

Burning Mouth Syndrome: A Comparative Cross-sectional Study

Abstract

Background and Aim: Burning mouth syndrome (BMS) may be defined as a burning sensation in the oral mucosa usually unaccompanied by clinical signs. Multiple conditions have been attributed to a burning sensation. The aim of this study was to determine the role of age and sex in BMS. **Materials and Methods:** A total of 195 consecutive patients with BMS and 95 healthy patients without burning sensation were recruited in this study. Patients with BMS had experienced oral, burning sensations for at least 6 months without oral clinical signs, and with a normal blood count. Multiple logistic regression analyses were utilized to define the main predictors. **Results:** Menopause, candidiasis, psychological disorders, job status, denture, and dry mouth were significantly frequent in BMS patients. Multivariate logistic regression indicated age (odds ratio (OR) = 1.12, 95% confidence interval (CI): 1.08–1.15, $P < 0.0001$) and sex (OR = 3.14, 95% CI: 1.4–6.7, $P < 0.002$) significantly increase the odds of BMS. Psychological disorders (OR = 3.39, 95% CI: 1.2–9.5, $P < 0.02$) and candidiasis remain as predictive factors. Ultimately, age was defined as a critical predictor. Moreover, we can therefore predict that a 60-year-old woman with psychological disorders is 25 times more likely to suffer from BMS than a man 10 years younger who has no psychological disorder. **Conclusion:** Age and sex were the main predictors in BMS. Psychological disorders and candidiasis were significantly associated with the occurrence of BMS.

Keyword: *Burning mouth syndrome, mouth disease, risk factors*

Introduction

Burning mouth syndrome (BMS) is a chronic oral dysesthesia characterized by a burning sensation of the oral cavity with clinically normal mucosa.^[1,2] BMS is an interesting condition as its etiology is multifactorial.^[1-13] The estimated prevalence of BMS reported in recent studies ranges between 0.7% and 15% in the general population, while it made up 10% of the outpatients of oral medicine clinics.^[3,5,7,12] The vast majority of affected persons are older than 50 years and there is a preponderance of women (male-to-female ratio between 1 and 4) that were postmenopausal or had experienced sex hormonal change.^[3,9-12]

Most patients experience burning sensations of moderate-to-severe intensity with mean severity of about 4.6–8 cm on a 0–10 cm visual analog scale.^[1,8,14-16] The tongue is the most common site of the complaint, though it may be accompanied by other parts of the mouth.^[5,6,8,9,16]

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Physiological and psychological factors play a role in causing and/or exacerbating BMS with continuum, but the interaction between these remains poorly understood.^[1-8,13,17-21] Many studies also reported adverse life events in the onset of disease.^[6,9,15] BMS has negative impacts on the quality of life, while a placebo or different treatments may improve their quality of life.^[14,15] Anxiety and depression were the common features in BMS patients.^[3-8,17-23] Other characteristics of BMS included cancer phobia, gastrointestinal problems, and chronic fatigue.^[3,21] Emotional and environmental stress makes them vulnerable to chronic pain. Vulnerability is associated with the onset and presentation of BMS, but the interaction in details is not ascertained.^[21] They also referred to “oral sensorial complaints”.^[24] The BMS group presented higher cortisol levels, K⁺ and amylase, nerve growth factor, substance P, and tryptase activity in the saliva.^[16,23-25] Different etiologic factors are postulated in the onset of BMS with different strengths. In spite of this point, patient management is unreliable. This is the first study performed to access age or sex as factor associated with BMS.

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The aim of this study was to explore different etiologic factors contributing to BMS and to estimate the magnitude of their value by considering age and sex in a comparative cross-sectional study.

Materials and Methods

One hundred and ninety-five patients presenting with BMS and 95 individual without this symptom participated in this prospective cross-sectional study. BMS patients had been consecutively referred to Oral Medicine and the Oral Diagnosis Clinic at the Guilan University of Medical Sciences from 2001 to 2010. A total of 156 women (72.9%) and 39 men (27.1%) in the BMS group were recruited in this study by estimating sample size with power 90% and 95% confidence interval (CI).^[21]

All the patients diagnosed with BMS exhibited clinically normal oral mucosa associated with a burning oral sensation which they had had for at least 6 months as inclusion criteria. Clinical examination was investigated by two professors in oral medicine and oral pathology.

A detailed demographic history was undertaken by interview and patients underwent a thorough clinical oral examination. Their medical history was recorded and verified by a physician. The possible underlying causes were investigated, and all patients underwent routine hematologic screening tests to rule out all possible organic etiologies (serum iron, total iron-binding capacity, Vitamin B12, hemoglobin count, folic acid, fasting blood glucose, and thyroid profile values).

None of the patients presented any evidence of malignancy, connective tissue, metabolic or infectious disorders, or vitamin deficiency. Patients with dentures were assessed for fitness, function, and candidiasis. Swabs for *Candida* were taken before the diagnosis was made. Those with candidiasis were treated with antifungal therapy with common products used in Iran (Nistat 100,000 I.U./ml, Jaber Ebne Hayyan, Tehran, Iran) and if their burning sensation continued, they were included in patient groups as inclusion criteria.

Psychiatric assessment was on the basis of past medical and/or psychiatric history (preceding diagnosis) and presented psychogenic symptoms which were confirmed with their physician. Xerostomia was determined by questionnaire comprised four essential questions.^[26]

As mentioned, it is postulated that gender and age have profound influences on BMS, hence a prospective, comparative, cross-sectional study was carried out to account for age and sex as predictors. The comparative group “without BMS” comprised 95 patients without any complaint of burning mouth who had sought dental treatment at the Department of Oral Medicine, Guilan University of Medical Sciences. The study protocol was approved by the local Ethical Committee (Guilan University of Medical Science)

and consent was obtained. The characteristics of BMS patients and non-BMS controls were transferred to data sheets (SPSS v 17.SPSS Inc., Chicago, IL, USA) and analyzed statistically. Chi-squared test and *t*-test were used to evaluate differences in group characteristics. Odd ratio and CI were estimated for each predictor. Backward logistic regression model was applied for significantly altered parameters. Hosmer–Lemeshow test as a goodness-of-fit models approved the predictors. Statistical significance was set at *P* < 0.05.

Results

Table 1 illustrates the general profile of the study population. There was an unequal gender distribution in favor of females; 156 women (72.9%) and 39 men (27.1%) in the BMS group. There was a difference in distribution of patients according to age group; with preponderance in the age ≥50 years, with the mean age (56 ± 13.9 years) which was significantly different from the mean age of the non-BMS group (35.4 ± 12.6 years), *P* < 0.0001 [Figure 1].

Table 1: Profile of burning mouth syndrome patients and comparative group

	BMS patients (n=195)	Non-BMS patients (n=95)	Total
Sex			
Female	156 (80)	58 (61.05)	214
Male	39 (20)	37 (38.95)	76
Age			
<50	55 (28.20)	80 (84.21)	135
>50	140 (71.79)	15 (15.78)	155
Job			
Homemakers (jobless)	129 (66.15)	30 (31.57)	159
Employee	66 (33.84)	65 (68.42)	131
Residency			
Urban	171 (87.69)	89 (93.68)	260
Rural	24 (12.30)	6 (6.31)	30

BMS: Burning mouth syndrome

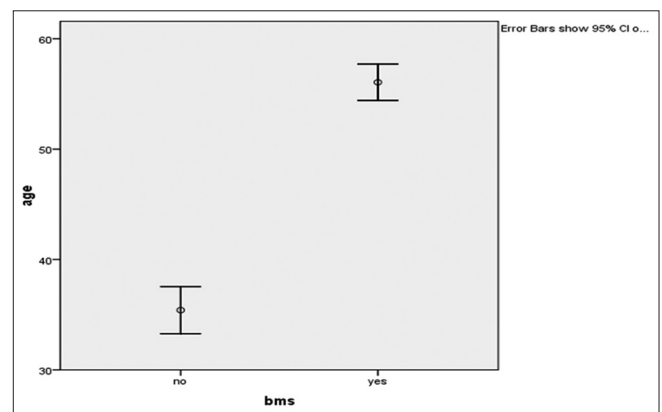


Figure 1: Comparison of age in burning mouth syndrome and nonburning mouth syndrome

The univariate analyses [Table 2] showed that menopause (OR = 20.72 95% CI: 8.32–51.61) was significantly associated with, while early indications of candidiasis (OR = 7.42 95% CI: 2.27–24.72), psychological disorders (OR = 5.45, 95% CI: 2.38–12.48), job status (OR = 4.23 95% CI: 2.50–7.5) ($P < 0.0001$), and sex, denture ($P < 0.001$) accompanied with dry mouth ($P < 0.002$) by order of mention exhibited higher incidence odd ratios for BMS. Stepwise multivariate logistic regression analysis was undertaken to estimate the relationship between the variables that were statistically significant in univariate analysis. This part was made up of two steps with subtle distinction. In the first step, the role of factors assessed in both sexes revealed that, age, sex, and psychogenic factors can be predictor factors of BMS in both sexes [Table 3]. The second step focused on the role of factors by excluding menopause from univariate remaining factors (special features for sex). Table 4 shows that only age remains as a predictor in BMS. Psychological disorders show less strength odd in this step but are kept as predictors. By taking outcomes into consideration in hierarchical approach, age is the specific ultimate measure which is significantly associated with

the onset of a disease, but after that psychogenic disorder may could be another risk factor which may increase the odds of BMS. Goodness-of-fit models were checked by the Hosmer–Lemeshow test ($P = 0.931$ and $P = 0.793$). By means of calculation based on Table 4, we can predict that the susceptibility (probability) of BMS in women may increase >3.38 fold by rise in age per decade (OR = 3.38, 95% CI: 2.39–4.8) and we can predict that a 60-year-old woman with a psychological disorder is 8.9 times more likely to suffer from BMS than a 50-year-old woman without psychological disease (OR = 8.9, 95% CI: 6.33–12.75). Based on Table 3, we can anticipate that a 60-year-old woman with a psychological problem is 25 times more susceptible to BMS than a 50-year-old man without a psychological problem (OR = 25, 95% CI: 19.76–33.4).

More than 70% of patients complained of burning sensation in their oral cavity with no distinct part (71.7%); tongue (12.8%): anterior part (46%), the lateral border of tongue (43%), and the center of the tongue (11%); lips and gingiva (2.5%).

Discussion

This study pointed out the importance of risk factors in BMS. The condition is complex and generated considerable debate. Eliciting predictors and highlighting them is of paramount importance in patient management. This study provides a new insight into these issues, defines that age and sex are the critical risk factors and has a substantial correlation with the occurrence of BMS.

Different studies implicitly acknowledge that patients in their mid to late fifties are prone to the burning sensation.^[3,6-10,12-23] However, different methodological research applied could only mention that patients with BMS are of older age without determining and outweighing this important risk factor. On the basis of multiple logistic regressions in this nonmatch cross-sectional study,

Table 2: Odds ratios and confidence intervals: Univariate analysis

Risk factors	OR	95% CI	P	Type of statistics
Menopause	20.72	8.32-51.61	0.0001	Chi-square test
Candidiasis	7.42	2.22-24.72	0.0001	Chi-square test
Psychological disorders	5.45	2.38-12.48	0.0001	Chi-square test
Job (homemakers)	4.23	2.50-7.5	0.0001	Chi-square test
Denture	3.45	1.56-7.64	0.0001	Chi-square test
Xerostomia	2.94	1.45-5.94	0.002	Chi-square test
Gender (female)	2.55	1.48-4.38	0.001	Chi-square test
Age	-	-	0.0001	t-test

OR: Odds ratio; CI: Confidence interval

Table 3: Backward Wald stepwise multiple logistic regression coefficient of odds ratio and confidence

Variables	B	SE	Wald	Significant	Exp (B)	95.0% CI for EXP (B)	
						Lower	Upper
Psychogenic factors	1.122	0.484	5.387	0.020	3.072	1.191	7.924
<i>Candida</i>	1.341	0.785	2.919	0.088	3.824	0.821	17.817
Age	0.098	0.013	53.782	0.000	1.103	1.075	1.133
Sex (female)	1.139	0.373	9.346	0.002	3.124	1.505	6.483
Constant	-4.850	0.689	49.498	0.000	0.008		

CI: Confidence interval; SE: Standard error

Table 4: Stepwise multiple logistic regression coefficient of odds ratio and confidence for variables

Variables	B	SE	Wald	Significant	Exp (B)	95.0% CI for Exp (B)	
						Lower	Upper
Psychogenic factors (1)	0.976	0.572	2.916	0.088	2.654	0.866	8.137
Age	0.122	0.018	46.471	0.000	1.130	1.091	1.170
Constant	-4.618	0.771	35.892	0.000	0.010		

Variable(s) entered on Step 1: Psychogenic factors, age, and menopause. CI: Confidence interval; SE: Standard error

results pointed out that age was a consistent predictor; the probability of BMS increases by passing decades of life. Gender difference was addressed in different studies;^[1,3-6,8-23] however, investigation into this issue was verified by outcomes; identifying that sex is the main risk factor to increase the odds of BMS. The male-to-female ratio in BMS group was 1:4. The female preponderance is in accordance with almost all studies.^[1,5,6,9,10]

Menopause is absolutely critical and accounted for the main predictor in concern to outcomes, in univariate analysis, provide support to other studies.^[1,3-14,21] The criterion for postmenopause was the time after which a woman has experienced 12 consecutive months of amenorrhea (lack of menstruation) without a period. Due to this phenomenon, women may be liable to physical and emotional changes including vasomotor changes (hot flushes, profuse perspiration, and palpitation), psychogenic disorders (depression, tiredness, irritability), and other complaints such as headaches.^[9] Different reports offer the prevalence of BMS as about 17.9%–93% in postmenopausal women.^[9] However, hormone supplement therapy could alter burning sensation in different studies without eliminating it completely.^[1,3,4,6,8,9,12] Virtually as a whole, young women who present multiple etiologic factors rarely experience BMS.

This investigation also verified that psychological disorders increase the chance of BMS especially in females, making them 25 times more susceptible than male. Although recent research indicates that psychological factors play a role in causing or exacerbating BMS, this study provides support that strengthens the role and odds of psychogenic disorders.

Different studies claim that patients with BMS suffered from psychological disorders.^[1,3-9,11,12,16-23] Psychological disorders, especially depression and anxiety, are the most common features reported in different studies. Psychological disturbances and adverse life events can decrease the patient's tolerance, making them more susceptible to different chronic diseases.^[1,3,5-8,10,15,18,19,22,23] Rational treatments are relying on controlling this causal factor. Although relief in different studies has been reported, nevertheless success in treatment with permanent remission dooms to failure and patients are always seeking for further medications.^[1,3,5,7,8,9,16,27,28] On the other hand, this study apparently showed that age and sex are inevitably the underlying risk factors which are out of control. Eventually, reasons for failure in treatment need to be explained to patients before initiating treatment.

Job status or in detail homemakers revealed a significant association within BMS and 66% of patients with BMS were unemployed. Implicitly, Grushka pointed out that a person's job may have an effect on BMS.^[13] Unemployed females older in age with postmenopausal history with or without psychological disorders may feel insecure and this

circumstance may rise the chance of BMS in them more than in fully employed women. It was verified by another study investigating into etiologic factors implicitly as adverse life events.^[6,13,21]

Significant relationship between candidiasis and BMS has been defined in this study; 19% of BMS patients had been treated for candidiasis. Many studies stated that patients are often triggered by other predisposing factors such as wearing a denture or having xerostomia.^[5,9,11,13,29] It was proposed that at least one-third of patients attributed the onset of their syndrome to a previous illness or a course of antibiotics or candidiasis.^[30] In this study, 24% of the patients with BMS used dentures though there were no ill-fitting dentures or other problems to cause candidiasis infection. Zegarelli indicated that 30% of patients were treated for candidiasis in relation to BMS,^[11] but another study showed that there was no significant relation between candidiasis and BMS. Twenty-two study on etiologic factors stated that parafunctional habits may elucidate an association with on BMS.^[6]

Another possible risk factor for BMS is xerostomia. There was a significant relationship between xerostomia and BMS in this investigation; 27% of BMS patients suffered from xerostomia. Many studies indicated that xerostomia was a principal contributing factor.^[1,3,9,6,10-12,23,29]

Most patients perceived burning in the whole oral cavity or in more than one site. This is an interesting finding and may be attributed to the culture of the respondents or the type of question. Nevertheless, we do not quantify pain in this study, and it was the limitation of the present study; therefore, a question may arise in concern to whether multiple etiologic factors increase the severity of the burning perception? Further studies need to assess pain by multiple conditions. The subsidiary sites of BMS were the tongue, especially the anterior part of the tongue. Different authors have shown that burning sensation can be reported in each location and in more than one site or in the whole mouth. They found that the tongue, especially its anterior part, the dorsum, and the anterior lateral margins are the most frequently affected areas.^{[1]-[3,5-7,13,14,16,18,25-29]} Although studies reveal that gustatory and somatosensory pain perception may decrease in BMS patients, especially in the tongue.^[31]

Conclusion

In this comparative study, in the absence of local and systemic underlying factors, we conclude that age and sex are the main factors in the onset of BMS. Postmenopausal women with psychological disorders may have higher likelihood for BMS. Other predictors such as candidiasis, job status, denture, and xerostomia revealed association by different odds for the occurrence of BMS strength to cause BMS.

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Conflicts of interest

There are no conflicts of interest.

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