

ORIGINAL ARTICLE

The Correlation between Subjective Complaint of Dry Mouth, Unstimulated Salivary Flow Rate, and Oral Mucosal Dryness in Patients with Sjogren's Syndrome

Felicia Paramita, Chininta Oktor Amani, Endah Ayu Tri Wulandari

Oral Medicine Division, Dentistry Department, Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia

Corresponding email to: felicia.paramita@gmail.com

ABSTRACT

Background: Sjogren's syndrome is an autoimmune disease characterized by the classic symptoms of dry mouth, dry eyes, and arthritis. The most common symptoms are called sicca symptoms, which consist of keratoconjunctivitis sicca, hyposalivation, and xerostomia. Many papers use the term xerostomia and hyposalivation interchangeably. However, these two terms define different conditions. Xerostomia describes the subjective complaint of dry mouth, whereas hyposalivation is objectively measured. **Objective:** To examine the correlation between xerostomia, unstimulated salivary flow rate, and oral mucosal dryness in patients with Sjogren's syndrome. **Results:** The Summated Xerostomia Inventory Indonesian version (SXI-ID) and Clinical Oral Dryness Score (CODS) correlate negatively with unstimulated salivary flow rate. Whereas SXI-ID is positively correlated with CODS. **Conclusion:** Xerostomia assessed using SXI-ID is not always followed by hyposalivation. Hyposalivation affects the wettability of oral mucosa, as it negatively correlates with dryness. Further study is needed to investigate the factors involved in the correlation between xerostomia and hyposalivation.

Keywords xerostomia, hyposalivation, Sjogren's syndrome, SXI-Id, CODS

INTRODUCTION

Sjogren's syndrome (SS) is an autoimmune disease characterized by the classic symptoms of dry mouth, dry eyes, and arthritis.^{1,2} Sjogren's syndrome has a wide variety of signs and symptoms. It can be divided into primary Sjogren's syndrome (pSS) and secondary Sjogren's syndrome (sSS).¹ Primary Sjogren's syndrome occurs alone, while secondary Sjogren's syndrome occurs in conjunction with other autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, and systemic sclerosis.¹

The most common symptom of Sjogren's syndrome is Sicca Syndrome, which consists of keratoconjunctivitis sicca, with a complaint about a foreign-body sensation in the eyes, increased sensitivity to light, marked hyposalivation, and xerostomia, with difficulties chewing and swallowing foods.¹ Salivary gland damage becomes one of the hallmarks of pSS. However, this process progresses slowly over the years and is frequently overlooked, resulting in an average delay of diagnosis of pSS for seven years.³

Two terms are commonly used in dry mouth: xerostomia and salivary gland hypofunction (hyposalivation). Many papers use these two terms interchangeably when, in fact, each term defines a different condition. Xerostomia is the term used to describe the sensation of dry mouth, a subjective complaint of patients.⁴ Since xerostomia is subjective, it can only be diagnosed by directly questioning the individual using the Summated Xerostomia Inventory (SXI); to Indonesians, it's the SXI-Id version.^{5,6} While objectively, hyposalivation is a condition of reduced salivary flow rate and can be measured by sialometry. Additionally, the clinical dryness of the oral cavity was objectively measured by the Clinical Oral Dryness Score (CODS).⁷

Xerostomia is not always necessarily experienced in hyposalivation; it can be found in patients with normal salivation.⁴ To the extent of our knowledge, no study correlates the subjective complaint of dry

mouth measured by SXI-ID, hyposalivation measured by sialometry and the objective dry mouth measured by CODS in Sjogren's syndrome patients. Thus, this study aims to correlate the subjective complaint of dry mouth (SXI-ID) and the objective finding of dry mouth (sialometry and CODS) in Sjogren's syndrome patients.

MATERIALS AND METHODS

This retrospective cross-sectional study includes Sjogren's syndrome patients presented to Oral Medicine Clinic of Dr. Cipto Mangunkusumo General Hospital from January 2021 to January 2023. The SXI-ID, unstimulated salivary flow rate (USSFR), and CODS examination were conducted as routine examinations in Sjogren's syndrome patients. Data will be presented as mean, standard deviation, or median and minimum maximum. Correlation between SXI-ID and USSFR, SXI-ID and CODS, and SXI-ID and USSFR will be analyzed using the Pearson's or Spearman Correlation Coefficient. The analysis is done using SPSS for Mac version 24. This study was approved by The Ethics Committee of the Faculty of Medicine, Universitas Indonesia-Cipto Mangunkusumo Hospital No. KET-1027/UN2.F1/ETIK/PPM.00.02/2023.

RESULTS

Four hundred thirty patients were included in this study. They were all consulted in the oral medicine clinic with suspected Sjogren's syndrome from January 2021 to January 2023. The age range of the patients was 17 to 80. Most patients were female, 386 (90%) vs 43 (10%) male. The demographic data is shown in Table 1.

Table 1. Demographic data of subjects

Subject Characteristics	Mean (\pm SD)	N (%)
Gender		
Male		43 (10)
Female		386 (90)
Age	43.3 (\pm 14.1)	

The SXI-ID's median score was 12, within the range of 5 to 25. Among all subjects examined, 38.4% had a lower unstimulated salivary flow rate but had not yet fallen into hyposalivation criteria, and 49.3% had hyposalivation. Only a few subjects had normal or even above-normal unstimulated salivary flow rates. The median score for CODS was 3, which is considered mild oral mucosal dryness, and only a few had severe oral mucosal dryness, as shown in Table 2.

Table 2. The Characteristics of Oral Condition

Oral conditions	Median (min-max)	N (%)
SXI-ID	12 (5 - 25)	
USSFR (ml/min)	0.12 (0 - 1.08)	
Above Normal (>0.4 ml/min)		15 (3.5)
Normal (0.3 - 0.4 ml/min)		38 (8.8)
Below Normal (<0.3 - >0.1 ml/min)		165 (38.4)
Hyposalivation (\leq 0.1 ml/min)		212 (49.3)
CODS	3 (0 - 8)	
Not Dry (0)		26 (6)
Mild (1-3)		252 (58.6)
Moderate (4-6)		134 (31.2)
Severe (7-10)		18 (4.2)

Study participants' responses to SXI-ID were recorded in five Likert Scale as shown in Table 3.

Table 3. Responses in the score of SXI-Id

SXI-ID	Responses				
	Never	Hardly Ever	Occasionally	Frequently	Always
SXI 1	147	14	19	70	180
SXI 2	328	11	10	19	62
SXI 3	320	13	12	32	53
SXI 4	296	13	21	32	68
SXI 5	132	28	30	58	182

The distribution of the SXI, USSFR, and CODS data was not normal, according to the normality test. Thus, we continue to analyze the correlation using Spearman's correlation.

The SXI-Id version is negatively correlated with USSFR with a correlation coefficient of -0.185 ($p < 0.05$) and positively correlated with CODS with a correlation coefficient of 0.112 ($p < 0.05$). The correlation between SXI-Id and USSFR, as well as SXI-Id and CODS, are shown in Table 4.

Table 4. The correlation between SXI-Id and USSFR, SXI-Id and CODS

Variable	Correlation (r)	p-value
USSFR	-0.186	0.000
CODS	0.113	0.000

Unstimulated salivary flow rate negatively correlates with CODS with a correlation coefficient of -0.480 ($p < 0.05$). The correlation between USSFR and CODS is shown in Table 5.

Table 5. The correlation between USSFR and CODS

Variable	Correlation (r)	p-value
CODS	-0.480	0.000

DISCUSSION

Sjogren's syndrome is a systemic autoimmune disease which characterized by the inflammation and dysfunction of exocrine glands, with dry eyes and dry mouth as a hallmark called Sicca syndrome.^{8,9} SS predominantly affects women, with a 9:1 ratio to men, and our study was in accordance with previous data, with a women to men ratio of also 9:1.⁹ This high female-to-male ratio of SS was said to be common in Asia compared to other continents or races.⁹ SS is commonly diagnosed in the fifth decade of life, but somehow, the mean age of SS patients in this study was younger (43 years old) compared to other documented studies, which range from 51 to 62 years old.⁹

The salivary gland damage, as one of the hallmarks of pSS, progresses slowly over the years and is frequently overlooked, resulting in an average delay of diagnosis of pSS for seven years.³ The salivary gland dysfunction, which leads to hyposalivation, may hinder the eating and swallowing process, speaking, and taste perception and increase the risk of oral infection, eventually decreasing the patient's quality of life.¹⁰

There are two terms commonly used in dry mouth: xerostomia and salivary gland hypofunction (hyposalivation). Many papers use these two terms interchangeably when in fact, each term defines a different condition. Xerostomia is the term used to describe the sensation of dry mouth, a subjective complaint of dry mouth by patients.⁴ Since xerostomia is subjective, diagnosis of xerostomia can only be made by directly questioning the individual, using the Summated Xerostomia Inventory (SXI) to the Indonesian SXI-Id version.^{5,6} Hyposalivation is a condition of reduced salivary flow rate and can be measured by sialometry. The clinical dryness of the oral cavity was objectively measured using the clinical oral dryness score (CODS).⁷

SXI-ID was used to diagnose the presence of the perceived dry mouth, although it does not have a cut-off score to state the degree of the perceived dry mouth. The minimum score of the SXI-ID was

five, which is considered as no perceived dry mouth, and the maximum score was 25, which is considered the most severe perceived dry mouth. The median score of SXI-ID in this study was 12, which can be considered medium-perceived dry mouth. Among 430 subjects, 65.8% complained of dry mouth, and 69.3% had dry lips in the past month. Despite having a dry mouth, we found that most subjects had no eating and/or swallowing difficulties (74.42% and 68.84%, respectively). It is possible that the disease has not yet affected the stimulated salivary flow rate, but unfortunately, this study did not measure the stimulated salivary flow rate; thus, we do not have any evidence to prove this hypothesis.

Xerostomia does not always necessarily arise in hyposalivation; it can be found in patients with normal salivation.⁴ This study found only a few subjects with normal (8.8%) and above-normal (3.5%) unstimulated salivary flow rates. Almost half of the subjects (49.3%) suffered from hyposalivation, 38.4% of subjects had below normal unstimulated salivary flow rate, and the median unstimulated salivary flow rate of all subjects was 0.12 ml/minute, which is considered below normal. Although perceived dry mouth or xerostomia does not always arise in hyposalivation, subjects in this study mostly had xerostomia and hyposalivation. This is supported by the correlation analysis between SXI-Id and USSFR, as SXI negatively correlates with USSFR. However, this correlation is considered to be weak with a correlation coefficient of -0.185 ($p < 0.05$).

Hyposalivation logically will be followed by the dryness of oral mucosa. Thus, we analyze the correlation between unstimulated salivary flow rate and clinical oral dryness score. This study found that unstimulated salivary flow rate had a moderate negative correlation with CODS, with a correlation coefficient of -0.480 ($p < 0.05$). Although the majority of saliva is water (99%), it also contains protein called salivary pellicle.¹¹ This salivary protein adheres to oral mucosal surfaces and maintains an adsorbed salivary film.¹¹ Hyposalivation patients may suffer from the loss of saliva pellicle, resulting in poor surface hydration, reduced wettability and higher hydrophobicity of oral mucosal surfaces.¹¹

On the other hand, xerostomia (the perception of dry mouth) is not always associated with reductions in unstimulated salivary flow rate.^{12,13} One of the factors that influence xerostomia is thought to be the changes in salivary composition. The protein composition in the minor salivary gland is much higher than that of whole saliva, while the sialometry was performed by measuring the whole unstimulated saliva. Thus, unstimulated salivary flow rate alone does not explain xerostomia.¹³

The retrospective nature of this study constituted a drawback. Additionally, we cannot assess the inter-examiner reliability, and we did not examine the stimulated salivary flow rate or further analyze the salivary composition.

CONCLUSION

The hallmarks of Sjogren's symptoms are Sicca symptoms, which are dry eyes and dry mouth. Dry mouth can be subjective (xerostomia) and objective (hyposalivation); these terms are sometimes used interchangeably. Xerostomia is assessed using SXI-ID, which is not always followed by hyposalivation. The hyposalivation affects the wettability of oral mucosa, as it negatively correlates with oral mucosa dryness. Further study is needed to investigate the detailed correlation between xerostomia and hyposalivation and the factors affecting them.

REFERENCES

1. Stefanski AL, Tomiak C, Pleyer U, Dietrich T, Burmester GR, Dörner T. The Diagnosis and Treatment of Sjögren's Syndrome. *Dtsch Arztebl Int*. Published online May 19, 2017.
2. Vivino FB. Sjogren's syndrome: Clinical aspects. *Clin Immunol*. 2017;182:48-54.
3. Zandonella Callegher S, Giovannini I, Zenz S, et al. Sjögren syndrome: looking forward to the future. *Ther Adv Musculoskelet Dis*. 2022;14:1759720X2211002.
4. Baer AN, Walitt B. Sjögren Syndrome and Other Causes of Sicca in Older Adults. *Clin Geriatr Med*. 2017;33(1):87-103.
5. Hopcraft M, Tan C. Xerostomia: an update for clinicians: Xerostomia: an update for clinicians. *Aust Dent J*. 2010;55(3):238-244.

6. Wimardhani YS, Rahmayanti F, Maharani DA, Mayanti W, Thomson WM. The validity and reliability of the Indonesian version of the Summated Xerostomia Inventory. *Gerodontology*. 2021;38(1):82-86.
7. Jager DHJ, Bots CP, Forouzanfar T, Brand HS. Clinical oral dryness score: evaluation of a new screening method for oral dryness. *Odontology*. 2018;106(4):439-444.
8. Tan Z, Wang L, Li X. Composition and regulation of the immune microenvironment of salivary gland in Sjögren's syndrome. *Front Immunol*. 2022;13:967304.
9. Negrini S, Emmi G, Greco M, et al. Sjögren's syndrome: a systemic autoimmune disease. *Clin Exp Med*. 2022;22(1):9-25.
10. Ahmad M, Bhayat A, Zafar M, Al-Samadani K. The Impact of hyposalivation on quality of life (QoL) and oral health in the aging population of Al Madinah Al Munawwarah. *Int J Environ Res Public Health*. 2017;14(4):445.
11. Sarkar A, Andablo-Reyes E, Bryant M, Dowson D, Neville A. Lubrication of soft oral surfaces. *Curr Opin Colloid Interface Sci*. 2019;39:61-75.
12. Hijjaw O, Alawneh M, Ojjoh K, et al. Correlation between xerostomia index, clinical oral dryness scale, and ESSPRI with different hyposalivation tests. *Open Access Rheumatol Res Rev*. 2019;Volume 11:11-18.
13. Won SH, Kho HS, Kim YK, Chung SC, Lee SW. Analysis of residual saliva and minor salivary gland secretions. *Arch Oral Biol*. 2001;46(7):619-624.