Polish Annals of Medicine

Journal homepage: https://www.paom.pl

Research Paper

Risk factors and serum parameters associated with xerostomia in cardiac patients – a case-control study

Maryam Basirat[1], *Seyedeh Fatemeh Mirrazeghi*[2], *Faezeh Soleimani*[3], *Fereshteh Najar Karimi*[4]

[1] *Dental Sciences Research Center, Medical Education Research Center, Department of Oral and Maxillofaicial Medicine, Faculty of Dentistry, Guilan University of Medical Sciences, Rasht, Iran*

[2] *Cardiovascular Disease Research Center, Department of Cardiology, Heshmat Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran*

[3] *General dentist, Faculty of Dentistry, Guilan University of Medical Sciences, Rasht, Iran*

[4] *Department of Oral and Maxillofacial Medicine, Faculty of Dentistry, Alborz University of Medical Sciences, Karaj, Iran*

Article info

Article history
Received: April 14, 2023
Accepted: November 11, 2023
Available online: December 1, 2023

Keywords
Risk factors
Serum
Xerostomia
Heart diseases

Doi
https://doi.org/10.29089/paom/175108

Abstract

Introduction: Xerostomia is not a disease in itself but is caused by a change in the amount or composition of saliva or both. Some systemic diseases and the use of some medicines cause this complaint.

Aim: Considering the high prevalence of cardiac diseases, the present study aimed to examine risk factors and serum parameters associated with xerostomia among hospitalized cardiac patients.

Material and methods: In this case-control study, 369 hospitalized cardiac patients were divided into two groups (with and without xerostomia) using a valid FOX questionnaire. Demographic information and laboratory analysis results were extracted from the subjects' medical records. Finally, data were analyzed using SPSS v. 24 software at a significance level of 0.05.

Results and discussion: According to the findings, 187 (50.7%) patients were suffering from xerostomia, whose prevalence was significantly higher in patients with a history of hypertension ($P = 0.017$) and thrombocytosis ($P = 0.023$). However, no significant relationship was observed between xerostomia and other serum parameters.

Conclusions: Xerostomia is associated with a history of hypertension and the use of certain medications, such as nitroglycerin. Other serum parameters seem to be unrelated to xerostomia, except thrombocytosis. Therefore, it is recommended to check the quantity and quality of saliva to evaluate the presence of hyposalivation along with xerostomia more accurately.

Corresponding author: Fereshteh Najar Karimi; Department of Oral and Maxillofacial Medicine, Faculty of Dentistry, Alborz University of Medical Sciences, Shahid katouiezade st., Golshahr avenue, karaj, Iran.
Postal code: 3198684868. Tel.: +26 3350 0080.
E-mail address: mastane_fk91@yahoo.com

1. INTRODUCTION

Hyposalivation and xerostomia are common oral problems, especially in the elderly, as an objective finding and a subjective perception, respectively.[1,2]

Xerostomia, as an unpleasant sensation in the mouth and throat, can only be assessed through direct questioning of patients. Moreover, it can significantly reduce the patient's quality of life and lead to symptoms such as bad breath, burning sensation in the mouth, difficulty in speaking and swallowing, and changes in the sense of taste.[1] Xerostomia is not necessarily always associated with an actual decrease in saliva flow rate, but in cases where it coincides, it can lead to an increase in various oral and dental diseases, including dental caries and oral infections. This complication may occur in elderly patients for various reasons, including depression, malnutrition, some chronic diseases, and the use of multiple medications.[1,2]

Cardiovascular diseases are one of the most important causes of death and disability worldwide, especially in Iran. Today, as a result of modern treatment methods, which have led to the improvement of life expectancy and survival rate, the number of people suffering from chronic diseases with physical limitations and treatment complications has increased.[3,4] Routine tests such as blood glucose (especially fast blood sugar – FBS), lipid profile (cholesterol, triglyceride, LDL, HDL), and kidney function (blood urea nitrogen – BUN , creatinine – Cr , and urinalysis) are used for screening and follow-up of cardiac patients.[5,6] Few studies have been conducted on the predisposing factors of xerostomia in cardiac patients, according to which this complication has been reported as a bothersome problem in these patients, which is probably caused by the use of multiple medicines, including some antihypertensive and diuretic medicines.[7,8]

2. AIM

Considering that changes in the level of serum parameters can affect the quality and quantity of saliva in patients, especially cardiac patients, this study aimed to determine the possibility of risk factors and serum parameters associated with xerostomia in hospitalized cardiac patients.

3. MATERIAL AND METHODS

This case-control study was conducted on a total of 369 cardiac patients admitted to Heshmat Hospital in Rasht, Iran. All hospitalized cardiac patients (any age and gender) were included in the study.

Patients with pregnancy, immune system deficiency, AIDS, Sjogren's syndrome, history of salivary gland surgery, head and neck radiotherapy and chemotherapy within the last month were excluded from the study. The reason for choosing cardiac patients is the high prevalence of xerostomia among these patients. On the other hand, since the results of serum analyses had been recorded in their medical records, there was no need to impose costs on researchers and patients. Among the limitations of this research was that if a cardiac patient was not suffering from other known systemic diseases, the serum parameters related to that systemic disease were not recorded in their medical record, and it was not possible to check the relevant parameters.

Demographic information of patients, including age, gender, history of hospitalization, medications, suffering from other systemic diseases, as well as the level of serum parameters including Na, BUN, K, LDL, HDL, TG, cholesterol, serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), FBS, white blood count (WBC), Hb, platelet count (PLT) and Cr were extracted from the subjects' medical records.

The diagnosis of cardiac diseases was made based on medical records confirmed by a cardiologist.

After completing the standard questionnaire for xerostomia (FOX questionnaire) by the interviewer through interviews with the patients, they were divided into two groups based on the presence/absence of xerostomia. Patients who answered positively to at least 3 questions were considered to have xerostomia, and those who answered positively to less than 3 questions were considered to have no xerostomia.[9] The general results were reported descriptively. Frequency and percentage were used to describe qualitative data, and mean and standard deviation were used for quantitative data. Based on the variable type, all data were analyzed using χ^2, ANOVA and Kruskal–Wallis tests with SPSS v. 24 software at a significance level of 0.05 ($P \leq 0.05$).

4. RESULTS

A total of 369 hospitalized cardiac patients participated in the study among whom 187 (50.7%; mean age 62.36 ± 11.59 years) including 94 (46.8%) men and 93 (55.4%) women, had xerostomia and 182 (49.3%; mean age 61.20 ± 12.23 years) including 107 (53.2%) men and 75 (44.6%) women did not have xerostomia. The χ^2 test results showed that the distribution of age ($P = 0.350$) and gender ($P = 0.100$) were not significantly different between the two groups.

According to the findings, 50.7% of hospitalized cardiac patients (187 of 369) complained of xerostomia. As shown in Table 1, the investigated serum parameters, except the number of platelets, were not significantly different between the two groups, while the number of platelets in the xerostomia group was significantly higher than the control group ($P = 0.023$).

In addition, no significant relationship was observed between diabetes, hypertension, hyperlipidemia, kidney, and gastrointestinal and thyroid diseases with xerostomia ($P > 0.05$). However, the number of subjects with a history of hypertension in the case group was significantly higher than the control group ($P = 0.017$; Table 2).

As shown in Figure 1, there was no significant relationship between the type of treatment received by hospitalized cardiac patients and the incidence of xerostomia ($P = 0.434$).

Table 1. Comparison of the serum parameters averages in two study groups (with and without xerostomia).

Variables	With X		Without X		Total	Laboratory measure	Test statistic*	*P*
	N	laboratory, mean ± SD	*N*	laboratory, mean ± SD	*N*			
Na^+	162	136.89 ± 3.40	161	136.84 ± 3.42	323	mg/dL	0.13	0.895
K^+	170	4.20 ± 0.53	164	4.31 ± 0.74	334	mg/dL	–1.48	0.139
BUN	168	19.22 ± 9.27	166	18.87 ± 9.81	334	mg/dL	0.32	0.743
Cr	168	122 ± 0.47	160	127 ± 0.87	328	mg/dL	–0.65	0.514
LDL	103	83.47 ± 33.69	111	88.91 ± 37.35	214	mg/dL	–1.11	0.267
HDL	104	40.78 ± 15.85	111	38.99 ± 12.02	215	mg/dL	0.93	0.350
TG	90	175.30 ± 95.24	102	158.65 ± 82.07	201	mg/dL	1.30	0.195
CHol	112	154.58 ± 41.76	129	159.86 ± 50.60	241	mg/dl	–0.87	0.382
FBS	157	132.91 ± 69.83	154	126.51 ± 51.55	311	mg/dl	0.90	0.366
SGOT	111	34.64 ± 46.86	126	45.11 ± 60.62	237	IU/L	–1.47	0.142
SGPT	113	27.91 ± 22.07	127	30.83 ± 25.54	240	IU/L	–0.94	0.347
Hb	110	11.77 ± 1.89	134	12.1 ± 2.2	244	mg/dL	0.52	0.063
Plt	149	222523.48 ± 78489.16	145	214641.37 ± 68015.79	294	count/mm^3	0.91	0.023
WBC	143	9594.87 ± 10883.29	149	9032.88 ± 5063.28	292	count/mm^3	0.49	0.330

Comments: * Independent samples test; X – xerostomia; Na^+ – sodium, K^+ – potassium, BUN – blood urea nitrogen, Cr – creatinine, LDL – low-density lipoprotein, CHol – cholesterol, TG – triglyceride, HDL – high density lipoprotein cholesterol, FBS – fasting blood sugar, SGOT – serum glutamic-oxaloacetic transaminase, SGPT – serum glutamic-pyruvic transaminase, Hb – hemoglobin, Plt – platelet count, WBC – white blood count.

Table 2. Comparison of the number of heart patients with other systemic diseases (diabetes and …) in the two study groups.

Variables		Xerostomia *N* (%)		Pearson χ^2	*P* value
		Yes	No		
Diabetes	Yes	72 (56.7)	55 (43.3)	0.13	0.895
	No	114 (47.1)	128 (52.9)		
Hypertension	Yes	81 (58.7)	57 (41.3)	–1.48	0.139
	No	106 (45.9)	125 (54.1)		
Kidney disease	Yes	18 (60.0)	12 (40.0)	0.32	0.743
	No	169 (49.9)	170 (50.1)		
Gastrointestinal disease	Yes	11 (47.8)	12 (52.2)	–0.65	0.514
	No	176 (50.9)	170 (49.1)		
Respiratory disease	Yes	6 (42.9)	8 (57.1)	–1.11	0.267
	No	181 (51.0)	174 (49.0)		
Thyroid disease	Yes	18 (50.0)	18 (50.0)	0.93	0.350
	No	169 (50.8)	164 (49.2)		
Dyslipidemia	Yes	71 (57.7)	52 (42.3)	1.30	0.195
	No	116 (47.2)	130 (52.8)		

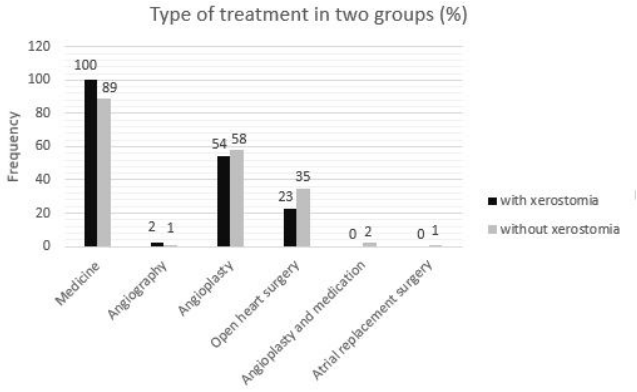

Figure 1. Type of treatment in the two groups. No significant relationship between the type of treatment received by hospitalized cardiac patients and the incidence of xerostomia.

The most commonly used medications in the group of patients with and without xerostomia are illustrated in Figure 2.

According to the results of the present study, using the independent samples *t*-test, the mean number of medications used in patients with and without xerostomia was 2.48 ± 2.59 and 2.39 ± 2.54, respectively, which was not significantly different between the two groups ($P = 0.0845$).

The use of medicines such as amlodipine, captopril, calcicare (calcium, magnesium, zinc, vitamin D3), domperidone, enalapril, isosorbidenitrate, gabapentin, losartan, fluticasone propionate and salmeterol xinafoate (Seroflospray), salbutamol, rivaroxaban, tranqopine, tamsulosin, metformin, novomix, gliclazide, and rosuvastatin was significantly higher in the group without xerostomia compared to the group with xerostomia (in all cases $P < 0.05$).

5. DISCUSSION

Investigating the presence or absence of xerostomia is determined by asking specific questions. Various questionnaires have been designed to evaluate salivary gland dysfunction and xerostomia.[10] Since the questionnaire developed by Fox

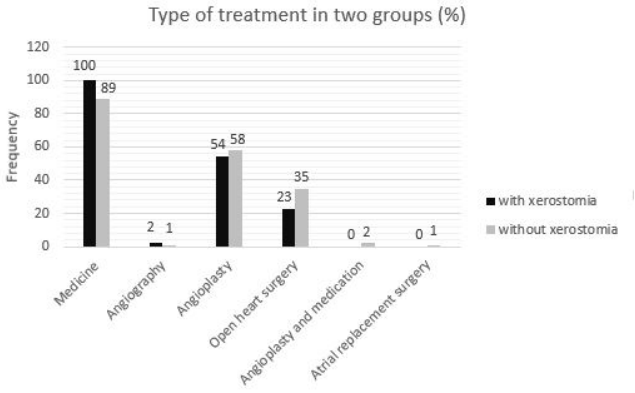

Figure 2. The most commonly used medicines in the two groups. The most frequently used medications in the group of patients with xerostomia are aspirin (ASA), atorvastatin, nitrocardin, losartan, clopidogrel, metformin, warfarin, and pantoprazole, respectively, and in the group without xerostomia, the medications are ASA, losartan, atorvastatin, nitrocardin, clopidogrel, metformin, pantoprazole, and warfarin, respectively.

et al. has the most usage and validity compared to other questionnaires,[10] it was used in the present study.

The results showed that 50.7% of hospitalized cardiac patients complained of xerostomia. A similar result was observed in the study of Molania et al., who reported the prevalence of xerostomia in 48.1% of cardiovascular patients who also had other systemic diseases.[3] Reporting xerostomia symptoms by the patients depends on specific aspects of their tolerance level, mental state, personality, and level of stress and anxiety.[11] Therefore, based on the conditions of the studied populations, there may be some exaggerations in the reports of different studies.

In this study, no significant relationship was observed between xerostomia with mean age ($P = 0.350$) and gender ($P = 0.100$), which is consistent with the findings of some studies.[12,13] However, the results of most previous studies indicate that the prevalence of xerostomia is significantly higher among women and the elderly.[1,2,14] Aging in itself does not increase the incidence of xerostomia but is attributed to other reasons such as medications.[2,15] As a result, the difference in the results of the studies can be due to the difference in the studied populations in terms of age, race, type of disease, mental status, examination tools, type of nutrition, and differences in the inclusion and exclusion criteria of different studies.

The findings showed that the number of platelets was significantly higher in the xerostomia group than the control group; however, other serum parameters, including Na, K, etc., were not significantly different between the two groups. Following the reduction of blood volume, the concentration of platelets and other blood cells falsely increases. In other words, the higher mean number of platelets in patients with xerostomia could be due to their lower plasma volume, especially in patients taking diuretics. It should be noted that an increase in the number of platelets can be seen in many systemic diseases, which can indicate that a person suffers from autoimmune disorders, infectious diseases, etc., which in turn can cause xerostomia.[16]

In addition, no significant relationship was observed between some systemic diseases and xerostomia in this study. At the same time, the number of subjects with a history of hypertension was significantly higher in the xerostomia group compared to the control group. This finding is in line with some studies,[17–19] but the results of some other studies are inconsistent with present study.[13,20,21] The difference in the prevalence of xerostomia between the present study and other studies can be due to the difference in various factors such as age, disease stage, disease duration, disease control level, and the number and type of medicines.

In this study, the mean number of antihypertensives taken by subjects was not significantly different between the two groups. Also, the use of medicines such as metoprolol (metoral), diltiazem, nitroglycerin, and propranolol was more prevalent in subjects with xerostomia. While the use of amlodipine, captopril, losartan, enalapril, and isosorbide nitrate was more common in patients without xerostomia. A more detailed examination of the medicines used showed that in patients with xerostomia, the use of medicines from the β-blocker family (propranol and metoprolol) was higher, which may be due to the stimulation of α2-adrenergic receptors in the salivary glands and CNS. Moreover, qualitative changes in saliva, including a decrease in total protein composition and salivary amylase activity, have been reported as the side effects of these medicines. In addition, some antihypertensives, including calcium channel blockers (e.g., diltiazem), have also been reported to cause xerostomia due to their effect on calcium regulation, which plays an essential role in saliva secretion.[17]

In contrast, patients without xerostomia used more ACE inhibitors (captopril, enalapril), calcium channel blockers (amlodipine), and angiotensin receptor blockers (losartan), which have been proven not to be associated with xerostomia side effect.[22] Although both groups of ACE enzyme inhibitors and angiotensin receptor blockers can decrease the serum level of Na^+ and increase the serum level of K^+,[23] in the present study, no significant relationship was observed between the mean serum concentration of Na^+ and K^+ with xerostomia. On the other hand, a direct relationship between the serum levels of these two ions and hypertension has also been reported.[23]

In the present study, no significant relationship was observed between the type of treatment received by hospitalized cardiac patients and the incidence of xerostomia. Considering that xerostomia is influenced by the level of systemic disease control and the type of medicines the patient uses, more studies are needed in this field.

The results of our study showed that the use of some medicines, including neuroleptics, was more in patients with xerostomia. Also, it has been reported that the use of some psychiatric medicines can cause xerostomia,[2] which is consistent with the results of our study. According to the findings of the present study, the use of neuropsychiatric medicines such as pregabalin, duloxetine, perphenazine,

and fluoxetine was significantly higher in patients with xerostomia. In contrast, the use of medicines such as gabapentin and tranqopine was more common in patients without xerostomia. Some antipsychotics, such as perphenazine, have a selective affinity for D2 receptors, which causes their anticholinergic side effects, including xerostomia.

On the other hand, about 4% of patients receiving pregabalin experience xerostomia without known pharmacomechanism, which has been reported to be dose-dependent. Selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine and duloxetine may also cause xerostomia by blocking histaminergic, cholinergic, and α1-adrenergic receptor sites.[17,24,25] These results can be considered in the prescription of medicines.

The saliva rate may vary with blood volume.[26] Also, changes in the quantity or quality of saliva can affect the occurrence of xerostomia.[27] Considering the lack of significant difference in the mentioned serum compounds of the two groups, it seems that despite the availability of their analyses performed routinely in hospitals, the incidence of xerostomia in cardiac patients cannot be predicted because several factors can affect the quantity and quality of saliva. Therefore, it is suggested to pay attention to salivary parameters such as enzymes and compounds that have an effect on the incidence of xerostomia.

The limitations of this study were not specifying which of the cardiac diseases were the cause of hospitalization of the assessed patients and which one was predisposed to xerostomia. Therefore, it is suggested to determine the type of cardiac diseases and their relationship with xerostomia in the future.

6. CONCLUSIONS

(1) The prevalence of xerostomia among hospitalized cardiac patients was 50.7%.
(2) Xerostomia is associated with a history of hypertension and the use of certain medications, including antihypertensives, especially β-blockers (propranolol and metoprolol) or psychiatrics, especially sedatives, antiepileptics, and antidepressants such as perphenazine or fluoxetine.
(3) Other serum parameters are not associated with xerostomia except for increased blood platelet count.
(4) It is recommended to check the quantity (by sialometry methods) and quality of saliva to more accurately evaluate the presence of hyposalivation along with xerostomia.

Conflict of interest

According to the authors of this article, there is no conflict of interests.

Funding

No external funding was available for this study.

Acknowledgment

The authors would like to thank Dr. Rasoul Tabari Khomeiran for his helpful comments and Dr Mohammad Ghaffari for performing statistical analysis throughout the paper.

Ethics

After providing adequate explanations over the phone about the study process and assuring the confidentiality of the subjects' information, written informed consent was obtained from all participants. The study has been approved by the Ethics Committee of the Research and Technology Vice-Chancellor of Guilan Faculty of Medical Sciences and Health Services (Ethics code: IR.GUMS.REC.1400.315).

References

1 Hopcraft M, Tan C. Xerostomia: an update for clinicians. *Aust. Dent. J.* 2010;55(3):238–244. https://doi.org/10.1111/j.1834-7819.2010.01229.x.
2 López-Pintor RM, Ramírez Martínez-Acitores L, Serrano Valle J, et al. Xerostomia and hyposalivation. *Oral Health Aging.* 2022:85–108. https://doi.org/10.1007/978-3-030-85993-0_5.
3 Molania T, Malekzadeh Shafaroudi A, Taghavi M, et al. Oral health-related quality of life (OHRQoL) in cardiovascular patients referring to Fatima Zahra Hospital in Sari, Iran. *BMC Oral Health*. 2021;21:1–9. https://doi.org/10.1186/s12903-021-01756-0.
4 Jezierska-Woźniak K, Wojtkiewicz J. Stem cells in clinical practice for cardiovascular diseases. *Pol Ann Med.* 2016;23(1):49–56. https://doi.org/10.1016/j.poamed.2015.09.001.
5 Blinderman CD, Homel P, Billings JA, Portenoy RK, Tennstedt SL. Symptom distress and quality of life in patients with advanced congestive heart failure. *J Pain Symptom Manage.* 2008;35(6):594–603. https://doi.org/10.1016/j.jpainsymman.2007.06.007.
6 Tarashoki ZB, Kamyari N, Zahedi A, et al. Investigating laboratory biochemical factors in different types of patients with cardiovascular diseases. *Dis Diagn*. 2022;12(1):35–41. https://doi.org/10.34172/ddj.2023.455.
7 Christine H, Dewi TS, Hidayat W. Management of severe xerostomia and oral candidiasis in patient with valvular heart disease: a case report. *Dentino: J Ked Gigi.* 2021;6(2):209–215. https://doi.org/10.20527/dentino.v6i2.12008.
8 Wolff A, Joshi RK, Ekström J, et al. A Guide to Medications Inducing Salivary Gland Dysfunction, Xerostomia, and Subjective Sialorrhea: A Systematic Review Sponsored by the World Workshop on Oral Medicine VI. *Drugs R D.* 2017;17:1–28. https://doi.org/10.1007/s40268-016-0153-9.
9 Villa A, Polimeni A, Strohmenger L, Cicciù D, Gherlone E, Abati S. Dental patients' self-reports of xerostomia and associated risk factors. *J Am Dent Assoc.* 2011;142(7):811–816. https://doi.org/10.14219/jada.archive.2011.0269.

[10] Kapourani A, Kontogiannopoulos KN, Manioudaki A-E, et al. A review on xerostomia and its various management strategies: the role of advanced polymeric materials in the treatment approaches. *Polymers*. 2022;14(5):850. https://doi.org/10.3390/polym14050850.

[11] Jamieson LM, Thomson WM. Xerostomia: its prevalence and associations in the adult Australian population. *Aust Dent J*. 2020;65(S1):S67–S70. https://doi.org/10.1111/adj.12767.

[12] Diep MT, Jensen JL, Skudutyte-Rysstad R, et al. Xerostomia and hyposalivation among a 65-yr-old population living in Oslo, Norway. *Eur J Oral Sci*. 2021;129(1):e12757. https://doi.org/10.1111/eos.12757.

[13] Salehi M, Akha O, Mousavi J, Ziaee M, Molania T. Frequency of burning mouth and subjective xerostomia in patients with diabetes mellitus type 2. *J Inflamm D*. 2017;21:18–11.

[14] Talha B, Swarnkar SA. *Xerostomia*. Treasure Island (FL): StatPearls Publishing; 2023. https://pubmed.ncbi.nlm.nih.gov/31424871/. Accessed: October 30, 2023.

[15] de Campos WG, Esteves CV, Costa K, de Andrade ACP, Domaneschi C, Lemos CA. Xerostomia in the older adult population, from diagnosis to treatment: a literature review. *Clin Lab Res Dent*. 2019. https://doi.org/10.11606/issn.2357-8041.clrd.2019.157759.

[16] Jameson J FA, Kasper DL, Hauser SL, Longo DL, Loscalzo J, eds. *Harrison's Principles of Internal Medicine*. 20 ed: McGraw-Hill Education; 2018.

[17] Einhorn O, Georgiou K, Tompa A. Salivary dysfunction caused by medication usage. *Physiol Int*. 2020;107(2):195–208. https://doi.org/10.1556/2060.2020.00019.

[18] Ramirez L, Sánchez I, Munoz M, et al. Risk factors associated with xerostomia and reduced salivary flow in hypertensive patients. *Oral Dis*. 2023;29(3):1299–1311. https://doi.org/10.1111/odi.14090.

[19] Villa A, Connell CL, Abati S. Diagnosis and management of xerostomia and hyposalivation. *Ther Clin Risk Manag*. 2015;11:45–51. https://doi.org/10.2147/TCRM.S76282.

[20] Fornari CB, Bergonci D, Stein CB, Agostini BA, Rigo L. Prevalence of xerostomia and its association with systemic diseases and medications in the elderly: a cross-sectional study. *Sao Paulo Med J*. 2021;139(4):380–387. https://doi.org/10.1590/1516-3180.2020.0616.r3.1902021.

[21] Krajewska Wojciechowska J, Krajewski W, Zatoński T. Otorhinolaryngological dysfunctions induced by chronic kidney disease in pre-and post-transplant stages. *Eur Arch Oto-Rhino-L*. 2020;277(6):1575–1591. https://doi.org/10.1007/s00405-020-05925-9.

[22] Little JW MC, Rhodus NL. *Dental management of the medically compromised patient*. Elsevier Health Sciences; 2017.

[23] Iqbal S, Klammer N, Ekmekcioglu C. The Effect of Electrolytes on Blood Pressure: A Brief Summary of Meta-Analyses. *Nutrients*. 2019;11(6):1362. https://doi.org/10.3390/nu11061362.

[24] Toth C. Pregabalin: latest safety evidence and clinical implications for the management of neuropathic pain. *Ther Adv Drug Saf*. 2014;5(1):38–56. https://doi.org/10.1177/2042098613505614.

[25] Kumar NN, Panchaksharappa MG, Annigeri RG. Modified schirmer test–a screening tool for xerostomia among subjects on antidepressants. *Arch Oral Biol*. 2014;59(8):829–834. https://doi.org/10.1016/j.archoralbio.2014.05.008.

[26] Aframian DJ, Baaton S, Mazor S, et al. Improvement of dry mouth following intraductal irrigation of salivary glands. *Oral Dis*. 2019;25(7):1735–1743. https://doi.org/10.1111/odi.13152.

[27] Lee Y-H, Auh QS, Park H-K. Determination of Xerostomia with Cutoff Value for Salivary Flow Rate using Machine Learning Algorithm. *Res Square*. 2022. https://doi.org/10.21203/rs.3.rs-2404122/v1.