02 enalapril and diuretics	1 (1%)	4 (5.8%)	0.16	6.03 (0.66–55.17)	0.11
C09D ARBs, combinations	10 (10.1%)	17 (24.6%)	0.01	2.91 (1.24–6.83)	0.01
C09DX arbs, other combinations	3 (3%)	6 (11.8%)	0.05	4.20 (1.07–16.44)	0.04
C09DX03 olmesartan medoxomil, amlodipine, and hydrochlorothiazide	2 (2%)	5 (7.2%)	0.12	3.79 (0.71–20.18)	0.12
C10B lipid modifying agents, combinations	15 (15.2%)	3 (4.3%)	0.03	0.25 (0.07–0.92)	0.04
C10BA combination of various lipid-modifying agents	14 (14.1%)	3 (4.3%)	0.04	0.28 (0.08–1)	0.05
C10BA05 atorvastatin and ezetimibe	11 (11.1%)	1 (1.4%)	0.02	0.12 (0.01–0.93)	0.04
H systemic hormonal preparations, excl. sex hormones and insulins	19 (19.2%)	20 (29%)	0.13	1.72 (0.83–3.54)	0.14
H02AB glucocorticoids	1 (1%)	7 (10.1%)	0.01	11.06 (1.3–92.11)	0.03
H02AB07 prednisone	1 (1%)	4 (5.8%)	0.16	6.03 (0.66–55.17)	0.11
N02AX other opioids	3 (3%)	6 (8.7%)	0.16	3.05 (0.73–12.63)	0.12
N05 psycholeptics	23 (23.2%)	26 (37.7 %)	0.04	2 (1.02–3.9)	0.04
N05BA08 bromazepam	7 (7.1%)	11 (15.9.%)	0.06	2.49 (0.91–6.8)	0.07
N05C hypnotics and sedatives	0 (0%)	4 (5.8%)	0.03	5.48 (1.10–27.22)	0.04
N05CF benzodiazepine related drugs	1 (1%)	4 (5.8%)	0.16	6.03 (0.66–55.17)	0.11
N06 psychoanaleptics	13 (13.1%)	19 (27.5%)	0.02	2.33 (1.06–5.16)	0.04
N06A antidepressants	12 (12.1%)	18 (26.1%)	0.02	2.37 (1.05–5.35)	0.04
N06AB SSRIs antidepresessants	7 (7.1%)	11 (17.4.%)	0.05	2.77 (1.03–7.44)	0.04
5B57Z vitamin D deficiency, unspecified	15 (15.2%)	2 (2.9%)	0.01	0.17 (0.04–0.76)	0.02

(Continues)

TABLE 4 | (Continued)

	No UWS hyposalivation ($n = 99$)	UWS hyposalivation ($n = 69$)	p	Crude OR (95% CI)	p
6A7Z depressive disorders, unspecified	9 (9.1%)	11 (15.9%)	0.17	1.9 (0.74–4.86)	0.18
9C61 glaucoma	8 (8.1%)	2 (2.9%)	0.2	0.34 (0.07–1.65)	0.07

Note: Chi-squared test or Fisher's exact test were used for categorical variables and Mann–Whitney *U* test for numerical variables.
Abbreviations: ARB, angiotensin II receptor blockade; HbA1c, hemoglobin A1c; SSRIs: selective serotonin reuptake inhibitors; T1DM, diabetes mellitus Type 1; T2DM, diabetes mellitus Type 2; UWS, unstimulated whole saliva.

[8, 25–28]. Similarly, the prevalence of hyposalivation varies between 11.5% and 56% [8, 25, 29]. In the present study we found prevalences of xerostomia and hyposalivation of 52.4% and 41.1%, respectively, which are within the previously mentioned ranges. This variability could be attributed to differences in the studied populations, patient age, heterogeneity in the type of DM, and diverse methodologies employed to asses xerostomia and salivary hypofunction.

It should be noted that in the present study a higher prevalence of hyposalivation was observed in patients with T1DM than in patients with T2DM (69.23% vs. 38.70%) reaching statistical significance in the univariate analysis but not in the multivariate analysis. There are no previous results in this line, but Ben Aryeh et al. found lower salivary flow rates in insulin-dependent patients compared to non-insulin-dependent patients [30]. We believe that further studies analyzing salivary disorders in T1DM and T2DM are needed in the future.

We have not found a significant association between DM control and xerostomia and/or hyposalivation, which is also observed in previous studies [27, 31]. Correlation between HbA1c values and severity of xerostomia (XI) and UWS salivary flow levels were also not found. Like Molaina et al. [29], we found higher levels of HbA1c in DM patients with hyposalivation than in those without hyposalivation, but the results were not significant. But Chávez et al. [32] in a previous study found that DM patients with poor glycaemic control had lower salivary flow. Given that HbA1c is a good indicator of long-term control and follow-up of DM, it would be good to perform longitudinal studies to evaluate whether changes in glycemic control (HbA1c) could lead to changes in salivary flow.

On the other hand, XI results showed significantly higher total values in patients with xerostomia and hyposalivation. However, in the case of xerostomia 9 out of 11 XI items were significantly higher and for hyposalivation only 7 out of 11. This might suggest that the XI is better aligned with the subjective sensation of dry mouth or xerostomia.

Most of the previous studies about xerostomia and/or hyposalivation in patients with DM have not considered other associated risk factors that can act as confounding factors, such as the intake of multiple drugs and suffering from other diseases. The patient with DM can suffer from other comorbidities, mainly T2DM patients, due to its relationship with a more advanced age, habits, or lifestyle. This study has considered these factors, and the diseases and drugs have been classified according to current criteria. DM patients use multiple drugs to treat their diabetes and the comorbidities they suffer from. It is reasonable to think that the greater the number of drugs, the greater the number of adverse reactions that can occur, including xerostomia. It has been reported that salivary flow rates decrease as the number of drugs and systemic diseases increases [33]. However, as in other studies [34], we did not find an association between the number of drugs taken and xerostomia or hyposalivation reaching in some cases contradictory results. It should be noted that all patients in our study were on medication, so comparisons could not be made with non-medicated patients.

A large percentage of the patients included in the present study were on antidiabetic medication. But it is noteworthy how we found no association between the drugs used to treat DM and salivary disorders. We have also not found studies that reported an association between antidiabetic medications and salivary disturbances. Therefore, it seems that antidiabetic treatments are not associated with xerostomia and hyposalivation.

We have identified an association in the univariate analysis between hyposalivation and certain medications, such as psycholeptics (hypnotics and sedatives), and psychoanaleptic antidepressants, including serotonin reuptake inhibitors. Although no significant results were obtained in the multivariate analysis, the results suggest that these drugs increase xerostomia and hyposalivation. Wolff's systematic review highlights the connection between various antidepressants and salivary dysfunction, including selective serotonin reuptake inhibitors, as well as hypnotics and sedatives, due to their action on the central nervous system and their effect on the autonomic nervous system, which regulates involuntary functions such as salivation [35]. Additionally, these drugs may have anticholinergic or antimuscarinic effects, leading to a decrease in saliva secretion. Moreover, antidepressants that enhance serotonin effects, such as fluoxetine, are strongly correlated with a reduced salivary flow [36].

Xerostomia has also been associated with different antihypertensive drugs [36], as observed in the multivariate analysis of our study. We found that patients taking ARBs and ACE inhibitors, both combined with other antihypertensives, suffered more xerostomia and hyposalivation, which may be explained by the drugs associated in these combinations (diuretics, calcium channel blockers, and others). On the other hand, we observed that patients taking ramipril, which is an

TABLE 5 | Multivariate logistic regression analysis of factors associated with UWS hyposalivation in DM patients.

	Multivariate analysis Crude model (95% CI)	*p*	Multivariate analysis Adjusted model (95% CI)	*p*
Gender (female)	2.47 (0.98–6.23)	0.05	2.44 (0.97–6.18)	0.06
Alcohol consumer (yes)	0.55 (0.16–1.95)	0.36	0.55 (0.15–1.94)	0.35
Type of diabetes (T2DM)	0.49 (0.09–2.56)	0.39	0.5 (0.09–2.66)	0.42
Poorly controlled diabetes (> 7%)	0.62 (0.25–1.53)	0.3	0.64 (0.25–1.61)	0.34
Number of drugs				
1–3 drugs	1		1	
4–6 drugs	0.08 (0.02–0.32)	0.001	0.08 (0.02–0.34)	0.001
7–9 drugs	0.09 (0.2–0.41)	0.002	0.09 (0.2–0.42)	0.002
> 10 drugs	0.25 (0.05–1.26)	0.09	0.26 (0.05–1.34)	0.11
A02 Drugs for acid related disorders	2.36 (0.96–5.82)	0.06	2.4 (0.96–5.84)	0.06
A10BX02 repaglinide	2.07 (0.21–19.94)	0.53	2.1 (0.22–20.3)	0.52
A12AX calcium, combinations with vitamin d and/or other drugs	1.99 (0.34–11.78)	0.45	1.94 (0.33–11.52)	0.46
C07AB03 atenolol	6.44 (0.41–100.23)	0.18	6.45 (0.42–99.97)	0.2
C09B ACE inhibitors combinations	4.3 (0.99–18.68)	0.05	4.44 (1–19.71)	0.05
C09D arbs, combinations	4.6 (1.54–13.83)	0.006	4.7 (1.55–14.14)	0.006
C10B lipid modifying agents, combinations	0.21 (0.04–1.24)	0.08	0.21 (0.03–1.27)	0.08
H02AB glucocorticoids	1.95 (0.14–26.43)	0.61	1.94 (0.14–26.26)	0.62
N02A opioids	2.02 (0.43–9.47)	0.37	2.06 (0.44–9.7)	0.36
N05 psycholeptics	1.5 (0.57–3.96)	0.4	1.51 (0.57–3.98)	0.41
N06 psychoanaleptics	2.75 (0.66–11.46)	0.16	2.82 (0.67–11.83)	0.16
5B57Z vitamin D deficiency, unspecified	0.08 (0.01–0.5)	0.007	0.08 (0.01–0.5)	0.007
6A7Z depressive disorders, unspecified	0.62 (0.12–3.32)	0.58	0.61 (0.12–3.27)	0.57
9C61 glaucoma	0.83 (0.13–5.48)	0.85	0.84 (0.13–5.51)	0.85

Note: Model I: crude model, no adjustment. Model II: adjusted for age.
Abbreviations: ACE, Angiotensin-converting enzyme; ARBs, Angiotensin II receptor blockers.

ACE inhibitor, suffered less xerostomia. ACE inhibitors prevent the degradation of bradykinin (a peptide with vasodilatory effects), which could increase perfusion to the salivary glands [37].

Some studies have reported a possible association between Gastroesophageal Reflux Disease and a decrease in stimulated saliva flow [38, 39]. Additionally, drugs for acid related disorders such as proton pump inhibitors, frequently used to treat this condition, have been associated with decreased saliva production [39]. Our results showed that DM patients taking these drugs were more likely to suffer from xerostomia and hyposalivation in the univariate analysis. Furthermore, it almost reached statistical significance in the case of hyposalivation.

The present study also observed that vitamin D deficiency could act as a protective factor against hyposalivation. This is contrary to the findings in Glijer et al. study [40]. It is essential to keep in mind that in the present study patients with these deficiencies are undergoing treatment and may have corrected their deficiency at the time of saliva collection, which could influence these results.

In the present study, patients taking lipid-modifying agents were less likely to have hyposalivation. These drugs improve lipid profiles, reduce LDL cholesterol accumulation, and prevent atheromatous plaques formation that causes inflammation and endothelial damage, which leads to the narrowing and hardening of blood vessels. Therefore, these drugs could improve perfusion to the glands by improving atherosclerosis [41].

Regarding oral lesions, we found a prevalence of 42.3%, which is consistent with the results of other studies [42–44]. Multiple lesions and infections of the oral mucosa have been found in DM patients, and one of the risk factors could be xerostomia [45, 46]. However, we did not observe any association between the presence of oral lesions and xerostomia or hyposalivation.

This study has different limitations. Firstly, the cross-sectional design does not allow us to evaluate the cause-and-effect relationships between the different variables studied and salivary disorders. Secondly, while the number of DM patients is considerable, they all belong to two specific centers in Community of Madrid (Spain). And the sample may not be representative of all DM patients in the region or beyond. The advanced age of the patients makes it challenging to find patients who have DM as their only comorbidity. However, we believe this reflects the reality of the problem, as most patients with T2DM usually have multiple comorbidities.

Another limitation is that, although the XI has been previously used to measure xerostomia in DM patients [47, 48], it is not specifically validated for this purpose. Furthermore, this questionnaire does not allow for grading xerostomia. The study also did not employ a validated outcome measure to assess whether the patient suffers from xerostomia, as no such validated question currently exists. Additionally, we acknowledge that relying solely on patient-reported symptoms of xerostomia through a single question may introduce bias due to the subjective nature of self-reporting [24]. We also highlighted that patients may interpret and respond to this question differently based on their individual perceptions and experiences, which could lead to variability in the assessment of xerostomia. In addition, considering that patients may have difficulties in accurately recalling the frequency or severity of xerostomia symptoms, especially when there are long intervals between experiencing symptoms and completing the questionnaire, recall bias is a potential limitation. This could impact the reliability of the reported prevalence and severity of xerostomia.

Finally, data collection occurred before and after the COVID-19 pandemic. Although no patients reported xerostomia, hyposalivation, or oral disorders associated with COVID-19 infection, different recruitment periods may have introduced some variability in the results following the pandemic. A strength of this study is that we have used the current criteria for the diagnosis and control of DM, as well as for the diagnosis of the salivary disorders studied.

It is important to note that many of the patients with DM are older patients, as this study shows. As we have seen, these patients have a high prevalence of xerostomia and hyposalivation, conditions often due to multiple comorbidities and the use of various medications. These findings highlight the critical need for oral medicine and geriatric specialists to develop personalized diagnostic algorithms and comprehensive management strategies for salivary disorders in the setting of DM. It is essential to address these issues appropriately, minimizing risk factors, and assessing which treatments for xerostomia are most appropriate in each case as certain systemic treatments may have side effects [49]. Finally, future research is needed to evaluate the efficacy of safe treatments for xerostomia and hyposalivation in elderly DM patients.

5 | Conclusions

In this study, a high prevalence of xerostomia and UWS hyposalivation was found in patients with DM. No association was observed between salivary disorders and DM control, or antidiabetic drugs. Associations were found with other comorbidities and their treatments. Therefore, the possible association between DM, xerostomia, and/or hyposalivation is complex and may be influenced by multiple factors. Further studies are needed to evaluate whether DM influences these salivary alterations.

Author Contributions

Isabel Sánchez Garrido: conceptualization; data curation; investigation; methodology; writing – original draft. **Lucía Ramírez:** investigation; methodology; writing – review and editing. **Marta Muñoz Corcuera:** investigation; writing – review and editing. **Estela Garrido:** investigation; writing – review and editing. **Lorenzo Sanchez:** investigation; writing – review and editing. **María Luisa Martínez Acitores:** investigation; writing – review and editing. **Gonzalo Hernández:** conceptualization; methodology; writing – review and editing. **Rosa María López-Pintor:** conceptualization; data curation; formal analysis; investigation; methodology; software; supervision; writing – original draft.

Disclosure

The authors have nothing to report.

Ethics Statement

The study protocol was approved by the Ethics Committee of the Hospital San Carlos of Madrid (IEC no. 17.067-E).

Consent

All patients signed the corresponding informed consent.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

All the data are available if needed.

Peer Review

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/jop.13583.

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