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Brief report

# Burning mouth syndrome and oral microbiota: A review

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**Abstract.** *Background and aim:* Burning mouth syndrome (BMS) is a chronic condition characterized by intraoral burning or dysesthetic sensations without evident causative lesions. The etiology of BMS remains unclear, and effective treatments are lacking. This review aimed to evaluate the correlation between BMS and oral microbiota by analyzing relevant studies. *Methods:* A literature search was conducted in PubMed, Embase, and Scopus databases from inception until 11 June 2023. *Results:* Two studies were identified, providing preliminary evidence of this association. The first study compared the oral microbial profiles of patients with primary BMS and healthy controls, revealing lower microbial diversity in the BMS group and specific microbial taxa associated with BMS. The second study assessed the incidence of oral infections in BMS patients and their impact on symptoms, finding no significant correlation between oral infections and BMS symptoms. *Conclusions*: The findings suggest a potential association between oral microbiota and BMS, with alterations in the oral microbial community possibly contributing to BMS pathogenesis. Disease-specific microbial markers may have diagnostic implications for BMS. However, the limited number of studies and heterogeneity among them emphasize the need for further well-designed research employing larger sample sizes, standardized methodologies, and consistent diagnostic criteria. (www.actabiomedica.it)

**Key words:** burning mouth syndrome, oral microbiota, oral bacteria

## Introduction

Burning mouth syndrome (BMS) is defined as an "intraoral burning or dysesthetic sensation, recurring daily for more than 2 h per day over more than 3 months, without evident causative lesions on clinical examination and investigation" (The Orofacial Pain Classification Committee 2020). The condition can be debilitating, leading to difficulty in eating, speaking, and performing daily activities, and can significantly impact the quality of life of affected individuals. The prevalence of primary BMS varies greatly and depends on the geographical area under consideration (1-3); globally it was estimated at around 1.73% (4). Despite being recognized as a distinct clinical entity for more than a century, the underlying causes of BMS are not yet fully understood, and effective treatments remain elusive (5). Recent studies have suggested that the gut microbiota may play a crucial role in regulating immune, neural, endocrine, and metabolic signalling pathways that contribute to the development of neuropathic pain (6). Alterations in gut microbiota are also associated with an anti-inflammatory state and were linked to reduced neuropathic pain (7). For what concern oral microbiota, which correlates well with gut microbiota from stools (8), is known to play a crucial role in maintaining oral health, taste perception (9) and its disruption has been implicated in various oral and

systemic diseases (10-12). It is suggested that oral microbiota may play a role in the development and pathogenesis of BMS (13-15). Understanding the potential role of oral microbiota in developing and progressing BMS could lead to developing novel diagnostic and therapeutic approaches for this debilitating condition. In this article, we will review the current state of the literature on the association between BMS and oral microbiota, summarize the key findings from relevant studies, and. This review aims to investigate the correlation between burning mouth syndrome (BMS) and oral microbiota. A comprehensive search strategy was employed to identify relevant studies. The selected studies were assessed for quality and data were synthesized to provide a comprehensive overview of the current evidence on the topic. The findings from this review will contribute to our understanding of the potential role of oral microbiota in the etiology of BMS discussing the possible implications for the diagnosis, management, and future research directions in BMS.

## Methods

A literature search was conducted in PubMed, Embase, and Scopus databases from inception until 11 June 2023. The search terms included "burning mouth syndrome," "oral microbiota," "oral microbiome," "oral flora," "oral bacteria," and "oral mycobiome." Articles were screened by title and abstract, and full-text articles were reviewed for eligibility. Inclusion criteria were clinical trials that evaluated the association between BMS and oral microbiota. The references of the identified articles were also searched manually for additional relevant studies. The search was limited to English language publications and studies conducted on human subjects. Studies were excluded if they were animal studies or in vitro experiments, were case reports or reviews or did not provide sufficient data to assess the correlation between BMS and oral microbiota. Two independent reviewers screened the titles and abstracts of the identified articles to determine their eligibility for full-text review. Discrepancies were resolved through discussion and consensus. The full texts of potentially eligible studies were then assessed for inclusion based on the predetermined criteria. A PRISMA flow diagram illustrating the study selection process is provided in Figure 1.

Data were extracted from the included studies using a standardized form. The following information was collected: study characteristics (authors, publication year, study design), participant characteristics (sample size, demographics), intervention or exposure (if applicable), outcome measures related to oral microbiota (composition, diversity, abundance), and key findings. Given the heterogeneity of the included studies, a narrative synthesis approach was employed to summarize the findings.

## Results

From 203 total results only two studies that investigated the association between burning mouth syndrome (BMS) and oral microbiota meet the inclusion criteria.

This first study (14) aimed to investigate the potential influence of the oral microbiome on the nervous system, specifically focusing on its association with BMS pathogenesis. Twenty-seven adult patients diagnosed with primary BMS and twenty-two healthy controls were recruited for the study. Saliva samples were collected from all participants, and the relative abundance and diversity of bacterial strains in the oral microbiome were analyzed using 16S rRNA gene sequencing. Statistical analysis was performed to compare the microbial profiles between the BMS and control groups and identify potential disease-specific microbial markers. The analysis revealed that the alpha diversity measures of the oral microbiome were lower in the BMS group compared to the control group. While the differences in observed species, Chao1, and abundance-based coverage estimator (ACE) were not statistically significant, Shannon's, Simpson's, inverted Simpson's, and Fisher's diversity indexes were significantly lower in the BMS group. Furthermore, the analysis identified specific microbial taxa that were significantly associated with BMS. The genus Streptococcus showed a significantly higher abundance in the BMS group, while genera such as Prevotella, Haemophilus, Fusobacterium, Campylobacter, and Alloprevotella were more prevalent in the healthy control

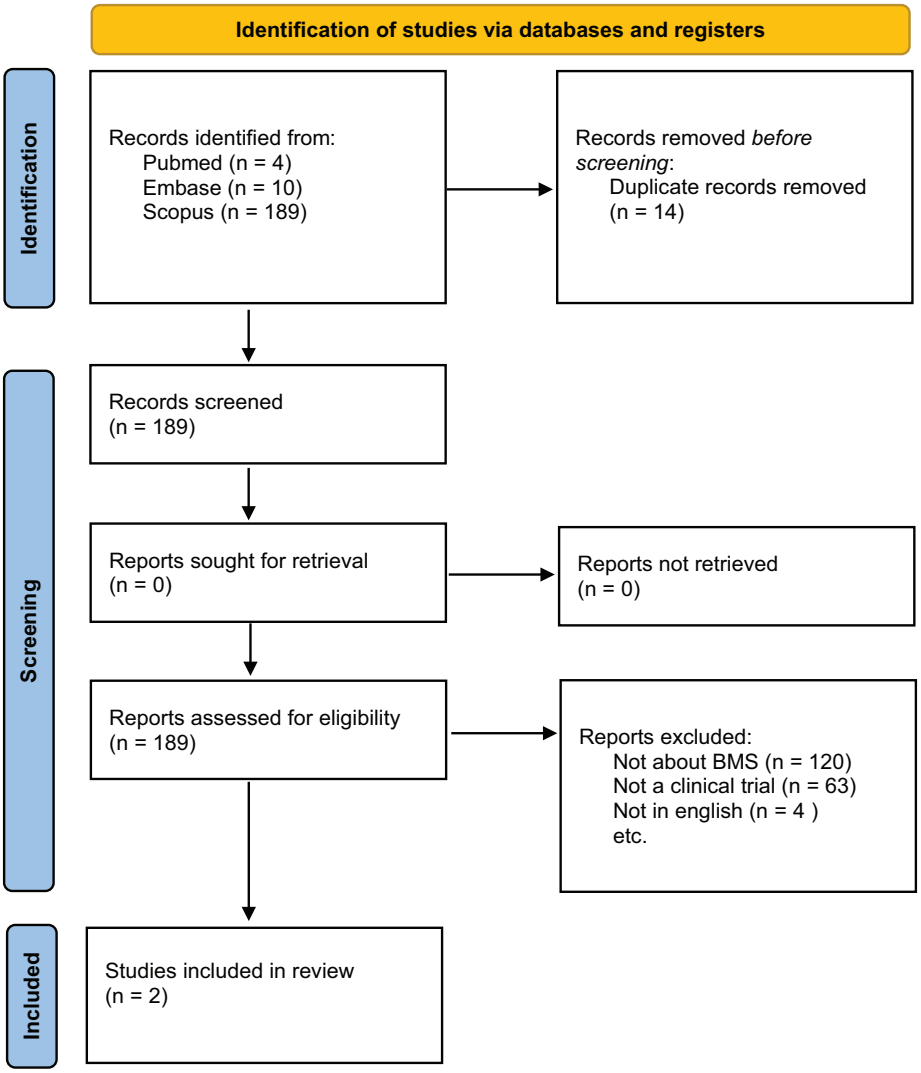


**Figure 1.** PRISMA flow diagram illustrating the study selection process.

group. In conclusion this study provides evidence for a potential association between the oral microbiome and BMS. The findings suggest that alterations in the oral microbial community may contribute to BMS pathogenesis and that the identification of disease-specific microbial markers may have diagnostic implications for BMS.

The second scientific article (15) aimed to determine the incidence of oral Candida or bacterial infections in patients with burning mouth syndrome (BMS) and their effect on pain/burning sensation and salivary flow levels. The study involved 173 BMS patients and 13 control patients. The median age of BMS patients was 57 years, with 29.5% below the age of 50 and 70.5% in the age group of 50 and above. The most affected area by the burning sensation was the tongue, followed by other parts of the oral mucosa. The median duration of the disease was 5 months. Pain/burning sensation levels were assessed in the morning, afternoon, and evening. The levels increased throughout the day, with scores rising from 2 in the morning to 5.5 in the evening. There were no significant differences in pain levels between different age groups or genders. Among BMS patients, 36.4% had an infection, with Candida albicans, Staphylococcus aureus, Enterobacter, Klebsiella pneumoniae, and

non-fermenting Gram-negative rods being the most frequent pathogens. In the control group, 61.5% had an infection, with S. aureus, Klebsiella species, and Candida albicans being the most common pathogens. The study also analyzed salivary flow levels and found that BMS patients had a median unstimulated salivary flow rate of 0.2 mL/min and a stimulated salivary flow rate of 0.9 mL/min, which were within the normal range. There was a statistically significant difference in unstimulated salivary flow between genders. In conclusion, this study found a relatively high incidence of oral Candida or bacterial infections in BMS patients. However, there was no significant correlation between the presence of these infections and pain/burning sensation or salivary flow levels. Further research is needed to better understand the relationship between oral infections and BMS symptoms.

## Discussion

The present review aimed to evaluate the correlation between BMS and oral microbiota by analyzing relevant studies. Two studies were identified, providing preliminary evidence of this association. The first study (14) focused on the potential influence of the oral microbiome on BMS pathogenesis. It compared the oral microbial profiles of patients with primary BMS and healthy controls using 16S rRNA gene sequencing. The analysis revealed lower alpha diversity measures in the BMS group, indicating reduced microbial diversity. Additionally, specific microbial taxa were found to be associated with BMS, with the genus Streptococcus showing a higher abundance in BMS patients, while other genera were more prevalent in the healthy control group. These findings suggest that alterations in the oral microbial community may contribute to BMS pathogenesis and highlight the potential diagnostic implications of disease-specific microbial markers.

The second study (15) focused on assessing the incidence of oral Candida or bacterial infections in BMS patients and their impact on pain/burning sensation and salivary flow levels. The study found a relatively high incidence of oral infections in both BMS patients and controls. However, there was no significant correlation between the presence of infections and pain/burning sensation or salivary flow levels in BMS patients. This suggests that oral infections may not directly contribute to BMS symptoms, although further research is needed to clarify this relationship.

The findings of these studies provide preliminary evidence supporting a potential association between oral microbiota and BMS.

## Conclusions

In conclusion, the limited evidence from the reviewed studies suggests a potential association between oral microbiota and BMS. Alterations in the oral microbial community, characterized by reduced diversity and specific microbial taxa variations, may contribute to BMS pathogenesis. Disease-specific microbial markers may have diagnostic implications for BMS. However, further research is needed to confirm these findings and elucidate the underlying mechanisms. Future studies should focus on larger sample sizes, standardized methodologies, and well-defined diagnostic criteria to provide more robust evidence regarding the role of oral microbiota in BMS.

## Limitations

Several limitations should be acknowledged in this review. Firstly, the number of studies included was limited, indicating the scarcity of research in this area. The limited evidence base highlights the need for additional well-designed studies to further investigate the association between oral microbiota and BMS. Secondly, there was heterogeneity among the included studies in terms of study design, sample characteristics, and outcome measures. This heterogeneity makes it challenging to draw definitive conclusions and emphasizes the need for caution when interpreting the results. Future studies should aim to address these limitations by employing larger sample sizes, standardized methodologies, and consistent diagnostic criteria. Additionally, the possibility of residual confounding factors cannot be ruled out, and the causal relationship between oral microbiota and BMS cannot be established based on the available evidence. Further

longitudinal studies and interventional trials are warranted to elucidate the temporal relationship and causality between oral microbiota alterations and BMS. Despite these limitations, this review provides valuable insights into the current state of knowledge on the association between BMS and oral microbiota and highlights areas for future research.

**Conflict of Interest:** Authors declare that they do not have any commercial associations that might pose a conflict of interest in connection with the submitted article.

**Authors Contribution:** DMF, FL and TA study design; RM and CP databases search and articles selection; All authors participate in the debate and consensus on the articles to be included. RM, BG, FM and RCK manuscript writing. DMF, FL, TA and CP proofreading of the manuscript.

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