

# Research Paper: Xerostomia in Schizophrenia and Bipolar Patients: Is There Any Relation?



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## ABSTRACT

### Article info

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**Introduction:** Psychiatric disorders such as bipolar disorder and schizophrenia cause vascular, neurological, and neurobiological changes. On other hand, salivary glands are influenced by changes in the autonomic nervous system. Therefore, this hypothesis was formed that psychiatric disorders can affect salivary glands through neurological pathways. This study aimed to evaluate if schizophrenia and bipolar disorder can cause xerostomia and lip dryness in patients who are not using psychiatric drugs.

**Materials and Methods:** This study included 54 bipolar and 50 schizophrenia whose disorder was confirmed, and the control group included 60 healthy individuals whose mental health was evaluated through GHQ21 questionnaire and a psychiatrist. The FOX questionnaire was also completed to diagnose Xerostomia and lip dryness. Data were analyzed by SPSS version 22 using Chi-square, t-independent, logistic regression, ANOVA, Tukey test, Kruskal–Wallis, Mann–Whitney and Spearman correlation.

**Results:** In this study, xerostomia was found in the bipolar group (57/40%), schizophrenia group (66%) and control group (18/33%). Xerostomia and dry lips were significantly higher in psychiatric patients than in the control group, but there was no significant difference between bipolar patients and schizophrenia patients. In this study, there was no significant relationship between Xerostomia and age and gender.

**Conclusion:** Neurological changes are factors that affect salivary secretions causing Xerostomia. Dentists must always consider psychological factors as a causative agent of Xerostomia.

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## Introduction

One of the objective or subjective complaint with changes in the quality or quantity of saliva is called Xerostomia, which can be caused by salivary and non-salivary factors.(1,2) Salivary gland dysfunction is the most common cause of Xerostomia-related complaints.(1) Non-salivary causes include dehydration, central perceptual changes and mental disorders.(2) The following factors can cause Xerostomia; nutritional factors (such as caffeine and alcohol), psychological factors (such as emotional reactions and stress), neurogenic factors, systemic factors (such as diabetes mellitus, Sjögren syndrome, anemia, vitamins' deficiency, head and neck radiotherapy), local factors (such as mastication reduction, smoking, salivary duct obstruction and aplasia or hypoplasia of salivary gland) and the medicines (such as Atropine, Antihypertensive drugs, Antidepressants).(3-9)

20% of the world's population and about 30% of women have Xerostomia.(3) 80% of medicines are potential to cause Xerostomia.(3,10) Xerostomia can cause speech disorder (aphasia), sense of taste disorder, swallowing disorder, malnutrition, increasing the risk of tooth decay, gingivitis, oral candidiasis and the intolerance of removable dentures.(5-8)

Xerostomia incidence in the mental disorders is because of the neural, physiological, biological and chemical changes; since the salivary glands are biologically regulated by the autonomic nervous system, the salivary glands are affected by the psychiatric disorders in several ways.(10-14) It is believed that in these diseases, changes in the blood flow and metabolism will simulate the lateral nucleus and paraventricular by the amygdala and consequently the autonomic system is simulated and the plasma cortisol is increased, which will result the changes in the salivary secretion and the decrease of its flow.(10,15) The neuropsychiatric disorders lead to endocrine changes like increasing the activity of the hypothalamic-pituitary-adrenal axis (HPA axis), which also increase the level of cortisol and as it was noted before the Xerostomia will develop.(15-16) Abnormal activity

of enzymes such as hemoglobin-oxygen affinity (p50) enzyme is also associated with neuropsychiatric disorders.(15) Molecular genetic studies show that the abnormal p50 will bind to the genes coding the cholinergic nicotinic receptors and will cause changes in the cholinergic neurotransmitters and then the salivary flow rate will change.(10)

Bipolar disorder with an incidence of 1% per year is along with severe and drastic mood changes between depression and mania and the increase of the activity of the HPA axis, the abnormal regulation between pre-frontal and limbic cortex regions especially amygdala the dopamine change.(17,18) Its incidence is the same in men and women.(19) Mania periods are more common in men and the depression periods are more common in women.(20) Researchers believe that the bipolar disorders have a genetic origin.(21) Factors increasing the risk of bipolar disorder incidence are having first-degree relatives with this disorder, periods of extreme stress and drug or alcohol abuse and the death of the loved ones. Factors like anxiety disorder, PTSD (Posttraumatic stress disorder), ADHD (Attention-deficit hyperactivity disorder) and addiction to drugs and alcohol will worsen it.(22)

Schizophrenia disorder is a mental disorder that has thought processes disturbance, poor emotional responsiveness, abnormal social behavior and the inability to understand the reality and it is along with changes in the frontal lobe, the hippocampus, the amygdala and the temporal lobe and the brain volume decrease.(23) Schizophrenia is often more common in men and has a worse prognosis in women and about 90% of schizophrenia (analysand) patients are between 15-50 years old.(24) Genetic and environmental factors (such as social isolation and immigration, racism, stressful environment, family problems/disorders and unemployment) can affect schizophrenia incidence.(25)

Veerabhadrappe et al. have done a cross-sectional case-control study and concluded that the emotional changes will affect the saliva secretion and cause the Xerostomia in anxious,

depressed, bipolar, and schizophrenic individuals.(16) In a study conducted by Kaur et al. examining the Xerostomia in adolescent psychiatric patients, they have found that the incidence rate of Xerostomia is 60% and has no significant relation with age and sex. (26) In 2011, Aditya et al. have studied the Xerostomia incidence and the burning sensation in psychiatric patients and have concluded that the Xerostomia is more common in these patients and they have recommended that the standard assessment of patients' psychological status be added to the examination protocol.(15)

Since few studies have been performed about the effect of the neural processes in causing Xerostomia in the psychiatric patients, this study has been conducted to determining the relationship between bipolar disorder and schizophrenia with Xerostomia in the patients before being treated by neural and psychiatric medicines. Our study aimed to identify the direct role of these diseases in causing Xerostomia.

## Materials and Methods

This observational cross-sectional analytical study with the aim of determining the relationship between bipolar disorder and schizophrenia with Xerostomia have been conducted on 164 people (54 bipolar patients, 50 schizophrenia patients, and 60 healthy people). Considering the statistical power of 80%, error level of 0.05 and variance of 86.49 and 70.56 and  $d = 6.2$ , the sample size was calculated at least 45.30, which was considered 46.

104 patients with bipolar disorder and Schizophrenia who visited the hospital and were diagnosed using their medical records or with a psychiatrist's examination were put on this study after filling a written testimonial. The inclusion criteria were patients' will to participate in the study, having bipolar disorder or Schizophrenia, and no history of using psychological drugs. Patient were excluded if they had chronic systemic disease (such as cancer and rheumatology diseases), had histo-

ry of neck radiotherapy, used drugs that cause xerostomia (such as blood pressure related drugs, psychological drugs and diabetes related drugs), smoked and used alcohol. The control group people were those who visited the International Campus Dental Clinic. They completed GHQ28 (General Health Questionnaire) whose validity and reliability have been confirmed, their scores were less than 22 and then they had mental health. In terms of age, gender and the occurrence of other systemic diseases, both control and patient groups were matched.

GHQ28 Questionnaire has 5 scales of physical symptoms, anxiety symptoms, sleep disorders, social function and depression symptoms. (27) This is a multiple-choice questionnaire; each question has four options. In order to sum up the scores we have added the following scores to each option, respectively: 1:0, 2:1, 3:2 and 4:3. On each scale, the score higher than 6 or a total score higher than 22 indicated the symptoms. Patients' characteristics include age, gender, medicine use and the associated underlying diseases were recorded. FOX Standard Questionnaire was used to examine the patients' sense of mouth dryness; its validity and reliability have been confirmed. Each patient who positively answered at least to 3 items out of 10 (Score 3-10) are considered a patient with Xerostomia. Lip dryness was evaluated by asking the patient and by observing chaps in the lib area, especially the angular-cheilitis.

SPSS software version 22 (SPSS Inc., Chicago, IL, USA) was used to analyze the data. Chi-square, t-independent, logistic regression, ANOVA, Tukey test, Kruskal-Wallis, Mann-Whitney and Spearman correlation were used in order to evaluate the relevance and compare the groups on the basis individuals score from the FOX Questionnaire (0-10) and compare the mean of groups.

## Results

In this study, 54 bipolar patients, 50 schizophrenia patients and 60 patients in control group were included. The data

distribution is presented in Table 1.

Table 1: Age, Gender and Group Size of Bipolar, Schizophrenia and Control Group

Study groups	Mean of Age $\pm$ SD	Gender Distribution: Percent (Number)		Group Size (Number)
		Female	Male	
Bipolar Group	30.0 $\pm$ 0.97	55.6% (30)	44.4% (24)	54
Schizophrenia Group	32.7 $\pm$ 1	48.0% (24)	52.0% (26)	50
Control Group	31.0 $\pm$ 0.9	40.0% (24)	60.0% (36)	60

Gender and age had no statistical relation with mental status of participants. (p value= 0.25 and p value= 0.15 respectively)

57.4% of bipolar patients, 66.0% of schizophrenia patients and 18.3% of control patients were found to have Xerostomia. Prevalence of Xerostomia was significantly higher in bipolar and schizophrenia patients compared to control

group. (p  $\leq$  0.001) However the difference between bipolar and schizophrenia patients was not statistically significant. (p = 0.26)

38.8% of bipolar patients, 44.0% of schizophrenia patients and 25.0% of control patients reported to have lip dryness. The relation of lip dryness and Xerostomia was significant. (p  $\leq$  0.001) (Table 2) FOX Standard Questionnaire was used to assess Xerostomia. (Table 3)

Table 2: Relation of Lip Dryness and Xerostomia in Bipolar, Schizophrenia and Control Group

Study groups		Lip Dryness: Percent (Number)	
		Yes	No
Bipolar Group	With xerostomia	61.3% (19)	38.7% (12)
	Without xerostomia	8.7% (2)	91.3% (21)
	Total	38.8% (21)	61.1% (33)
Schizophrenia Group	With xerostomia	60.0% (20)	40% (13)
	Without xerostomia	11.8% (2)	88.2% (15)
	Total	44.0% (22)	56.0% (28)
Control Group	With xerostomia	100% (11)	0% (0)
	Without xerostomia	8.2% (4)	91.8% (45)
	Total	25.0% (15)	75.0% (45)
Total	With xerostomia	66.6% (50)	33.3% (25)
	Without xerostomia	8.9% (8)	91.1% (81)
	Total	35.4% (58)	64.6% (106)

Table 3: Participants' Answer to FOX Questionnaire in Bipolar, Schizophrenia and Control Group

Questions of FOX questionnaire	Study group	Yes	No	P value
Question 1: Do you experience mouth dryness during meals?	Bipolar	31.5%	68.5%	0.001
	Schizophrenia	34%	66%	
	Control	6.7%	93.3%	
Question 2: Do you experience problems with swallowing foods?	Bipolar	18.5%	81.5%	0.016
	Schizophrenia	20%	80%	
	Control	3.3%	96.7%	
Question 3: Do you drink fluids while swallowing dry foods?	Bipolar	40.7%	59.3%	0.612
	Schizophrenia	46%	54%	
	Control	36.7%	63.3%	
Question 4: Do you feel that your saliva secretion has decreased?	Bipolar	55.6%	44.4%	0.001
	Schizophrenia	62%	38%	
	Control	18.3%	81.7%	
Question 5: Do you experience mouth dryness during the night or upon waking up?	Bipolar	40.7%	59.3%	0.294
	Schizophrenia	48%	52%	
	Control	33.3%	66.7%	
Question 6: Do you experience mouth dryness during vacation?	Bipolar	14.8%	85.2%	0.555
	Schizophrenia	8.0%	92.0%	
	Control	11.7%	88.3%	
Question 7: Do you use chewing gum and chocolate on a daily basis to eliminate a feeling of mouth dryness?	Bipolar	24.1%	75.9%	0.073
	Schizophrenia	18%	82%	
	Control	8.3%	91.7%	
Question 8: Do you keep a glass of water next to your bed?	Bipolar	25.9%	74.1%	0.015
	Schizophrenia	46%	54%	
	Control	21.7%	78.3%	



## Discussion

This study evaluated the relation of xerostomia with bipolar and schizophrenia disorders. Since there are various tools to measure the mouth dryness (Xerostomia) in different studies, therefore, a variety of values have been reported for its occurrence; so that in a review study of 13 articles in Scandinavia, the Xerostomia occurrence was reported about 0.9 to 64.8% and in most of these articles, Xerostomia was diagnosed by questionnaire.(28,29)

In the current study, Xerostomia was significantly more frequent in healthy participants compared to participants with bipolar disorder and schizophrenic patients. The results confirm that biological and chemical factors in neuropsychiatric patients can cause Xerostomia. In agreement to our study, Veerabhadrapa et al. reported that emotional changes affected the saliva secretion and caused Xerostomia.(16)

There was no significant relationship between age and Xerostomia in the current study. The results were in line with the results of Kaur et al. and Matear et al.(26,30) However, Field et al., Pajukoski et al., Rad et al. and some studies indicated that aging has a significant clinical effect on the secretion and flow of saliva.(16-19,31-33) Recent studies have stated that Xerostomia increases in elderly people because of systemic diseases and the side effects of their medicines, not simply due to aging and they have concluded that age has no direct effect on xerostomia.(26-30)

In the present study, there was no significant difference between females and males in terms of xerostomia, which is similar to the results of Kaur et al., Matear et al., and Gerdin et al. (26,30,34) But Ikebe et al., Rad et al. and Farsi suggested that Xerostomia was more frequent in males.(33,35,36) On contrary, Field et al., Nederfors et al., Hopcraft and Veerabhadrapa et al. claimed that the Xerostomia was more common in females.(16,28,31,37) This controversy can be due to different target population and the method to examining Xerostomia as well as the genetic, social and cultural differences in the studies.

Lip dryness is one of the symptoms of the Xerostomia.(38-39) During the clinical exam-

ination of the participants in this study, the lip dryness was observed in 44% of schizophrenic patients, 38.9% in bipolar patients, 25% in the control group and 35.4% in total. There is a significant relationship between the Xerostomia and lip dryness so that we can say most people with the Xerostomia had also the lip dryness. The results of this study are in agreement with the results of Berti-Couto et al. and Farsi.(39,40)

The first three questions out of ten questions of FOX questionnaire, assessed the salivary function (1. the sense of Xerostomia when eating, 2. difficulty in swallowing, 3. need to drink water when eating dry food). In the present study, the salivary dysfunction in schizophrenic and bipolar groups is significantly more than the healthy group. However, there is no significant difference in terms of salivary dysfunction between the two schizophrenic and bipolar groups.

In this study, most patients in bipolar and schizophrenic groups reported that they felt an decrement in their saliva which was in accordance to the results of Kaur et al. and Sreebny et al.(26,41) In many cases, the stimulated and un-stimulated salivary flow is normal, but they report Xerostomia, which can be due to changes in the nervous system and the autonomy stimulation or endocrine changes, etc. Since the sensitivity of this question is high in the diagnosis of the Xerostomia (93%), it is used in many scientific researches as an initial screening for patients to examine Xerostomia. This question can diagnose Xerostomia even when there are no acute symptoms and no obvious sign of salivary dysfunction (specificity = 68%). A negative answer to this question can make the therapist sure that the person has no salivary dysfunction (negative predictive value =98%).(10)

We have asked the participants of the present study that, do they use chocolate and gum to help them relieve their Xerostomia (question number 7); 24.07% of bipolar patients, 18% of schizophrenia and 8.3% of the control group and totally 16.4% answered “yes”; this is less than the results of Cho et al.(42) (37%). This can be due to that most of the patients prefer drinking water more than using gum and chocolate to relieve their Xerostomia, which is

probably because of their worries and concerns about tooth decay.(42)

Waking up feeling thirsty is significantly related to the un-simulated salivary flow rate and can affect individual's life quality.(43) For this reason, negative answer to this question is one of the effectiveness criteria to treat Xerostomia.(43) The sum of this question and the fourth question (Do you feel that your saliva secretion has decreased?) will increase the diagnostic ability of Xerostomia up to 94% and will indirectly show salivary dysfunction. In the present study, there is a significant relationship between the studied groups and the answers to question number 8 ( $p < 0.05$ ), so that the positive answer to this question in the schizophrenia group (46%) is significantly more than healthy (21.7%) and bipolar (25.9%) groups and this is less than the results of Cho et al. due to different sample population and inclusion and exclusion criteria.(42)

Xerostomia can affect life quality by dramatic dysgeusia (food taste impairment). In the present study, dysgeusia was observed in 16.6% of bipolar patients, 30% of schizophrenia and 5% of the control group, which is not consistent with the result of studies by Suh Ki et al. and Cho et al.(42,43) Suh Ki evaluated salivary flow rate and clinical symptoms of Xerostomia. They reported dysgeusia to be 4.65% in their participants. Cho et al. evaluated Xerostomia in different medicine-treated groups, radiotherapy groups and systemic-disease groups; the dysgeusia was observed to be 58%.(42) These divergences can be due to different sample population, the side-effects of medicines, systemic diseases, genetic and the method of measurement.

Many studies have shown that the burning sensation of the tongue is one of the common complications of Xerostomia. (44) Although the burning of the tongue can occur for many reasons, but the most likely cause is Xerostomia. 6.09% of the participants in the present study reported the burning of the tongue, 7.4% of them are bipolar, 10% schizophrenic and 1.7% healthy groups. This is less than the results of Aditya et al. (9.5%), which can be due to differences in the sample population, study method,

climatic and cultural factors as well as eating habits.(15,45)

## Conclusion

The Xerostomia in the present study was significantly more in bipolar and schizophrenic patients than the control group, but there was no difference between bipolar and schizophrenic patients. Swallowing difficulties, dysgeusia, burning sensation in the mouth and the need to drink water during the night were more in schizophrenic and bipolar patients than in healthy controls. As a result, the mental illness like bipolar disorders and schizophrenia may be considered as a cause of Xerostomia, but there was no significant difference between Xerostomia, gender and age.

It can be also seen that the dentists should always consider the psychological factors as a cause of Xerostomia; therefore, a standard evaluation of the psychological status of patients who complaint of Xerostomia, dysgeusia, burning sensation in the mouth, the need to drink water during the night as well as during food swallowing must be added to the patients' oral examination protocol.

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### Authors' contributions

**Maryam Basirat:** Conceptualization, Methodology, Writing - Review & Editing **Robabe Soleimani:** Resources, Investigation, Visualization **Dina Maleki:** Methodology, Visualization **Elahe Alipour:** Writing - Original Draft, Data Curation **Sattar Akbari:** Funding acquisition, Project administration, Supervision

### Conflict of Interests

The authors declare no conflict of interest.

### Ethical declarations

Not applicable

### Financial support

None

### Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request

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