Journal of Dental Sciences 20 (2025) 2245–2249

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-jds.com

Original Article

Increased medications in the aged patients with burning mouth syndrome: A potentially overlooked risk factor

Chun-Pin Chiang [a,b,c,d], Chih-Chung Chien [e], Yu-Hsueh Wu [f,g*]

[a] *Department of Dentistry, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan*
[b] *Institute of Oral Medicine and Materials, College of Medicine, Tzu Chi University, Hualien, Taiwan*
[c] *Graduate Institute of Oral Biology, School of Dentistry, National Taiwan University, Taipei, Taiwan*
[d] *Department of Dentistry, National Taiwan University Hospital, College of Medicine, National Taiwan University, Taipei, Taiwan*
[e] *Department of Dentistry, Far Eastern Memorial Hospital, New Taipei City, Taiwan*
[f] *Department of Stomatology, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan*
[g] *Institute of Oral Medicine, School of Dentistry, National Cheng Kung University, Tainan, Taiwan*

Received 7 June 2025
Available online 18 June 2025

KEYWORDS
Burning mouth syndrome;
Medications;
Polypharmacy

Abstract *Background/purpose:* Burning mouth syndrome (BMS) is a chronic oral mucosal burning and pain disorder, predominantly affecting the middle-aged and elderly women. This study aimed to explore the association between polypharmacy and BMS, with consideration of the patients' age and sex.
Materials and methods: Medical data from 115 BMS patients and 115 age- and sex-matched control subjects were collected. Medications were categorized into four groups based on the number of medications taken. The chi-square test, Student's *t*-test, and binary logistic regression were performed to evaluate the association between polypharmacy and BMS, after adjustment for age and sex.
Results: A higher proportion of individuals with medications was observed in the BMS group than in the control group ($P = 0.0015$). Among BMS patients, the older group ($\geq$ 65 years), especially the female BMS patients, tended to take more medications. Binary logistic regression analysis revealed a significant association between polypharmacy and increased odds of having BMS. After adjustment for age and sex, the patients in the minor polypharmacy group (1–4 medications) had significantly higher odds of having BMS compared to those in the non-pharmacy group (no medications), with an adjusted odds ratio of 5.015 ($P < 0.001$).

* Corresponding author. Institute of Oral Medicine, School of Dentistry, College of Medicine, National Cheng Kung University, No. 1, University Road, Tainan City 701, Taiwan.
E-mail address: z10908025@ncku.edu.tw (Y.-H. Wu).

https://doi.org/10.1016/j.jds.2025.06.008

Conclusion: These findings suggest a potential association between multiple medications and the risk of having BMS and supported the need to consider polypharmacy as a contributing factor for the older BMS patient. However, future studies should be conducted to explore the exact dose—response trend and the influence of other associated factors on BMS.

Introduction

Burning mouth syndrome (BMS) is a chronic pain disorder characterized by a recurring burning, scalded or stinging sensation affecting the clinically normal-appearing oral mucosa for more than three months.[1] Affected individuals may also report sensations of oral dryness or altered taste, such as a bitter or metallic flavor. These symptoms may be aggravated by hot, spicy, or irritating foods and beverages.[2] Though BMS can involve any region of the oral mucosa, the tongue, particularly the tip and lateral borders, is the most frequently affected site, followed by the hard palate and the lower labial mucosa.[2,3]

The prevalence rate of BMS in the general population ranges from 0.11% to 5.4%, with variation reported across different studies.[4–6] It has been shown to be more common in the middle-aged and elderly individuals, with women more frequently affected than men.[3,7] BMS has a significant impact on patients' daily lives.[8] The persistent discomfort and prolonged disease courses often lead to frustration.[9] The absence of remarkable mucosal findings makes the condition difficult to diagnose and treat, leaving patients feeling helpless. Despite its clinical relevance, the etiology of BMS remains poorly understood. Various local, systemic, neurological, and psychological factors have been proposed, reflecting its multifactorial nature.[3,10] This complexity may contribute to the variability in treatment outcomes and challenge effective management.[2]

Medication is one of the proposed associated factors.[6,10] Besides, the elderly are generally considered to be the frequent users of medications.[11] Thus, it is noteworthy to explore medication use in BMS patients, who are predominantly middle-aged and elderly individuals. Soares et al. reported an increased number of medications used in the BMS patients, with 95% identified as xerogenic agents.[12] Our previous study demonstrated that a substantial proportion of BMS patients exhibited polypharmacy, with older individuals, particularly older female BMS patients, showing a higher mean number of medications used. Psychotropics, gastroprotectors and gastrointestinal tract (GI)-associated drugs, and antihypertensives were the most frequently used drug classes.[13] These findings may suggest that medications, especially multiple medications, may play an important role in the development of BMS, especially for the older female BMS patients. Therefore, this study aimed to further explore the associations between polypharmacy and BMS, with consideration of the patients' age and sex.

Materials and methods

Patient selection

This study was reviewed and approved by the Institutional Review Board at the National Cheng Kung University Hospital (IRB number: B-ER-109-420). A total of 115 patients diagnosed with BMS, aged between 45 and 80 years, were recruited from the Department of Dentistry at National Cheng Kung University Hospital (Tainan City, Taiwan) and the Far Eastern Memorial Hospital (New Taipei City, Taiwan). Each participant underwent a clinical interview followed by a comprehensive oral examination performed by an oral pathologist or a qualified dentist. Standardized clinical examinations were conducted using cotton swabs, tongue depressors, and mouth mirrors under adequate illumination.

Inclusion criteria consisted of patients reporting persistent symptoms associated with BMS (recurring burning, scalded or stinging sensation, oral dryness, or altered taste) of the oral mucosa for a minimum duration of six months, in the absence of any clinically apparent oral mucosal lesions. The diagnosis of BMS was established not only based on the lack of visible oral mucosal abnormalities but also through the exclusion of any systemic disease or condition that may cause insidious oral mucosal disorders, such as a history of cigarette smoking, betel quid chewing, or autoimmune diseases (systemic lupus erythematosus, rheumatoid arthritis, Sjögren's syndrome, pemphigus vulgaris, cicatricial pemphigoid, etc.). Additionally, none of the patients had received any prescription medications for BMS within at least three months prior to enrollment.

For comparison purposes, data from 115 age- and sex-matched individuals without BMS were collected to serve as the control subjects. These control subjects were randomly selected from the dental patients who visited the outpatient department at the National Cheng Kung University Hospital for routine dental treatment.

Data collection and processing

The patients' medical and dental histories, as well as their psychosocial statuses, were carefully reviewed, collected, and documented, with particular attention to their medication records. Regarding medications, drugs prescribed for short-term or sporadic illnesses, such as antibiotics or analgesics, were excluded from analysis. In addition, the medications initiated after the onset of BMS, or those taken specifically to relieve BMS symptoms, were also excluded.

The medications prescribed were recorded to evaluate the association between the number of medications taken and BMS. The BMS patients were categorized into four groups based on their medication usage: non-pharmacy (no medication), minor polypharmacy (1–4 medications), polypharmacy (5–8 medications), and excessive polypharmacy (≥ 9 medications).[11]

Statistical analysis

The chi-square goodness-of-fit test was used to evaluate whether the distribution of BMS patients across different medication count groups (non-pharmacy, minor polypharmacy, polypharmacy, and excessive polypharmacy) was statistically uniform. The chi-square test of independence was applied to compare the status of medication use (with or without use of medications) between BMS patients and control subjects. It was also used to assess whether the distribution of medication count groups differed significantly between male and female BMS patients. The Student's *t*-test was performed to examine differences in the mean number of medications taken between BMS patients and control subjects, as well as between relatively younger (45–64 years) and older (≥ 65 years) BMS patients. The same test was also applied separately within each sex group to compare the younger and older subgroups of BMS patients. Binary logistic regression analysis was conducted to evaluate the association of medication count, age, and sex with the likelihood of BMS diagnosis. The results were considered significant if the *P*-value was less than 0.05.

Results

The mean age of the 115 BMS patients was 62.8 years. Of the 115 BMS patients, 29 were men and 86 were women. The observed distribution of 115 BMS patients across the four medication count groups significantly deviated from the expected uniform distribution ($P < 0.001$, Table 1). There was no significant difference observed in the distribution of four different medication count groups between 29 male and 86 female BMS patients ($P = 0.164$, Table 1). Because the number of the male BMS patients was relatively small (n = 29), the interpretation of the results may be limited. Moreover, the proportion of individuals with medications was significantly higher in the BMS patients (n = 100, 87.0%) than in the control subjects (n = 79, 68.7%, $P = 0.0015$) (Table 1). These results indicated a potential association of an increased medication use with the BMS, suggestive of a trend toward increased medication use in the BMS patients.

The mean number of medications taken was 5.08 ± 6.14 in the 115 BMS patients and 4.16 ± 4.03 in the 115 control subjects ($P = 0.180$, Table 2). Despite no significant difference, the mean number of medications taken was higher in the BMS patients than in the control subjects. Among 115 BMS patients, the mean number of medications use was significantly higher in the older age group (≥ 65 years, n = 50) compared to the relatively younger age group (45–64 years, n = 65) ($P = 0.002$, Table 2). When stratified by the sex, a significant age-related difference in the medication use was observed in the 86 female BMS patients ($P = 0.002$, Table 2). For the 29 male BMS patients, although the mean number of medication was higher in the older age group (≥ 65 years, n = 12) than in the relatively younger age group (45–64 years, n = 17), the difference was not significant ($P = 0.479$, Table 2).

A binary logistic regression analysis was conducted to evaluate the association of the age, sex, and medication count groups with the likelihood of having BMS. The male sex, relatively younger age group, and the non-pharmacy group were set as the reference groups. The overall effect of the four medical count groups of 115 BMS patients was statistically significant ($P < 0.001$, Table 3), indicating that the increased number of medications was significantly associated with the outcome (BMS). Furthermore, compared to the non-pharmacy group, the minor polypharmacy group showed a significantly elevated odds ratio (odds ratio (OR) = 5.015, 95% confidence interval (CI): 2.330–10.797, $P < 0.001$, Table 3). Although there was no statistically significant difference at the conventional level ($P < 0.05$), the polypharmacy group exhibited a marginally significant association with an increased risk of having BMS (OR = 2.066, 95% CI: 0.922–4.630, $P = 0.078$, Table 3). Similarly, the excessive polypharmacy group also demonstrated an increased risk of having BMS (OR = 2.203, 95%

Table 1 Distribution of the 115 patients with burning mouth syndrome (BMS) and 115 control subjects by the sex and the number of medications used.

Group	Patient number (%)				*P*-value
	Non-pharmacy (no medication)	Minor polypharmacy (1–4 medications)	Polypharmacy (5–8 medications)	Excessive polypharmacy (≥9 medications)	
BMS patients (n = 115)	15 (13.0)	54 (47.0)	28 (24.3)	18 (15.7)	<0.001[a]
Male (n = 29)	5 (4.3)	14 (12.2)	8 (7.0)	2 (1.7)	0.164[b]
Female (n = 86)	10 (8.70)	40 (34.8)	20 (17.4)	16 (13.9)	
Control subjects (n = 115)					
Male (n = 29)	9 (7.8)	8 (7.0)	7 (6.1)	5 (4.3)	0.872[b]
Female (n = 86)	27 (23.5)	18 (15.7)	26 (22.6)	15 (13.0)	

[a] Chi-square goodness-of-fit test.
[b] Chi-square test of independence.

Table 2 Stratified comparison of the mean number of medications taken by the 115 patients with burning mouth syndrome (BMS) and 115 control subjects according to different sex and age groups.

Groups	Mean medications ± Standard deviation			*P*-value[a]
	Total (n = 115)	Male (n = 29)	Female (n = 86)	
BMS patients				
45–64 years	3.51 ± 3.48 (n = 65)	3.53 ± 3.20 (n = 17)	3.50 ± 3.60 (n = 48)	
≥65 years	7.12 ± 8.03 (n = 50)	4.58 ± 4.72 (n = 12)	7.92 ± 8.72 (n = 38)	
P-value[a]	0.002	0.479	0.002	
BMS patients	5.08 ± 6.14 (n = 115)	3.97 ± 3.86 (n = 29)	5.45 ± 6.72 (n = 86)	0.261
Control subjects	4.16 ± 4.03 (n = 115)	4.14 ± 4.39 (n = 29)	4.16 ± 3.93 (n = 86)	0.977
P-value[a]	0.180	0.874	0.126	

[a] Student's *t*-test.

Table 3 Binary logistic regression analysis of burning mouth syndrome (BMS) risk based on demographic characteristics and the number of medications used for the 115 BMS patients.

Variable	Odds ratio [95% confidence interval]	*P*-value
Sex		0.958
Male	Reference	
Female	1.017 [0.544, 1.899]	
Age		0.875
45–64 years	Reference	
≥65 years	0.997 [0.963, 1.032]	
Groups		<0.001
Non-pharmacy (no medication)	Reference	
Minor polypharmacy (1–4 medications)	5.015 [2.330, 10.797]	<0.001
Polypharmacy (5–8 medications)	2.006 [0.922, 4.630]	0.078
Excessive polypharmacy (≥9 medications)	2.203 [0.880, 5.518]	0.092

CI: 0.880–5.518, Table 3), although the association reached only a marginally significant level ($P = 0.092$). Neither the sex nor the age showed a significant association with the outcome ($P = 0.958$ and $P = 0.875$, respectively) (Table 3). These findings suggest an association between the increased medication use and the risk of having BMS, after adjustment for the age and the sex.

Discussion

In this study, we found that an increased medication use was significantly associated with the risk of having BMS. Compared to BMS patients without medication, those with any level of medication use demonstrated an increased risk of having BMS, even after adjusting for the age and the sex. While the risk of having BMS was most pronounced in the minor polypharmacy group, the BMS patients in higher medication groups (the polypharmacy and excessive polypharmacy groups) also showed elevated risks of having BMS with marginal significance.

It is generally considered that BMS is more prevalent among middle-aged and older individuals.[3,7] Nevertheless, based on the findings of this study, it might suggest that the increased medication use, instead of the age itself, is the key associated factor of having BMS; that is, the higher prevalence of BMS in the older adults may be attributed to the greater number of medications taken by this age group of patients, rather than to the aging process itself as an independent risk factor. Moreover, the cumulative exposure to certain medication has been proved to be an associated factor of some diseases or adverse health conditions.[14,15] However, the associated research about BMS is so scarce that the lack of comprehensive investigation makes the exact relationship between the cumulative exposure effect and BMS being validated. Our results showed that the older patients tended to take more medications and this in turn increased the likelihood of developing BMS. This challenges the traditional age-based interpretation and highlights the need to consider polypharmacy as a key underlying contributor in the pathogenesis of BMS.

Moreover, we observed no significant difference in the mean number of medications taken between male and female BMS patients. These findings failed to explain the higher prevalence of BMS in women than in men, but pointed out the involvement of other biological or systemic variables, such as sex hormonal influence or deficiencies in vitamins or other hematinics.[16–18] These observations underscore the multifactorial nature of BMS, where systemic, local, psychological, and pharmacological factors are involved in the development of BMS.[3,10,19]

In conclusion, a higher proportion of individuals with medications was observed in the BMS group than in the control group ($P = 0.0015$). Among the BMS patients, the older group ($\geq$ 65 years), especially the female BMS patients, tended to take more medications. Binary logistic regression analysis revealed a significant association between polypharmacy and increased odds of having BMS. After adjustment for the age and the sex, the patients in the minor polypharmacy group (1—4 medications) had significantly higher odds of having BMS compared to those in the non-pharmacy group (no medications), with an adjusted odds ratio of 5.015 ($P < 0.001$). This study mainly focused on those middle-aged or elderly BMS patients, so that the inclusion criterion restricted participants to those aged 45 years and older. As a result, the impact of young age groups on the risk of having BMS could not be fully assessed. Our previous study has addressed the difference in the mean blood hemoglobin, serum levels of vitamin B12, folic acid and iron between the younger and the older BMS patients.[20] Future studies including the BMS patients with a broader age range are required to further confirm whether the polypharmacy factor persists to cause an increased risk of having BMS in all age groups of subjects. Moreover, other proposed factors to date may merit incorporation into the analysis to clarify their interactions and the underlying mechanisms among them.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

Acknowledgments

This study was partially supported by the grant [NSTC 111-2314-B-006-037-MY2] and [MOST 110-2314-B-006-015] from the National Science and Technology Council, Taiwan.

References

1. Chmieliauskaite M, Stelson EA, Epstein JB, et al. Consensus agreement to rename burning mouth syndrome and improve International Classification of Diseases-11 disease criteria: an international Delphi study. *Pain* 2021;162:2548—57.
2. Savage NW, Boras VV, Barker K. Burning mouth syndrome: clinical presentation, diagnosis and treatment. *Australas J Dermatol* 2006;47:77—81. quiz 82-3.
3. Sun A, Wu KM, Wang YP, et al. Burning mouth syndrome: a review and update. *J Oral Pathol Med* 2013;42:649—55.
4. Bergdahl M, Bergdahl J. Burning mouth syndrome: prevalence and associated factors. *J Oral Pathol Med* 1999;28:350—4.
5. Kohorst JJ, Bruce AJ, Torgerson RR, Schenck LA, Davis MDP. The prevalence of burning mouth syndrome: a population-based study. *Br J Dermatol* 2015;172:1654—6.
6. Brailo V, Vuéiaeeviae-Boras V, Alajbeg IZ, et al. Oral burning symptoms and burning mouth syndrome-significance of different variables in 150 patients. *Med Oral Patol Oral Cir Bucal* 2006;11:E252—5.
7. Rabiei M, Kasemnezhad E, Masoudi Rad H, Shakiba M, Pourkay H. Prevalence of oral and dental disorders in institutionalised elderly people in Rasht, Iran. *Gerodontology* 2010;27:174—7.
8. Souza FT, Santos TP, Bernardes VF, et al. The impact of burning mouth syndrome on health-related quality of life. *Health Qual Life Outcome* 2011;9:57.
9. Barker KE, Savage NW. Burning mouth syndrome: an update on recent findings. *Aust Dent J* 2005;50:220—3. quiz 288.
10. Coculescu EC, Tovaru S, Coculescu BI. Epidemiological and etiological aspects of burning mouth syndrome. *J Med Life* 2014;7:305—9.
11. Walckiers D, Van Der Heyden J, Tafforeau J. Factors associated with excessive polypharmacy in older people. *Arch Public Health* 2015;73:50.
12. Soares MS, Chimenos-Küstner E, Subirá-Pifarrè C, Rodríguez De Rivera-Campillo ME, López-López J. Association of burning mouth syndrome with xerostomia and medicines. *Med Oral Patol Oral Cir Bucal* 2005;10:301—8.
13. Wu YH, Chiang CP. Association of medications with burning mouth syndrome in Taiwanese aged patients. *J Dent Sci* 2023;18:833—9.
14. Han L, Agostini JV, Allore HG. Cumulative anticholinergic exposure is associated with poor memory and executive function in older men. *J Am Geriatr Soc* 2008;56:2203—10.
15. Sylvestre MP, Abrahamowicz M, Čapek R, Tamblyn R. Assessing the cumulative effects of exposure to selected benzodiazepines on the risk of fall-related injuries in the elderly. *Int Psychogeriatr* 2012;24:577—86.
16. Dahiya P, Kamal R, Kumar M, et al. Burning mouth syndrome and menopause. *Int J Prev Med* 2013;4:15—20.
17. Wu YH, Jin YT, Wu YC, et al. Anemia, hematinic deficiencies, and hyperhomocysteinemia in male and female burning mouth syndrome patients. *J Dent Sci* 2022;17:935—41.
18. Chiang CP, Wu YH, Wu YC, et al. Anemia, hematinic deficiencies, hyperhomocysteinemia, and serum gastric parietal cell antibody positivity in 884 patients with burning mouth syndrome. *J Formos Med Assoc* 2020;119:813—20.
19. Jin YT, Wu YH, Wu YC, et al. Higher gastric parietal cell antibody titer significantly increases the frequencies of macrocytosis, serum vitamin B12 deficiency, and hyperhomocysteinemia in patients with burning mouth syndrome. *J Dent Sci* 2022;17:57—62.
20. Wu YH, Wu YC, Chang JY, et al. Anemia, hematinic deficiencies, and hyperhomocysteinemia in younger and older burning mouth syndrome patients. *J Dent Sci* 2022;17:1144—50.