Limited Jaw Movements and Somatization (But Not Pain) May Play a Role in Salivary Flow in Female Patients with Temporomandibular Disorders

Irena Mladenovic, PhD, MSc, DDS
Assistant Professor
Department of Oral Rehabilitation
Faculty of Medicine
University of East Sarajevo
Foca, Bosnia and Herzegovina

Jelena Krunic, PhD, MSc, DDS
Assistant Professor
Department of Dental Pathology
Faculty of Medicine
University of East Sarajevo
Foca, Bosnia and Herzegovina

Nikola Stojanovic, PhD, MSc, DDS
Associate Professor
Department of Dental Pathology
Faculty of Medicine
University of East Sarajevo
Foca, Bosnia and Herzegovina

Dusanka Markovic, DM
Center for Medical Biochemistry
Clinical Center Nis
Nis, Serbia

Silvia RDT de Siqueira, PhD, DDS
Associate Professor
Orofacial Pain Team of Hospital das Clinicas and Neurology Department
Interdisciplinary Pain Center Medical School;
School of Arts, Science and Humanities
University of São Paulo
São Paulo, Brazil

Correspondence to:
Dr Irena Mladenovic
Department of Oral Rehabilitation
Faculty of Medicine
5 Studentska St.
73300 Foca
Bosnia Herzegovina
Fax: +387 58 210 420 ext. 203
Email: eirene14a@yahoo.com

Aims: To explore the unstimulated salivary flow rate and subjective feeling of oral dryness in young adult women with temporomandibular disorders (TMD) and their relation to the presence of chronic pain, depression, somatization, and limited mandibular mobility. **Methods:** Unstimulated whole saliva flow rate and presence of oral dryness were determined in 45 women with TMD and 30 healthy controls. The Research Diagnostic Criteria for TMD (RDC/TMD) were used for assessment of TMD, chronic pain, depression, somatization, and mandibular mobility. Factors with $P < .05$ in the bivariate analysis were included in multivariate modeling. **Results:** The TMD patients showed significantly diminished unstimulated salivary flow ($P = .010$) in comparison to controls, but there was no difference in subjective oral dryness. Within the TMD group, patients with mandibular hypomobility and free from somatization exhibited significantly lower salivary output ($P = .037$; $P = .015$, respectively). No relationship between salivary flow and depression or TMD pain was observed. Multivariate linear regression identified somatization as the single variable contributing to salivary flow ($P = .044$) in the TMD patients. **Conclusion:** The present study shows a relationship between TMD and lower salivary flow but no evidence of a relationship between TMD and subjective oral dryness in young adult women. Somatization was the single variable to emerge from the evaluation of potential factors contributing to salivary output in TMD patients. *J Oral Facial Pain Headache 2018;32:123–129. doi: 10.11607/ofph.1918*

Keywords: *mouth dryness, RDC/TMD, salivation, temporomandibular disorders, women*

Temporomandibular disorders (TMD) are a set of conditions affecting the masticatory muscles, temporomandibular joints (TMJs), and adjacent structures.[1] Several studies have shed new light on the clinical aspects of TMD by directing attention to the appearance of reduced salivation and complaints of xerostomia in these patients.[2–4]

It has been suggested that chronic pain conditions in the orofacial region might be related to orofacial sensory abnormalities[5] or that chronic pain and sensory disturbances share a common neural substrate.[6] However, the relationship between orofacial pain and changes in salivary flow has not yet been fully clarified. Potential mechanisms include neurovegetative phenomena due to pain chronification or to anxiety and depression, which are common comorbidities of pain. This may happen due to central sensitization involving areas of the limbic system and hypothalamus, which can alter hormonal secretion from the hypothalamic-hypophyseal-adrenal axis and may result in increased serum levels of cortisol and adrenaline, causing neurovegetative signs such as altered blood pressure and heart rate.[7] Pain-related TMD has been associated with taste disturbances[6] and subjective oral dryness.[2,4,8] Orofacial pain patients, including those with TMD, have been found to report more oral complaints and reduced unstimulated salivary flow in comparison to healthy subjects.[3] Decreased production of unstimulated whole saliva has been associated with TMD in rheumatoid arthritis patients.[9] Furthermore, an increase in stimulated salivary flow was observed after successful treatment of unmedicated TMD patients,[10] although this was not confirmed in a more recent study of patients with myogenic TMD.[11] In addition, Siviero et al[5] found that oral neuropathic pain

syndromes were not related to unstimulated salivary secretion. This disparity in findings suggests that other factors besides chronic pain might be involved in salivary impairment among TMD patients.

Psychosocial disturbances—including somatization and depression, which present important aspects of a TMD patient's profile[12–14]—have also been related to the modulation of salivary flow and/or subjective oral dryness in TMD patients.[15–18] Depressive symptoms have been associated with both reduced unstimulated salivary output[16] and dry mouth complaints.[15] Patients with somatoform disease may have many salivary complaints, but the underlying pathologic cause is unknown.[18] However, except for a single study dealing with stress,[11] previous studies have not investigated salivary flow and/or oral complaints of TMD patients in relation to psychosocial variables.

Mandibular hypomobility is a well-established symptom of TMD.[1,19–21] Patients avoid jaw motions due to pain or mechanical interference, limiting the amplitude of jaw movements. As a local factor, oromotor activity may play a role in salivary production. While mandibular activities stimulate salivary secretion,[22] prolonged reduction in masticatory muscle activity is associated with a decrease in unstimulated and stimulated salivary flow[23,24] or persistent dry mouth.[25]

There seems to be widespread agreement that TMD, TMD pain, salivary output, and subjective oral complaints are gender dependent. Women are 3 to 9 times more prevalent in TMD treatment-seeking subjects,[26] and the prevalence of TMD pain is higher in adult women than in adult men, with increased rates in the reproductive age range.[27,28] In the case of saliva, women are usually more affected with dry mouth and diminished unstimulated and stimulated salivary flow than men.[15,29]

Thus, the current study aimed to explore the unstimulated salivary flow and subjective feeling of oral dryness in young adult women with TMD and their relation to the presence of chronic pain, depression, somatization, or limited mandibular mobility. The authors hypothesized that TMD patients show a decreased salivary flow and a higher prevalence of xerostomia than TMD-free controls and that these changes are related to the presence of chronic TMD pain, psychosocial disability, or restricted mandibular movements.

Materials and Methods

Study Population

The study protocol was approved by the ethical committee of the Faculty of Medicine, University of East Sarajevo and conformed to the principles embodied in the Declaration of Helsinki. The participants received detailed information about the study and signed an informed consent form.

This study involved two groups of subjects. The size of the sample was calculated on the basis of a pilot study involving 30 subjects. The mean and standard deviation (SD) of unstimulated salivary flow rate was reported for young adult females with TMD and healthy controls. A level of significance of 5% for a two-tailed *t* test for means and a power of 80% were adopted. At least 22 persons were calculated to be needed per group.

For the study group, women aged from 20 to 40 years with a diagnosis of TMD were recruited from a population of patients seeking treatment at the Department of Prosthodontics. A considerable proportion (37.8%) of the patients were dental students. Control subjects were healthy women without a TMD diagnosis and with an overall age distribution similar to the study group; they were selected from patients attending yearly routine check-ups at the Department of Restorative Dentistry.

Exclusion criteria for all study participants were: a current or past medical history of systemic disease; other painful physical conditions; obesity (body mass index > 30); pregnancy, lactation, or irregularity in menstrual cycle; any medication intake, including contraceptives and over-the-counter medication, in the past 6 months; current use of tobacco products; presence of tooth decay; Silness-Löe plaque index (PI) score > 1; community periodontal index > 2; < 21 teeth; or wear of dentures/orthodontic appliances.

Clinical Examination

Assessment of TMD, Depression, Somatization, and Mandibular Mobility. The assessment of TMD, psychosocial status, and mandibular mobility was performed in accordance with the Research Diagnostic Criteria for TMD (RDC/TMD).[19] The RDC/TMD has a dual-axis approach: Axis I obtains the clinical diagnosis of TMD, and Axis II assesses the levels of chronic pain, depression, and somatization. Additionally, data considering characteristic pain intensity (present, worst, and average pain intensity as reported on a 0 to 10 verbal numeric rating scale [NRS], with 0 representing no pain and 10 indicating the worst pain the subject has ever experienced) and pain duration were extracted from the RDC/TMD history questionnaire. Vertical jaw motion and lateral and protrusive excursions were assessed according to Axis I. Minimum normal jaw opening was considered to be 35 mm, minimum lateral motion 7 mm to both right and left sides, and minimum protrusion 6 mm.[19,20]

Salivary Flow and Oral Dryness. Sialometry was carried out at a fixed time of the day: between 9:00 and 11:00 am. The subjects were instructed to refrain from eating, drinking, and any oral hygiene

for 2 hours preceding the saliva sampling. The subjects were seated in a dental chair and relaxed for 5 minutes and were then instructed to make as few movements as possible, including swallowing, during the saliva collection procedure. Unstimulated whole saliva was collected using the spit method as described by Navazesh.[30] The collection was initiated immediately after an initial swallow. Subsequently, saliva was allowed to accumulate in the floor of the mouth without stimulation of saliva secretion by means of orofacial movements. The participants then expectorated into 10-mL plastic containers once per minute over a 5-minute period and were asked to expectorate residual saliva into the container. The saliva-filled plastic containers were reweighed, and the original weight of the containers subtracted from the new weight. Whole unstimulated saliva flow was expressed in milliliters per minute (which is nearly equivalent to grams/minute).[30] A salivary secretion rate of 0.1 mL/minute or less was considered low unstimulated saliva flow (hyposalivation).[31] The question "Does your mouth usually feel dry?" was used as the means to assess subjective oral dryness, as recommended previously.[32]

TMD, depression, somatization, and mandibular mobility were recorded by an examiner (I.M.), while salivary flow and subjective oral dryness were assessed by another investigator (J.K.) who was masked to the subject's group.

Statistical Analyses

Statistical calculations were performed by using Statistical Package for Social Sciences (SPSS) 19.0 for Windows (IBM). The means, SDs, and frequencies were calculated. Kolmogorov-Smirnov test showed that salivary output data were normally distributed ($P = .598$). For intergroup analysis, the following tests were used: independent Student *t* test for comparison of age, salivary flow, and opening range; Fisher exact tests for comparison of dry mouth and hyposalivation; and Mann-Whitney test to analyze differences in depression and somatization scores.

Differences in salivary flow were further investigated with respect to TMD pain, depression and somatization, diagnostic group as determined by the RDC/TMD, and mandibular mobility. To simplify the interpretation of the relationships with salivary flow and to avoid difficulties arising out of low cell frequencies, Axis II variables were dichotomized into: chronic pain grade 0 vs chronic pain grade ≥ 1; and normal vs moderate/severe depression or somatization. Similarly, patients with any of the investigated movements below limit values were classified as patients with restricted mandibular movements. To evaluate differences in salivary flow, independent Student *t* test was used for Axis II variables and hypomobility, while one-way analysis of variance (ANOVA) was performed between RDC diagnostic categories in the TMD group. Correlation was quantified through calculation of Spearman's correlation coefficient, as the sample size was too small to use Pearson's correlation. In addition, Cohen's d was calculated to assess the magnitude of effect of TMD, TMD-related pain, depression, somatization, and restricted jaw movements on salivary flow rate.

Factors with $P < .05$ in the bivariate analysis were included in the multivariate modeling. Multivariate linear regression was used to investigate the joint effect of the predictor variables on the unstimulated salivary flow rate. Age was also included, as it is known to influence salivary flow. For all analyses, the significance level was $\alpha = 5\%$.

Results

The overall age distribution was similar among the controls and TMD patients (patients vs controls, mean ± SD = 26.3 ± 4.5 years vs 27.3 ± 4.9 years; $P = .368$). TMD diagnoses, as well as other clinical characteristics of the patients, are presented in Table 1. Chronic TMD pain was observed in 48.9% of the patients, with worst pain intensity being 4.59 ± 1.79 on the NRS.

The frequency distributions for depression/somatization scores and range of pain-free and maximal mandibular opening for the TMD patients and controls are presented in Table 2. Altogether, 66.2% of the TMD patients and 36.7% of the controls reported depressive symptoms, and the difference in depression scores was significant ($P = .018$). Somatization was evident in 40% of the TMD subjects and 36.7% of the controls. Among the TMD patients, 6 (13.3%) showed limited unassisted opening without pain, 1 (2.2%) limited maximal opening, 13 (28.9%) limited laterotrusion, and 3 (6.7%) limited protrusion. In total, 19 (42.2%) of the TMD patients showed restriction in at least one mandibular movement. The range of unassisted opening without pain was significantly lower ($P = .041$) in the TMD group.

The mean unstimulated salivary flow rate for the TMD group was significantly lower than that of the control group, giving a medium effect size ($P = .010$, Cohen's d = 0.59). Hyposalivation values (< 0.1 mL/minute) were found in only one subject in each group, while subjective feeling of dry mouth was reported by three subjects in the TMD group and two in the control group (Table 3). None of the subjects with observed hyposalivation reported oral dryness.

Within the TMD group, unstimulated salivary flow was significantly lower in patients with limited mandibular movements ($P = .037$) and in those free from

Table 1 Prevalence of Axis I Diagnoses[a] and Pain Characteristics in TMD Patients

	TMD group (n = 45)	
Axis I diagnosis	n	%
Myofascial pain		
Without limited opening	11	24.4
With limited opening	5	11.1
Disc displacement		
With reduction	17	37.8
Without reduction, with limited opening	0	0.0
Without reduction, without limited opening	6	13.3
Other joint conditions		
Arthralgia	13	28.9
Arthritis	0	0.0
Arthrosis	0	0.0
Combined	7	15.6
Graded Chronic Pain Scale[b]		
Grade 0	23	51.1
Grade I	17	37.8
Grade II	5	11.1
Grade III	0	0.0
Grade IV	0	0.0
Pain intensity in TMD patients with pain (0–10 NRS) (mean ± SD)		
At present	2.05 ± 2.32	
Worst	4.59 ± 1.79	
Average	3.68 ± 2.03	
Duration of pain in TMD patients with pain (mo) (mean ± SD)	34.18 ± 28.24	

NRS = numeric rating scale; SD = standard deviation.
[a]Since the patients may have had several TMD diagnoses, the sum of the columns may not match the number of patients in each column.
[b]Graded Chronic Pain Scale: Grade 0 = no TMD pain in the last 6 months; Grade I = low disability, low intensity of pain (characteristic pain intensity < 50 and < 3 disability points); Grade II = low disability, high intensity of pain (characteristic pain intensity > 50 and < 3 disability points); Grade III = high disability, moderately limiting (3 to 4 disability points regardless of characteristic pain intensity); Grade IV = high disability, severely limiting (5 to 6 disability points regardless of characteristic pain intensity).

Table 2 Depression, Somatization, and Mandibular Movements in TMD Patients and Controls

	TMD group (n = 45)	Controls (n = 30)	*P*
Depression, n (%)			
Normal	17 (37.8)	19 (63.3)	.018
Moderate	18 (40.0)	9 (30.0)	
Severe	10 (22.2)	2 (6.7)	
Somatization, n (%)			
Normal	27 (60.0)	19 (63.3)	NS
Moderate	8 (17.8)	9 (30.0)	
Severe	10 (22.2)	2 (6.7)	
Unassisted opening without pain, mean ± SD (mm)	45.68 ± 9.21	49.83 ± 7.20	.041
Maximum unassisted opening, mean ± SD (mm)	49.57 ± 6.73	49.83 ± 7.20	NS

SD = standard deviation; NS = nonsignificant. Depression: normal < 0.535; moderate 0.535–1.105; severe > 1.105; Somatization (pain items included): normal < 0.500; moderate 0.500–1.000; severe > 1.000.

Table 3 Unstimulated Salivary Flow Rate, Hyposalivation, and Dry Mouth Sensation in TMD Patients and Controls

	TMD group (n = 45)	Control group (n = 30)	*P*
Unstimulated salivary flow rate, mean ± SD (mL/min)	0.34 ± 0.17	0.46 ± 0.23	.010
Hyposalivation, n (< 0.1 mL/min)	1	1	NS
Dry mouth, n	3	2	NS

NS = nonsignificant; SD = standard deviation.

Table 4 Unstimulated Salivary Flow Rate with Respect to Presence of Depression, Somatization, Chronic Pain, and Restricted Mandibular Movements in TMD Patients (n = 45)

	n	Salivary flow rate mean ± SD (mL/min)	*P*
Depression			
With	28	0.38 ± 0.15	NS
Without	17	0.28 ± 0.19	
Somatization			
With	18	0.42 ± 0.14	.015
Without	27	0.29 ± 0.17	
Chronic pain			
With	22	0.37 ± 0.16	NS
Without	23	0.31 ± 0.17	
Restricted mandibular movements			
With	19	0.28 ± 0.18	.037
Without	26	0.39 ± 0.15	

NS = nonsignificant.

somatization (P = .015) (Table 4). Salivary output was not related to chronic pain (P = .208), depressive symptoms (P = .064), or any of the TMD subdiagnoses (ANOVA, F = 0.970, P = .416). Correlation analysis revealed that salivary flow in TMD patients was not correlated with range of pain-free opening (r_s = .073; P = .632) or maximal mandibular opening (r_s = 0.226; P = .136). In comparison to the controls, unstimulated salivary flow was lower in TMD patients with depressive symptoms, somatization, chronic pain, and restricted mandibular movements, but this difference was significant only for mandibular hypomobility, with a large effect size (P = .005, Cohen's d = 0.87). When an additional comparison was performed in subjects free from both depression and somatization, salivary output remained significantly lower in TMD patients with limited mandibular movements (n = 11; unstimulated salivary flow rate mean ± SD = 0.22 ± 0.15) than in the controls (n = 17; unstimulated salivary flow rate mean ± SD = 0.46 ± 0.24) (P = .006).

The results of the multivariate linear regression analysis are presented in Table 5. Somatization was retained as the independent predictor of unstimulated salivary flow values, irrespective of age, while limitation in mandibular movements was not a predictor of unstimulated salivary flow (P = .077).

Table 5 Factors Entered into the Multivariate Models (P < .05 on Bivariate Analysis) for Unstimulated Salivary Flow Rate

Model	R^2	B (95% CI)	β	P
1	0.182			
Somatization		0.100 (0.003–0.197)	0.295	.044
Restricted mandibular movements		−0.087 (−0.185–0.010)	−0.258	NS
2[a]	0.182			
Somatization		0.102 (0.002–0.201)	0.300	.047
Restricted mandibular movements		−0.089 (−0.188–0.011)	−0.262	NS

[a]Adjusted for age. B = regression coefficient; 95% CI = confidence interval; β = standardized regression coefficient; R^2 = coefficient of determination; NS = nonsignificant.

Discussion

The present study has shown that young adult women with TMD presented lower unstimulated salivary flow when compared with healthy controls. This finding was related to mandibular mobility and somatization, but not to TMD pain or depressive symptoms. Although there was lower salivary flow in the TMD sample, it was above the criteria for hyposalivation (< 0.1 mL/minute). However, it is still significant and warrants discussion in view of the influence on salivation caused by pain and co-related factors. When entered into the multivariate models, only somatization remained significant.

In order to control for age and gender, which can influence salivary flow, dry mouth sensation, and TMD signs and symptoms, the study included only adult women (aged 20 to 40 years). Additionally, exclusion criteria were applied to control for other factors known to impair salivary flow and/or cause xerostomia. Only unstimulated saliva was collected because it is present in the mouth for about 14 to 16 hours of the day and plays an important role in the maintenance of oral health. Furthermore, the unstimulated whole saliva flow rate has been proposed as a test of choice for detecting reduced salivary flow, since it may be reduced even when the stimulated whole saliva is unaffected.[33] Reduced salivary flow did not correspond to hyposalivation in this study; however, it is relevant as a factor associated with oral discomfort and xerostomia, common symptoms in chronic orofacial pain.[3] The TMD group included patients with and without TMD pain in order to investigate whether the presence of pain was related to salivary findings. Although pain is the most prominent symptom of TMD, barely half of the investigated TMD patients reported chronic TMD pain. This could partly be explained by the fact that a considerable portion of the patients consisted of dental students, who could be more aware of and seek advice/treatment for various TMD symptoms besides pain. In addition, patients with pain-related disability and/or psychological impairment more likely refused to participate or were excluded from the study for taking medications. The control group was selected without any regard to psychosocial status to mimic the general population, and the possible differences are more likely to be obscured than overestimated. Additional analysis for salivary findings, performed in comparison to controls without investigated psychosocial disturbances, showed similar findings.

The mean salivary flow rate of 0.46 ± 0.23 mL/minute in healthy females is within the values observed in previous studies.[34,35] Patients with TMD appeared to have lower salivary flow than the controls, but this value was still close to normal values. Although the differences in salivary flow values were statistically significant, a large inter-individual variation in salivary flow, indicated by a large SD, was observed in both groups. This variation in flow rate has also been previously documented and is in line with the findings of da Silva et al,[3] who reported lower unstimulated salivary output in orofacial pain patients, including those with TMD, compared to control subjects; in addition, TMD cases reported more oral complaints.[2,4,8] However, in the current study, only a few subjects had complaints of oral dryness or showed hyposalivation. This discrepancy in results may be attributed to the difference in study populations.

The nature of the relationship between TMD and salivary flow has not yet been identified. It has been suggested that central sensitization, which plays a role in chronic pain states, might be responsible for reduced unstimulated salivary secretion observed in patients with chronic orofacial pain.[3] Pain chronification due to activation in the central nervous system of limbic regions and including the hypothalamus and hypothalamic-hypophyseal-adrenal axis promotes the increase of release of cortisol and adrenaline, causing neurovegetative phenomena,[7] and the reduction of saliva secretion may occur as a neurovegetative effect. However, this could not be supported by the results of the present study, as no relation was found between unstimulated salivary flow rate and the presence, intensity, or duration of TMD pain. The disparity in findings between the current and previous study[3] might be related to many factors, including differences in age and gender ratio, type of pain condition,

additional medical diagnoses, use of medications, teeth loss, and/or wearing dentures. In addition, the absence of a relationship between pain symptoms and salivary output in the present study might partially be explained by less severe pain in the present patient population. In accordance with the current findings, Siviero et al[5] found that the most common neuropathic pain syndromes did not differ in unstimulated salivary output in comparison to age-matched controls.

Somatization has been suggested to be an underlying factor of diverse salivary complaints for which no organic pathologic cause can be found. Excessive salivation is a common complaint observed among patients with somatoform disease, but salivary flow measurements have failed to verify the presence of sialorrhea.[18] Salivary output in somatized patients was significantly higher in the TMD group in the present study, but was still similar to that of the controls. Somatization was the only factor that remained significant as an independent predictor of salivary flow rate. Repeated sampling technique and the combination of unstimulated/stimulated saliva could have improved the results in this aspect.

Evidence from human studies suggests that masticatory muscle activity with or without tooth contact stimulates salivary secretions from salivary glands,[22] while a prolonged decrease in mastication may diminish resting and stimulated salivary output.[23,24] Hemodynamic changes in the masseter muscle have been suggested to be related to altered salivary secretion in TMD patients.[11] Within the TMD group in the present study, salivary output was lower in patients showing restricted mandibular movements, and these results were confirmed with respect to healthy counterparts as well when somatization was eliminated. These findings support the hypothesis that limited mandibular movement might play a role in reduced salivation. However, when entered into the multivariate model, restriction in mandibular movement was not a predictor of unstimulated salivary flow. Stimulated whole saliva produced by chewing is a reflex secretion, which might be impaired in the presence of hypomobility and should be investigated in future studies.

There are several limitations in the present study that should be addressed. Variables that might also be considered when evaluating salivary findings in TMD patients are anxiety and stress, since these factors are related to lower salivary output,[15,17] are elevated in subjects with TMD,[12,36] and could be present independently of depressive disorders in some patients.[37] Secondly, the present study was limited to young adult women, so the findings cannot be generalized. Experimental sessions were done regardless of the menstrual phase, and possible effects of estrogen on salivary flow in a group of women of reproductive age cannot be neglected. Finally, the assessment of jaw mobility was based only on RDC/TMD parameters. These issues should be addressed in future studies.

Conclusions

Despite the limitations mentioned above, this study showed an association between TMD and lower salivary flow, but no evidence was found of its relationship with subjective oral dryness in young adult women. Salivary flow rates for women with TMD were approximately 26% lower than those for the healthy controls, but still close to normal values according to the literature. Somatization was the single variable to emerge from the evaluation of potential factors contributing to salivary output in TMD patients. The hypothesis that TMD patients would show decreased salivary flow and increased xerostomia and that these changes would be related to the experience of chronic pain or presence of depression could not be supported. Other studies must be designed to confirm the present findings and fully explain the mechanisms by which TMD exerts its effects on salivary gland function.

Acknowledgments

The authors declare no conflicts of interest.

References

1. Romero-Reyes M, Uyanik JM. Orofacial pain management: Current perspectives. J Pain Res 2014;7:99–115.
2. de-Pedro-Herráez M, Mesa-Jiménez J, Fernández-de-Las-Peñas C, de-la-Hoz-Aizpurua JL. Myogenic temporomandibular disorders: Clinical systemic comorbidities in a female population sample. Med Oral Patol Oral Cir Bucal 2016; 21:e784–e792.
3. da Silva LA, Teixeira MJ, De Siqueira JT, De Siqueira SR. Xerostomia and salivary flow in patients with orofacial pain compared with controls. Arch Oral Biol 2011;56:1142–1147.
4. Unell L, Johansson A, Ekbäck G, Ordell S, Carlsson GE. Prevalence of troublesome symptoms related to temporomandibular disorders and awareness of bruxism in 65-and 75-year old subjects. Gerodontology 2012;29:e772–e779.
5. Siviero M, Teixeira MJ, de Siqueira JT, Siqueira SR. Somesthetic, gustatory, olfactory function and salivary flow in patients with neuropathic trigeminal pain. Oral Dis 2010;16:482–487.
6. Nixdorf DR, John MT, Schierz O, Bereiter DA, Hellekant G. Self-reported severity of taste disturbances correlates with dysfunctional grade of TMD pain. J Oral Rehabil 2009;36: 792–800.
7. Chapman CR, Tuckett RP, Song CW. Pain and stress in a systems perspective: Reciprocal neural, endocrine, and immune interactions. J Pain 2008;9:122–145.

8. Osterberg T, Carlsson GE. Relationship between symptoms of temporomandibular disorders and dental status, general health and psychosomatic factors of 70-year-old subjects. Gerodontology 2007;24:129–135.
9. Moen K, Bertelsen LT, Hellem S, Jonsson R, Brun JG. Salivary gland and temporomandibular joint involvement in rheumatoid arthritis: Relation to disease activity. Oral Dis 2005;11:27–34.
10. Le Bell Y, Söderling E, Kirveskari P, Alanen P. Flow rate, pH and buffer capacity of whole saliva before and after treatment of TMJ dysfunction. Proc Finn Dent Soc 1985;81:226–229.
11. Doepel M, Söderling E, Ekberg EL, Nilner M, Le Bell Y. Salivary cortisol and IgA levels in patients with myofascial pain treated with occlusal appliances in the short term. J Oral Rehabil 2009;36:210–216.
12. Bertoli E, de Leeuw R. Prevalence of suicidal ideation, depression, and anxiety in chronic temporomandibular disorder patients. J Oral Facial Pain Headache 2016;30:296–301.
13. Fillingim RB, Ohrbach R, Greenspan JD, et al. Potential psychosocial risk factors for chronic TMD: Descriptive data and empirically identified domains from the OPPERA case-control study. J Pain 2011;12(suppl):T46–T60.
14. Reiter S, Emodi-Perlman A, Goldsmith C, Friedman-Rubin P, Winocur E. Comorbidity between depression and anxiety in patients with temporomandibular disorders according to the research diagnostic criteria for temporomandibular disorders. J Oral Facial Pain Headache 2015;29:135–143.
15. Bergdahl M, Bergdahl J. Low unstimulated salivary flow and subjective oral dryness: Association with medication, anxiety, depression, and stress. J Dent Res 2000;79:1652–1658.
16. Takiguchi T, Yoshihara A, Takano N, Miyazaki H. Oral health and depression in older Japanese people. Gerodontology 2016; 33:439–446.
17. Bergdahl J, Bergdahl M. Environmental illness: Evaluation of salivary flow, symptoms, diseases, medications, and psychological factors. Acta Odontol Scand 2001;59:104–110.
18. Votta TJ, Mandel L. Somatoform salivary complaints. Case reports. N Y State Dent J 2002;68:22–26.
19. Dworkin SF, LeResche L. Research diagnostic criteria for temporomandibular disorders: Review, criteria, examinations and specifications, critique. J Craniomandib Disord 1992;6: 301–355.
20. Fricton JR. Temporomandibular muscle and joint disorders. Pain: Clinical Updates 2004;12:1–6.
21. Schiffman E, Ohrbach R, Truelove E, et al. Diagnostic criteria for temporomandibular disorders (DC/TMD) for clinical and research applications: Recommendations of the International RDC/TMD Consortium Network and Orofacial Pain Special Interest Group. J Oral Facial Pain Headache 2014;28:6–27.
22. Thie NM, Kato T, Bader G, Montplaisir JY, Lavigne GJ. The significance of saliva during sleep and the relevance of oromotor movements. Sleep Med Rev 2002;6:213–227.
23. Hall HD, Merig JJ Jr, Schneyer CA. Metrecal-induced changes in human saliva. Proc Soc Exp Biol Med 1967;124:532–536.
24. Johansson I, Ericson T. Effects of a 900-kcal liquid or solid diet on saliva flow rate and composition in female subjects. Caries Res 1989;23:184–189.
25. Johansson AK, Johansson A, Unell L, Ekbäck G, Ordell S, Carlsson GE. A 15-yr longitudinal study of xerostomia in a Swedish population of 50-yr-old subjects. Eur J Oral Sci 2009;117:13–19.
26. Management of TMDs. In: De Leeuw R (ed). Orofacial Pain: Guidelines for Assessment, Diagnosis and Management, ed 4. Chicago: Quintessence, 2008:158–174.
27. LeResche L. Gender considerations in the epidemiology of chronic pain. In: Crombie IK, Croft PR, Linton SJ, LeResche L, Von Korff M (eds). Epidemiology of Pain. IASP: Seattle, 1999:43–52.
28. Gillborg S, Åkerman S, Lundegren N, Ekberg EC. Temporomandibular disorder pain and related factors in an adult population: A cross-sectional study in southern Sweden. J Oral Facial Pain Headache 2017;31:37–45.
29. Parvinen T. Stimulated flow rate in relation to size and sex. Proc Finn Dent Soc 1984;80:127–130.
30. Navazesh M. Methods for collecting saliva. Ann N Y Acad Sci 1993;694:72–77.
31. Sreebny LM, Valdini A. Xerostomia. Part I: Relationship to other oral symptoms and salivary gland hypofunction. Oral Surg Oral Med Oral Pathol 1988;66:451–458.
32. Toida M, Nanya Y, Takeda-Kawaguchi T, et al. Oral complaints and stimulated salivary flow rate in 1188 adults. J Oral Pathol Med 2010;39:407–419.
33. Wang SL, Zhao ZT, Li J, Zhu XZ, Dong H, Zhang YG. Investigation of the clinical value of total saliva flow rates. Arch Oral Biol 1998;43:39–43.
34. Prodan A, Brand HS, Ligtenberg AJ, et al. Interindividual variation, correlations, and sex-related differences in the salivary biochemistry of young healthy adults. Eur J Oral Sci 2015; 123:149–157.
35. Carvalho PM, Castelo PM, Carpenter GH, Gavião MB. Masticatory function, taste, and salivary flow in young healthy adults. J Oral Sci 2016;58:391–399.
36. Rollman GB, Gillespie JM. The role of psychosocial factors in temporomandibular disorders. Curr Rev Pain 2000;4:71–81.
37. Cowen PJ. Cortisol, serotonin and depression: All stressed out? Br J Psychiatry 2002;180:99–100.