

Original Article



Prevalence of xerostomia in patients with a history of COVID-19 infection: A cross-sectional study

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Abstract

Introduction: Dysfunction of salivary glands in patients with a history of coronavirus disease (COVID-19) infection are a prevalent clinical finding. However, the impact of these salivary disorders on the clinical experience of xerostomia has been less frequently investigated. This study aimed to investigate the prevalence of xerostomia in patients recovered from COVID-19.**Methods:** In this retrospective cross-sectional study, data were collected through interviews with 350 patients referred to the Department of Dentistry at Urmia from March to August 2023 who had a history of COVID-19 infection. Demographic information, previous systemic diseases, medication history, and history of COVID-19 infection were provided by patients through a checklist of preliminary descriptive information. The Persian version of the Fox et al questionnaire was used to assess xerostomia, and the Thomson et al questionnaire was used to assess the severity of xerostomia. The total scores were used to evaluate the severity of xerostomia. The final data were entered into SPSS version 29 for analysis.**Results:** Participants were 211 males and 139 females with a mean age of 32.19±12.14 years. The mean xerostomia score in patients based on the Thomson Index was 21.7±7.50 out of 44. No significant difference in xerostomia severity was observed between males and females ($P=0.278$), but with increasing age, the likelihood of xerostomia occurrence increased ($P=0.009$). The severity of xerostomia was significantly higher in recipients of the Sinopharm vaccine compared to recipients of the AstraZeneca vaccine ($P=0.028$). Still, no difference was observed between the frequency of vaccinations and the severity of xerostomia ($P=0.757$).**Conclusion:** Based on the results of this study, age and type of vaccine can have an impact on the severity of xerostomia after contracting COVID-19 infection. Therefore, the type of received vaccine and the age of the patient during vaccination and assessments of patients should be considered.

Introduction

COVID-19 is a viral infection similar to influenza caused by infection with the SARS-CoV-2 virus. COVID-19 can affect multiple organs upon systemic spread. and in cases of acute infection, severe cases may result in death within 2 weeks. The mortality rate and hospitalization due to this unprecedented viral infection were significant.¹⁻³

Infection spreads person-to-person through respiratory droplets resulting from sneezing or coughing. Initial symptoms in an infected individual include fever, dry cough, sore throat, shortness of breath, and muscle pain.³ Furthermore, other symptoms are observed following disease onset, such as loss of smell, and gastrointestinal disturbances like vomiting and constipation.^{4,5} Studies show that viral infection alters salivary glands and saliva content. Essential components of saliva, such as proteins and enzymes, and other substances play a crucial role

in flavor perception. Therefore, loss of taste sensation following COVID-19 infection appears to be linked to salivary gland infection.⁵

The mechanism of COVID-19 has been investigated in previous studies and referenced to various conditions such as interference with angiotensin-converting enzyme 2 (ACE2) inhibitors found in the lungs, blood vessels, brain, and salivary glands.⁶ Additionally, tissues presenting ACE2 receptors are not immune to viral infection invasion, and usually, symptoms of their involvement are observable. Xerostomia symptoms are the clinical manifestations of decreased or altered salivary secretion from the salivary glands associated with oral cavity functional disorders.⁷ Xerostomia is accompanied by a burning sensation in the mouth, taste disorders, loss of taste, and bad breath, all of which reduce oral health-related quality of life in the affected patient.^{5,8,9} In most cases, xerostomia is associated

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with systemic diseases such as diabetes, acquired immune deficiency, kidney failure, vitamin deficiencies, and some chronic and acute viral infections.^{10,11} Advancing age and the use of various medications, especially inhalable asthma medications, predispose individuals to xerostomia.¹²

COVID-19 infection, due to its viral nature, can cause long-lasting sequelae even after recovery, impacting the quality of life of patients. Patients may continue to experience xerostomia, dietary restrictions, and impaired speech function post-recovery, leading to decreased saliva flow and subsequent reduction in saliva's protective effects against decay, increasing the risk of developing more severe symptoms like progressive decay. Therefore, by identifying risk factors, supportive programs can be designed to improve xerostomia or identify patients at risk of deteriorating oral health due to persistent xerostomia, ultimately enhancing oral health-related quality of life in these patients even after recovery.

The prevalence of xerostomia resulting from COVID-19 infection in various studies conducted in different countries has been reported rates ranging from 40% to 60%.^{7,13-15} The severity of xerostomia was found to be associated with the severity of COVID-19 infection.¹⁶ On the other hand, the findings of the study by Saleem et al revealed that the prevalence of xerostomia was associated with decrease in the quality of life in patients with COVID-19 and has posed challenges in the treatment course of the viral infection.¹⁷ Factors such as stress resulting from infection have been found to influence the occurrence of xerostomia in patients.¹⁸ Therefore, it can be concluded that vaccination may have a separate impact on the severity of xerostomia. Considering the mentioned aspects, the present study aimed to investigate the risk factors of xerostomia in patients recovered from COVID-19.

Methods

A descriptive cross-sectional study was conducted on 350 patients referred to the Department of Dentistry at Urmia University of Medical Sciences in 2023, with a history of COVID-19 infection in the period from March to August 2023. After obtaining necessary approvals from the ethics and research committee of Urmia University of Medical Sciences, the researcher visited the dental clinic and interviewed all patients who provided informed consent to participate in the study. The sample size was determined based on the findings of Saleem et al¹⁷ and calculated using the Cochran formula.

The inclusion criteria for the study were a history of COVID-19 infection, age over 18 years, and informed consent to participate in the study. Also, patients with a history of systemic inflammatory diseases that could confound research results were excluded from the study. These diseases included diabetes mellitus, rheumatologic diseases such as rheumatoid arthritis, lupus, Sjogren's syndrome, untreated anemias, hepatitis, Parkinson's

disease, and severe neurological and psychiatric disorders such as major depression. A history of COVID-19 infection was confirmed by a previous positive COVID-19 RT-PCR test or self-reported hospitalization due to COVID-19. Demographic information, previous systemic disease history, medication history, history of getting COVID-19 infection, and history of vaccination were collected through a preliminary descriptive information checklist. To evaluate xerostomia, a shortened Persian version of the Fox et al questionnaire was used.¹⁹

The questionnaire consists of 3 binary questions (yes, no) and one Likert 3-point question (very little, very much, I do not understand). A response of "yes" to at least one of the first 3 main questions was considered as xerostomia. Moreover, for evaluating the severity of xerostomia, the Thomson et al questionnaire was used.²⁰ This questionnaire consists of 11 questions scored on a 5-point Likert scale (never, rarely, sometimes, often, always) from 1 to 5 (with 1 being the lowest score and 5 being the highest score) to each question, and the total scores were then used to assess xerostomia severity. The questions were scored from 4 to 0 in order of the mentioned options. The validity and reliability of the Fox et al questionnaire have been confirmed by considering the acceptable level of Cronbach's alpha and item correlation scale (0.4 and 0.6, respectively) as the desired level in previous research.¹⁵ The validity and reliability of the Thomson et al questionnaire was considered to be 0.71 based on previous studies according to Cronbach's alpha coefficient.

Statistical analysis of the data was performed using SPSS version 29. Parameters related to the Fox and Thomson questionnaire were reported in terms of mean and standard deviation. To compare the median and deviation from the mean of questionnaire scores by gender, the Mann-Whitney U test was used, and by vaccine type, the Kruskal-Wallis test and post hoc Mann-Whitney test were applied. The Spearman correlation coefficient was used to assess correlations between age, vaccine dosage, and questionnaire scores. A significance level of 0.05 was considered for statistical significance.

Results

A total of 350 patients participated in this study. The distribution of patient's demographic information is presented in [Table 1](#). The age range of the patients was 18 to 71 years with a mean of 32.19 ± 12.14 years. 211 participants (60.4%) were male and 139 participants (39.6%) were female. The most prevalent underlying condition among the participants was hypertension with a prevalence of 7.4%. Azithromycin (8.4%) was reported as the most commonly prescribed medication among the patients. 54% of the patients were vaccinated with AstraZeneca. Additionally, 51.4% of the patients had a history of receiving three doses of the vaccine.

Initially, the assessment of xerostomia was examined

using the Fox questionnaire. In the first question of this questionnaire, participants were asked about using fluids to help swallow dry foods, to which 121 individuals (34.6%) responded positively. Furthermore, 144 participants (41.1%) reported drinking water after consuming dry foods. Additionally, 73 participants (20.9%) reported feeling that their mouths generally felt dry after eating. Furthermore, 134 participants (34.3%) noted that their mouths became dry while eating after recovering from COVID-19. To investigate the correlation between the Thomson test scores and the age of the patients, the Spearman correlation coefficient was utilized. The results are presented in Table 2, indicating that as the age increases, the severity of xerostomia in patients significantly improves ($P=0.009$). Approximately 134 participants (34.3%) reported experiencing dryness in their mouths while eating after recovering from COVID-19.

The severity of the xerostomia was analyzed based on the gender of the patients using the Mann-Whitney test. The results of this test are presented in Table 3. The results indicated that there was no statistically significant

Table 1. Demographic information of the participants

Characteristics		Frequency (Percent)
Gender	Male	211 (60.4)
	Female	139 (39.6)
Chronic disease	Hypertension	26 (7.4)
	Pulmonary problems	7 (2)
	Cardiac insufficiency	6 (1.7)
Medication history	Azithromycin	29 (8.4)
	Dexamethasone	13 (3.7)
	Losartan	12 (3.4)
	Propranolol	11 (3.1)
Type of vaccine	AstraZeneca	189 (54)
	Sinopharm	107 (30.6)
	Barakat	54 (15.4)
Consumed medications	First	20 (5.4)
	Second	130 (37.1)
	Third	180 (51.4)
	Fourth	20 (5.4)

Table 2. Analyzing the correlation between the age of patients and the severity of xerostomia based on the Spearman test

	Number	Raito	P value
Age	350	0.146	0.009
Vaccine dosage	350	0.032	0.757

Table 3. Comparison of the severity of xerostomia in recovered COVID-19 patients based on gender

	Number	SD	Total	P value
Male	211	161.39	3503	0.288
Female	139	150.31	1836	

difference between the median and standard deviation of Thomson test scores between the two genders ($P=0.288$).

To investigate the correlation between the Thomson test scores and the age of the patients, the Spearman correlation coefficient was utilized. The results are presented in Table 2, indicating that as the age increases, the severity of xerostomia in patients significantly improves ($P=0.009$). On the other hand, the severity of xerostomia showed no significant association with the dosage of the administered vaccine.

To investigate the correlation among the type of vaccine used and the severity of xerostomia in recovered patients, the Kruskal-Wallis test was employed. The results of this test are presented in Table 4. The Kruskal-Wallis test results indicated a significant difference in the mean score of xerostomia severity among the three groups ($P=0.028$). Therefore, pairwise comparisons were conducted using the Mann-Whitney test. The post hoc Mann-Whitney test revealed that the median score of xerostomia severity in patients receiving the AstraZeneca vaccine was significantly lower compared to those receiving the Sinopharm vaccine ($P=0.018$). However, the severity of xerostomia in patients receiving the Barakat vaccine showed no significant difference when compared to either the AstraZeneca vaccine ($P=0.112$) or the Barakat vaccine ($P=0.088$).

Discussion

Recently, COVID-19 has been one of the greatest natural threats endangering human life. Despite the end of the COVID-19 pandemic, post-coronavirus manifestations in recovered patients continue to pose significant challenges to healthcare systems. Given that xerostomia has been identified as one of the persistent manifestations following recovery from COVID-19 infection, this study aimed to investigate the correlation between demographic parameters and the severity of xerostomia in recovered COVID-19 patients referred to a dental clinic.

The results of this study indicated that the severity of xerostomia increased in recovered patients with advancing age. On the other hand, the severity of xerostomia in recipients of the AstraZeneca vaccine was significantly lower in those who received Sinopharm vaccine. Moreover, our results showed that the severity of xerostomia had no significant association with gender or the dose of vaccine received by the patients.

In this study, the severity of xerostomia based on the Thomson index in recovered COVID-19 patients was 21.7 out of 44, indicating moderate severity. The study by Saleem et al demonstrated that the prevalence of xerostomia in recovered COVID-19 patients based on the XI index was 39.53% (17) which is consistent with our findings. The prevalence of xerostomia in Iraqi recovered patients was reported to be 50.9%, which was much higher compared to our finding.²¹ The prevalence of xerostomia in patients with active COVID-19 infection was reported

Table 4. Comparison of xerostomia intensity in patients receiving different vaccine formulations

Parameter	Number	SD (Mean ± SD)	Kruskal-Wallis P value	Mann-Whitney	Mann-Whitney P value	
AstraZeneca	189	15.71	0.028	AstraZeneca	Sinopharm	0.018
Sinopharm	107	26.75		AstraZeneca	Barakat	0.112
Barakat	54	21.50		Sinopharm	Barakat	0.088

to be between 35% and 50%^{15,22} which was similar to our results, indicating no difference in xerostomia between recovered patients and patients with active infection. Overall, it can be concluded that xerostomia is a persistent clinical finding in patients recovering from COVID-19.

Previous studies have shown that xerostomia manifests itself in the early stages of COVID-19, and xerostomia cannot be used as an indicator for diagnosing COVID-19.^{15,19} On the other hand, xerostomia is also associated with various other viral infections,²³ and it has also been reported that SARS-CoV-2 involves the salivary gland epithelial cells of primates.²⁴ Additionally, some risk factors for xerostomia and COVID-19 are shared,^{1,7,23} which disturbs the direct correlation between xerostomia and viral infection. For example, psychological stress and depression due to quarantine and COVID-19 infection during active viral infection can create a basis for the persistence of xerostomia in the recovered individual in the long term.²⁵

The results of the present study showed that a significant difference in the prevalence of xerostomia in male and female patients recovered from COVID-19 was not observed, which is consistent with the findings of Al-Magsoosi et al.²¹ This finding contradicts the results of the studies by Saleem et al¹⁷ and Biadsee et al,²⁶ which reported a higher prevalence of xerostomia in female recovered patients compared to males.

The results of microscopic examinations have shown that the viroid of COVID-19 uses ACE2 receptors to enter cells and activate their genome for replication.²⁷ The receptor for this enzyme is highly expressed on the surface of epithelial cells of salivary glands, and therefore inhibiting it can have a long-term significant impact on salivary gland atrophy.²⁸ The identification of COVID-19 viral particles in the saliva of infected patients confirms this finding.²⁹ Furthermore, studies on patients hospitalized in intensive care units 48 hours after admission have shown that the viral particle density of COVID-19 in saliva samples was higher than in their blood samples.³⁰ It has also been reported that the penetration of viral particles into the salivary glands sets the stage for salivary gland atrophy.¹⁴ Studies on primates have also shown that COVID-19 viral particles have been observed in the salivary glands of patients with high density before the onset of pulmonary lesions.⁸ The neurotropic role of the COVID-19 virus has also been mentioned as one of the possible hypotheses for its role in reducing salivary gland function or causing xerostomia in infected patients, and this hypothesis is further strengthened by the persistence

of this sensation.²² Additionally, the inflammatory process that aids in viral infection clearance can itself lead to reduced saliva secretion.¹⁶ Some case reports have also shown that salivary gland swelling in patients with COVID-19 can lead to obstruction of Stensen's duct and decreased saliva secretion.²² Furthermore, nasal congestion due to COVID-19 infection can lead to mouth breathing and xerostomia in patients.⁴ Psychological factors and stress are also not effective in this context.²²

Limitations and suggestion

This study, despite its valuable results, also had some limitations. Various factors such as stress, anxiety, caffeine consumption, alcohol and tobacco use, and carbonated beverages, which hold a constant place in people's daily lives, are among the risk factors for xerostomia that were not examined in the current study. Additionally, the sample size was low, and many patients did not have the possibility to participate in the study due to lack of consent. Most importantly, an arbitrary criterion and questionnaire were used in this study to assess xerostomia in patients, which is not a precise measure. It is recommended that future studies focus on quantitative and qualitative analyses of saliva and use more precise methods to investigate the severity of xerostomia in patients and related risk factors.

Longitudinal studies with extended follow-up periods would provide valuable insights into the persistence and progression of xerostomia symptoms over time. Additionally, including a well-matched control group of individuals who have not experienced COVID-19 infection would allow for a direct comparison of xerostomia prevalence and severity between those with and without a history of COVID-19, enabling a more comprehensive understanding of the impact of the virus on salivary gland function.

Conclusion

In conclude, according to the findings of this study, factors such as age and vaccine type may serve as stable risk factors for xerostomia in recovered COVID-19 patients in Urmia city. Therefore, it is recommended that supportive programs for improving xerostomia, such as routine examinations and prescription of xerostomia-relieving medications, be implemented in elderly COVID-19-recovered patients who have received the Sinopharm vaccine, targeting a broad spectrum of the Iranian population, to enhance the quality of life associated with xerostomia in these patients.

Study Highlights

What is current knowledge?

- Previous research has established that salivary gland disorders are common in individuals with a history of COVID-19 infection. However, the impact of these salivary disorders on the prevalence and severity of xerostomia in these individuals has been less investigated. Xerostomia is a condition characterized by reduced saliva production, which can lead to discomfort and various oral health problems.

What is new here?

- This study contributes to the existing knowledge by investigating the prevalence and severity of xerostomia specifically in patients who have recovered from COVID-19. The study found that the severity of xerostomia was influenced by the age of the patient at the time of vaccination and the type of COVID-19 vaccine received. Increasing age was associated with a higher likelihood of experiencing xerostomia, while recipients of the Sinopharm vaccine exhibited a greater severity of xerostomia compared to recipients of the AstraZeneca vaccine. These findings highlight the potential impact of age and vaccine type on post-COVID-19 xerostomia, suggesting that considering these factors could be important inpatient screening and management.
- Overall, this study adds to our understanding of the clinical experience of xerostomia in individuals recovering from COVID-19, emphasizing the relevance of age and vaccine type in assessing the severity of this condition.

Authors' Contribution

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Competing Interests

None.

Consent for Publication

Not applicable.

Data Availability Statement

The dataset analyzed in the current study is available from the corresponding author upon a reasonable request.

Ethical Approval

The study process was reviewed and approved by the Ethics Committee of Urmia University of Medical Sciences, in accordance with the Declaration of Helsinki (Ethics Code: IR.UMSU.REC.1402.122).

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