

Xerostomia impacts oral health-related quality of life in individuals with end-stage renal disease

Xerostomia impacta a qualidade de vida relacionada à saúde bucal de indivíduos em estágio final de doença renal crônica

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ABSTRACT

Objective: This two-centre cross-sectional study aimed to evaluate whether xerostomia occurrence is associated with oral health-related quality of life (OHRQoL) in patients with end-stage renal disease (ESRD) after the adjustment for potential confounders.

Methods: Oral examinations were performed by calibrated examiners for untreated dental caries, periodontitis and tooth loss in 180 adults with ESRD. The presence of xerostomia was determined using the global question "How often does your mouth feel dry?". OHRQoL was evaluated by the simplified version of the Oral Health Impact Profile (OHIP14) questionnaire. Multivariate zero-inflated negative binomial regression analysis was used to calculate the incidence rate ratios (IRR) for the nonzero scores and odds ratios (OR) of having no impact in OHIP14 scores according to the presence of exposure. **Results:** In the adjusted model, xerostomia (IRR = 1.57; 95% CI: 1.12 to 2.20) was associated with poorer OHRQoL. The adjusted domain-specific analysis revealed that xerostomia occurrence significantly impacted the psychological disability and social disability, and the chance of having no impact was lower for the psychological discomfort domain (OR = 0.84; 95% CI: 0.12 to 0.98). **Conclusion:** Xerostomia exert an impact on OHRQoL in patients with ESRD, mainly in the psychological and social disabilities constructs.

Indexing terms: Kidney failure, chronic. Oral health. Quality of life. Renal dialysis. Xerostomia.

RESUMO

Objetivo: Este estudo transversal realizado em dois centros teve como objetivo avaliar se a ocorrência de xerostomia está associada à qualidade de vida relacionada à saúde bucal (QVRSB) em pacientes com doença renal crônica em estágio final (DRCEF) após o ajuste

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para potenciais fatores de confusão. **Métodos:** Exames bucais foram realizados por examinadores calibrados para cárie dentária não tratada, periodontite e perda dentária em 180 adultos com DRCEF. A presença de xerostomia foi determinada por meio da pergunta global "Com que frequência você fica com a boca seca?". A QVRSB foi avaliada pela versão simplificada do questionário Oral Health Impact Profile (OHIP-14). A análise multivariada de regressão binomial negativa inflacionada por zero foi usada para calcular as taxas de incidência (IRR) para os escores diferentes de zero e os razões de chance (OR) de não haver impacto nos escores do OHIP-14 de acordo com a presença da exposição. **Resultados:** No modelo ajustado, a xerostomia (IRR = 1,57; IC 95%: 1,12 a 2,20) foi associada a pior QVRSB. A análise específica por domínio revelou que a ocorrência de xerostomia impactou significativamente a incapacidade psicológica e a incapacidade social, e a chance de não haver impacto foi menor para o domínio desconforto psicológico (OR = 0,84; IC95%: 0,12 a 0,98). **Conclusão:** A xerostomia exerce impacto sobre a QVRSB em pacientes com DRCEF, principalmente nos construtos de deficiência psicológica e social.

Termos de indexação: Insuficiência renal crônica. Saúde bucal. Qualidade de vida. Diálise renal. Xerostomia.

INTRODUCTION

Chronic kidney disease (CKD) causes structural damage and a reduction in kidney function and is a major public health problem that consumes substantial financial and social resources [1]. CKD is ranked among the fifteen leading causes of death and 1.5% of deaths worldwide are credited to this disease [2]. When an individual reaches end-stage renal disease (ESRD), kidney function becomes unable to sustain life over the long term and there is a need for renal replacement therapy (RRT) [3]. Pre-emptive kidney transplantation, which can lead to a longer life expectancy and better quality of life [4], is an option only if a living donor is available. Thus, peritoneal dialysis and haemodialysis are the most common treatment modalities offered to patients requiring RRT.

The provision of a support system for kidney function compromises the social, physical, parental and economical aspects of a patient's life [5]. It requires adjustment to the intensive alterations caused by the disease occurrence and progression, such as restrictions affecting lifestyle, the use of multiple therapies, the effects of dialysis and disease-related complications, which generally increase over time [6]. Thus, health-related quality of life is often markedly reduced in patients with ESRD [7].

As a key factor of general health as well as mental and physical wellness, oral health is influenced by an individual's changing perceptions, relieves, expectations and capability to readapt to adverse situations. Oral health-related quality of life (OHRQoL) is a multidimensional construct employed to measure the impact of oral health conditions on wellbeing [8]. Due to potentially influence on individual's general perception of life, OHRQoL has been widely used as an adjunct to clinical examination when appraising public oral health strategies [9].

Recent evidence has shown that patients with ESRD have a greater frequency of oral conditions, such as xerostomia, which is defined as the subjective feeling of a dry mouth, compared to systemically healthy individuals [10]. Although this condition leads to difficulties in chewing, swallowing, tasting and speaking and thus may exert negative impacts on OHRQoL [11], to the best of our knowledge, no previous study has explored this relationship in patients undergoing haemodialysis using multivariate models. Thus, we aimed to analyze whether xerostomia is associated with OHRQoL in ESRD patients. We hypothesized that this condition exerts an impact on OHRQoL in this population.

METHODS

Design and sampling process

This study received approval from the Human Research Ethics Committee of the Federal University of Santa Maria (certificate number: 2.429.552) and all activities were conducted in conformity with the precepts stipulated in the Declaration of Helsinki. All participants obtained a full explication regarding the aims and procedures of the study and agreed to participate by signing a statement of informed consent.

This cross-sectional analysis was conducted from January to August 2018 involving ESRD patients [estimated glomerular filtration rate: < 15 ml/min per 1.73 m² for more than three months [12]], in two treatment units (Caridade Hospital and Casa de Saúde Hospital) of the city of Santa Maria, which is located in southern Brazil. This city offers coverage to 32 municipalities and is considered a reference for RRT. Both treatment units are covered by the Brazilian Unified National Healthcare System.

The aim of the major project was to include as many patients as possible. All patients (n = 301) undergoing regular haemodialysis at renal clinics during the study period were screened for eligibility. The inclusion criteria were (1) individuals with at least 18 years old, (2) presenting at least five teeth and (3) absence of neoplasia. The final sample was constituted of 180 individuals aged from 21 to 82 years.

Four examiners (C.S., D.S., L.M.O. and S.S.S.) performed the clinical examinations after undergoing training exercises to measure dental plaque, gingival bleeding and dental caries. Intra-examiner and inter-examiner agreement were determined for probing depth (PD), clinical attachment loss (CAL) and number of present teeth. The weighted Kappa (K) test was used (± 1 mm) to measure reproducibility for PD and CAL and the intraclass correlation coefficient (ICC) was used for the teeth count. Intra-examiner reproducibility was determined through repeated examinations of 10 subjects after one hour interval and the values ranged from 0.84 to 0.96. An experienced examiner (A.P.G.) was considered the “gold standard” during the calibration process, which involved the examination of 20 patients, and each of the four examiners evaluated two quadrants in the same patient for CAL and PD, totalling a minimum of 1,000 sites (K = 0.83–0.98) and a full-mouth teeth count (ICC = 0.94–0.98).

Data collection

Face-to-face structured interviews were conducted with the participants for the collection of demographics, socioeconomic, medical and dental data. Xerostomia was assessed subjectively based on the global item: “How often does your mouth feel dry?” [13]. The participants were positioned on a portable dental chair under artificial light. A mouth mirror and Williams periodontal probe (Neumar, São Paulo, SP, Brazil) were used for the examination. The oral conditions assessed were number of teeth (total number of permanent sound, decayed and filled teeth), untreated dental caries [D component of the Decayed, Missing and Filled Teeth (DMFt) index] and periodontal status [probing depth (PD), bleeding on probing (BP) and clinical attachment loss (CAL)]. All teeth, except third molars, were examined in six sites per tooth [14]. The body mass index, haemodialysis vintage time, diabetes mellitus and cardiovascular disease were collected from the hospital records.

Dependent variable: OHRQoL

The Brazilian simplified, well-validated version of the multidimensional Oral Health Impact Profile (OHIP14) was used to determine the frequency of problems related with the oral cavity in seven dimensions: functional limitation (e.g., chewing problems), physical pain (oral pain and discomfort while eating), psychological discomfort (feeling tense), physical disability (suspended meals and unsatisfactory diet), psychological disability (embarrassment and difficulty relaxing), social disability (averting social interactions) and handicap (disability to function) [15]. For each question, the participants were asked how frequently they had experienced the impact in the previous six months. The response options are scored on ordinal scale: 0 = never, 1 = hardly ever, 2 = occasionally, 3 = fairly often and 4 = very often. The total score was calculated as the sum of the item scores and ranged from 0 to 56, with a higher score indicating more negative impacts and lower OHRQoL [16].

Independent variables and covariates

The explanatory variables considered in the present study were age (less than 44, 45 to 54, 55 to 64 and 65 or more years), sex (male or female), self-reported skin colour (white or non-white), body mass index [normal weight

(BMI \leq 25 kg/m²), overweight (BMI = 25-29.9 kg/m²) or obese (BMI \geq 30 kg/m²), dental care in the previous two years (routine/maintenance, toothache or none), diabetes mellitus (present or absent) and cardiovascular disease (present or absent). Smoking status was categorized in pack-years (the number of cigarette packs smoked in a year and multiplying the number of smoking years by the mean number of packs a day) as non-smoker (0 pack-years), light smoker (0.1 to 20 pack-years) or heavy smoker ($>$ 20 pack-years). Schooling was categorized as \leq eight (corresponding to primary school) or $>$ eight years of study and household income was dichotomized as \leq 2.4 or $>$ 2.4 times the Brazilian minimum wage (BMW). Periodontitis was recorded in the presence of PD \geq 4 mm and CAL \geq 4 mm affecting non-adjacent interproximal sites of two or more teeth [17] and tooth loss was dichotomized as \leq 8 or $>$ 8 teeth lost [18]. Lastly, xerostomia was dichotomized as present [responses “frequently” (3) and “always” (4)] or absent [responses “never” (1) and “occasionally” (2)] [13].

Statistical analysis

All analyses were conducted with the aid of the Stata 14.0 software (StataCorp., College Station, TX, USA). Firstly, descriptive analysis yielded summary statistics of the study variables. The OHIP14 and its domain-specific scores were discrete count variables with excess zeros, overdispersion and skewness. Hence, we fitted zero-inflated negative binomial regression (ZINB) models to estimate the association between occurrence of xerostomia and OHIP14 scores. ZINB modelling generated two separate models and then combined them: first, a logit model was generated to predict the chance of having no event (OHIP14 = 0) by calculating odds ratios (OR); second, a negative binomial model was generated, predicting the severity of OHIP14 for those who presented scores \geq 1 by calculating the incidence rate ratios (IRR); finally, the two models were combined, and the respective 95% confidence intervals estimated. We calculated unadjusted estimates followed by adjusted analysis for potential confounders (covariates and remaining oral conditions). Variables with a p-value $<$ 0.20 in the unadjusted analysis were included in the adjusted models. Vuong test compared the standard negative binomial regression and ZINB modelling, indicating that the second fitted data better. Furthermore, ZINB provided a significant improvement in the fit when compared to zero-inflated Poisson model. The study is currently reported according to STROBE guideline.

RESULTS

The distribution of the sample characteristics is presented in table 1. Among the 180 participants, 78.3% had OHIP₁₄ scores \leq 1. From those, 62.4% studied more than eight years and 28.1% have a household income of more than 2.4 times the BMW. The prevalence of xerostomia was 28.3%, being 30.5% of those who presented OHIP₁₄ scores \geq 1 and 20.5% of those with OHIP₁₄ = 0.

The median OHIP14 score was 5 and the mean \pm standard error was 7.25 ± 0.56 , with scores ranging from 0 to 41. Individuals presenting xerostomia exhibited higher OHIP₁₄ overall (8.51 ± 1.13) and domain-specific scores, being psychological discomfort the construct with higher mean (2.20 ± 0.34) (table 2).

Table 3 displays the results of the unadjusted and adjusted multivariate zero-inflated negative binomial regression analyses. Xerostomia occurrence was associated with higher overall OHIP14 (IRR = 1.44; 95% CI: 1.07 to 1.94; $p <$ 0.05) and lower chance of having no impact (OHIP14 = 0) in physical disability (OR = 0.52; 95% CI: 0.18 to 0.97; $p <$ 0.05) and psychological disability (OR = 0.43; 95% CI: 0.08 to 0.93; $p <$ 0.05) domain-specific scores in the unadjusted analyses. After the adjustment for potential confounders, present xerostomia was associated with a 57% increase in OHIP14 overall score (IRR = 1.57; 95% CI: 1.12 to 2.20; $p <$ 0.05). When attention is given for the domain-specific, poorer psychological disability (IRR = 1.38; 95% CI: 1.03 to 1.67; $p <$ 0.05) and social disability (RR = 2.18; 95% CI: 1.01 to 4.69; $p <$ 0.05) were found among those with xerostomia. Lastly, they presented a 16% lower chance of having no impact in psychological discomfort domain (OR = 0.84; 95% CI: 0.12 to 0.98; $p <$ 0.05).

Table 1. Characteristics of study sample (n= 180).

1 of 2

	OHIP ₁₄ overall scores	
	OHIP ₁₄ = 0	OHIP ₁₄ ≥ 1
	N (%)	
Number of subjects	39 (21.7)	141 (78.3)
Mean age ± SE	51.31 ± 2.18	52.17 ± 1.23
Demographic and socioeconomic variables		
Sex		
Male	22 (56.4)	77 (54.6)
Female	17 (43.6)	64 (45.4)
Skin color		
White	29 (74.4)	81 (57.4)
Non-white	10 (25.6)	60 (42.6)
Age (years)		
≤ 44	9 (23.1)	43 (30.5)
45 – 54	14 (35.9)	29 (20.6)
55 – 64	10 (25.6)	42 (29.8)
≥ 65	6 (15.4)	27 (19.1)
Schooling		
≤ 8 years	19 (48.7)	53 (37.6)
> 8 years	20 (51.3)	88 (62.4)
Income		
≤ 2.4 x BMW ^a	27 (84.4)	87 (71.9)
> 2.4 x BMW	5 (15.6)	34 (28.1)
Behavioral and medical variables		
Body mass index		
< 25 kg/m ²	18 (46.2)	64 (45.4)
25 to 29.9 kg/m ²	13 (33.3)	44 (31.2)
> 30 kg/m ²	8 (20.5)	33 (23.4)
Diabetes mellitus		
Absent	29 (74.4)	90 (63.8)
Present	10 (25.6)	51 (36.2)
Cardiovascular disease		
Absent	19 (48.7)	48 (34.0)
Present	20 (51.3)	93 (66.0)
Smoking status		
Non-smoker	21 (53.9)	72 (51.1)
Light smoker	13 (33.3)	48 (34.0)
Heavy smoker	5 (12.8)	21 (14.9)
Dental care		
Routine	24 (61.5)	44 (31.2)
Toothache	6 (15.4)	49 (34.8)
No visit	9 (23.1)	48 (34.0)
Mean hemodialysis vintage time ± SE	53.26 ± 10.61	5.79 ± 4.72
Oral health-related variables		
Tooth loss		
Low extent (≤8 teeth lost)	28 (71.8)	79 (56.0)
High extent (>8 teeth lost)	11 (28.2)	62 (44.0)

Table 1. Characteristics of study sample (n= 180).

	OHIP ₁₄ overall scores	
	OHIP ₁₄ = 0	OHIP ₁₄ ≥ 1
	N (%)	
Oral health-related variables		
Untreated dental caries		
Absent	37 (94.9)	112 (79.4)
Present	2 (5.1)	29 (20.6)
Periodontitis		
Absent	7 (18.0)	23 (16.3)
Present	32 (82.0)	118 (83.7)
Xerostomia		
Absent	31 (79.5)	98 (69.5)
Present	8 (20.5)	43 (30.5)

Note: ^aBMMW: Brazilian monthly minimum wage ≈ US\$ 200.

Table 2. Distribution of overall and domain-specific OHIP14 scores for total sample and according to xerostomia occurrence.

	Mean (SE ^a)		
	Xerostomia		Total
	Absent	Present	
Overall OHIP-14 score	6.33 (0.64)	8.51 (1.13)	7.25 (0.56)
Functional limitation	0.53 (0.09)	0.61 (0.15)	0.55 (0.08)
Physical Pain	1.73 (0.20)	1.94 (0.28)	1.79 (0.16)
Psychological discomfort	1.49 (0.18)	2.20 (0.34)	1.69 (0.16)
Physical disability	0.56 (0.12)	1.06 (0.24)	0.70 (0.11)
Psychological disability	0.96 (0.14)	1.33 (0.24)	1.07 (0.12)
Social disability	0.50 (0.11)	0.59 (0.21)	0.53 (0.10)
Handicap	0.57 (0.13)	0.78 (0.23)	0.63 (0.11)

Note: ^aSE, standard error.

Table 3. Unadjusted and adjusted associations between xerostomia and overall/domain-specific OHIP14 scores, determined using multivariate zero-inflated negative binomial regression.

	Unadjusted estimates		Adjusted estimates ^d	
	IRR ^a	OR ^c	IRR	OR
	(95% CI ^b)	(95% CI)	(95% CI)	(95% CI)
Overall OHIP ₁₄ score	1.44 (1.07 – 1.94)*	0.62 (0.24 – 1.69)	1.57 (1.12 – 2.20)*	2.57 (0.12 – 6.83)
Functional limitation	1.07 (0.65 – 1.75)	0.38 (0.08 – 1.41)	0.75 (0.37 – 1.53)	0.23 (0.07 – 2.51)
Physical pain	1.11 (0.82 – 1.51)	0.58 (0.22 – 1.17)	1.05 (0.77 – 1.44)	0.41 (0.11 – 1.26)
Psychological discomfort	1.17 (0.88 – 1.57)	0.79 (0.07 – 1.52)	1.21 (0.89 – 1.66)	0.84 (0.12 – 0.98)*
Physical disability	1.40 (0.92 – 2.14)	0.52 (0.18 – 0.97)*	1.16 (0.69 – 1.95)	0.97 (0.22 – 1.97)
Psychological disability	1.11 (0.80 – 1.53)	0.43 (0.08 – 0.93)*	1.38 (1.03 – 1.67)*	0.65 (0.19 – 1.49)
Social disability	1.45 (0.62 – 3.42)	0.89 (0.17 – 1.24)	2.18 (1.01 – 4.69)*	0.97 (0.49 – 2.53)
Handicap	0.95 (0.59 – 1.53)	0.59 (0.11 – 1.38)	1.08 (0.65 – 1.79)	0.65 (0.12 – 1.61)

Note: ^aIRR, incidence rate ratio; ^bCI, confidence interval; ^cOR, odds ratio; ^dAdjusted for race, schooling, cardiovascular disease, smoking status, dental care, untreated dental caries, tooth loss and periodontitis. Reference category is absence of xerostomia; *p < 0.05.

DISCUSSION

The present findings support the hypothesis that xerostomia occurrence exerts a negative impact on the OHRQoL of individuals with ESRD. Previous studies found that haemodialysis patients with xerostomia had higher OHIP14 scores than those with no perception of dry mouth [19,20]. However, the comparison with these results is hindered by the inconsistent control for confounding variables and bivariate models, which affect the validity of the previous findings. In the present study, we analysed socioeconomic, behavioural and medical determinants along with periodontitis, tooth loss and untreated dental caries in the adjusted model, which lends strength to our findings.

Xerostomia is a continual, frustrating, debilitating symptom in patients with ESRD and can impact OHRQoL due to difficulties on chewing, swallowing and speaking as well as an altered sense of taste and halitosis [11]. Due to the concurrent use of multiple drugs, patients undergoing haemodialysis have a higher frequency of dry mouth sensation compared to systemically healthy individuals [21]. Besides the burning sensation, patients with xerostomia are more inclined to present periodontitis, untreated dental caries and lack of denture retention [22], which are also related to a reduction in OHRQoL [23]. These aspects, except denture retention, were addressed in the multivariate model as confounders and xerostomia was confirmed to be independently associated with higher OHIP14 scores. This condition also contributes to excessive fluid intake and interdialytic weight gain, which is a documented predictor of poorer general health quality of life [24] as well as the development of oral lesions [25].

The analysis of domains enables a better understanding of the distinct features of life that are influenced by oral diseases. Assessing each OHRQoL domain, xerostomia was positively associated with psychological disability and social disability. Moreover, we detected a lower chance to present no impact on the psychological discomfort construct. A similar pattern was observed in individuals with rheumatoid arthritis [26], although the study failed to adjust for confounders. These associations underscore that the main pathway of influence on OHRQoL is due to difficulties to relax, stress and averting social interactions. The overall OHIP14 score and specific domains affected should be used to set risk priorities and interventions should prioritize this group focusing on the described constructs. In this respect, the daily use of topical mouth gel was reported to improve the OHRQoL of patients undergoing haemodialysis by decreasing xerostomia symptoms [27]. Nevertheless, further clinical trials ought to test different interventions (i.e., sialogogues) and evaluate whether such therapies lead to fewer food restrictions and improve the quality of life of these patients.

Curiously, the prevalence of xerostomia (approximately 28% of the total sample) was lower when compared to a pooled estimate recently published [28], but higher than the reported in healthy individuals [29]. This difference may be explained due to the distinct instruments used to measure this variable. Indeed, high floor effects were identified, and the mean OHIP14 scores were comparable to reported from healthy individuals [30]. One possible explanation for this finding may be attributable to the mean haemodialysis vintage time found in the present sample, which was higher than a previous report [20]. Although longer waiting times on haemodialysis can exacerbate the emotional burden, it is also possible to increase characteristics of resilience and resistance [31]. In this perspective, it is possible that these individuals have higher likelihood to adapt to oral health problems as the systemic impairment may be more influential in the quality of life than the oral health.

The present manuscript has the intrinsic limitations of the cross-sectional design. The entire examination process was performed during the haemodialysis session. Thus, some assessments were difficult to perform due to not being in an adequate environment for a proper oral evaluation. Nevertheless, oral health variables are commonly measured without all favourable conditions for the assessment in epidemiological studies. Additionally, no psychological/coping (i.e., sense of coherence, resilience) or prosthetic status variables were investigated, and such factors can modify the effect of xerostomia on OHRQoL. Another limitation concerns xerostomia (subjective assessment), which was only determined using a single question, impeding a better interpretation of this variable according to the different severities. Importantly, our findings must be extrapolated only for ESRD individuals in haemodialysis regimens.

There is a deficit on engagement to address the oral health of ESRD individuals and the OHRQoL assessment can modify this scenario by the motivation to public health strategies proposed for this population. Longitudinal studies are

still required to endorse the elaboration of health programs intending to decrease the consequences of oral conditions and diseases among individuals with CKD. On the basis of the present findings, policy makers should consider the greater impact of xerostomia on OHRQoL during haemodialysis by giving additional priority to these patients.

CONCLUSION

The present findings indicate that xerostomia exert a negative impact on OHRQoL in individuals with ESRD, mainly in the psychological disability and social disability constructs.

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Collaborators

LM Oliveira, RP Antoniazzi and FB Zanatta, substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. C Schöffner, LC Argenta and SS Santi, drafting the work or revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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