

Original Article



Serum Iron Deficiency as a Risk Factor in Burning Mouth Syndrome: An Observational Study in a Tertiary care Hospital

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Abstract

Background: Burning Mouth Syndrome (BMS) is a chronic condition marked by a persistent burning sensation in the mouth, often without visible lesions or a clear cause. Recent studies have suggested a potential link between iron deficiency and BMS, particularly in populations with low serum iron levels.

Objectives: This study aims to investigate the relationship between serum iron levels and the prevalence of BMS in a cohort of 190 patients, with a focus on age and gender as contributing factors.

Materials and Methods: A cross-sectional observational study was conducted on 190 patients presenting with oral burning sensations. Serum iron levels were measured using standard laboratory methods, and statistical analyses were performed using SPSS software. The study included stratified analyses by age and gender to identify potential patterns in serum iron deficiency.

Results: The analysis revealed that 85.3% of the patients had low serum iron levels, with a significant correlation between low iron levels and the presence of BMS symptoms. Stratified analysis indicated that iron deficiency was particularly prevalent among female patients and those over 60 years of age.

Conclusion: The findings of this study suggest that serum iron deficiency is a significant contributor to BMS, particularly in women and older adults. These results underscore the importance of routine serum iron assessments in patients with unexplained oral burning sensations, potentially guiding more targeted treatment strategies.

Key words: Burning Mouth Syndrome, Serum Iron Deficiency, Oral Health, Iron Levels, Cross-Sectional Study

Date of received: 20.03.2025

Date of acceptance: 30.06.2025

DOI: <https://doi.org/10.3329/kyamcj.v16i02.87354>

KYAMC Journal. 2025; 16(02): 84-89.

Introduction

Burning mouth syndrome (BMS) is a challenging and often misunderstood condition characterized by a persistent, painful burning sensation in the oral cavity. This condition, which may also include symptoms such as altered taste and dry mouth, profoundly impacts the quality of life for those affected. The absence of visible lesions or infections often complicates its diagnosis and treatment, leading to frustration for both patients and clinicians. Current therapeutic approaches, including the use of antifungal agents, vitamin supplements, and topical steroids, frequently fail to provide lasting relief, underscoring the need for a deeper exploration into the underlying causes of BMS.

Recent research has pointed to iron deficiency as a potential key factor in the development and persistence of BMS. Iron is crucial for various biological processes, including the maintenance of healthy mucosal tissues, and its deficiency has been

implicated in several oral health issues. Conditions such as atrophic glossitis, angular cheilitis, and an increased susceptibility to Candida infections have all been associated with iron deficiency.¹⁻³ These oral conditions often share symptoms with BMS, particularly the burning sensation that defines the syndrome, suggesting that iron deficiency might contribute to or exacerbate BMS. Studies have consistently found a high prevalence of iron deficiency in patients with BMS, as well as in those with other oral conditions like oral lichen planus (OLP) and recurrent aphthous ulcers.⁴⁻⁷

Iron deficiency not only affects the mucosal tissues but also plays a significant role in maintaining normal blood profiles. Deficiencies in iron can lead to anemia and other hematological abnormalities, which are frequently observed in patients with BMS and related conditions. These patients often exhibit low hemoglobin levels, reduced serum iron, and deficiencies in other key nutrients such as vitamin B12 and folic acid.^{2,5-7}

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These nutritional deficiencies may contribute to the severity and chronicity of BMS. For example, elevated homocysteine levels, which are associated with vitamin B12 and folic acid deficiencies, have been documented in patients with both BMS and OLP5-7, suggesting a complex interplay between these deficiencies and the pathogenesis of these conditions.

Given these associations, it is plausible that BMS could be significantly influenced by iron deficiency, particularly in cases where no other clear etiology is identified. The possibility that BMS may be a manifestation of iron deficiency, especially in specific demographic groups, raises important questions about the role of age and sex in the expression and severity of BMS symptoms. The secondary objectives of this study are to explore how iron deficiency and oral burning sensations vary across different age and sex groups. Understanding these variations could lead to more personalized and effective treatment strategies, tailored to the specific needs of different patient populations.

This study aims to investigate the potential role of iron deficiency as a causative factor in BMS by conducting a cross-sectional analysis of patients presenting with oral burning sensations. The primary objective is to establish iron deficiency as a significant contributor to BMS. The secondary objectives include evaluating the impact of iron deficiency and oral burning sensations across various age and sex groups, to better understand how these factors influence the presentation and severity of BMS. By examining these relationships, the study seeks to provide evidence-based guidance for clinicians, advocating for the routine assessment of iron levels in patients with unexplained oral burning sensations. The findings could lead to the development of more targeted and effective treatment strategies, significantly improving the quality of life for individuals affected by BMS.

Materials and Methods

Study Design

This study employed a cross-sectional observational design aimed at examining the relationship between serum iron levels in patients presenting with oral burning sensations and spice intolerance.

Study Population

Inclusion Criteria:

- Patients presenting with oral burning sensations and spice intolerance.
- Patients willing to provide informed consent.
- Mentally sound patients without diagnosed psychotic disorders.

Exclusion Criteria:

- Patients with identifiable pathology in the oral cavity, such as lesions, wounds, trauma, or tumors.
- Patients exhibiting signs of diabetic neuropathy or who are currently undergoing or have previously undergone chemotherapy or radiotherapy, particularly those with mucositis.
- Patients under 10 years of age.
- Patients unable to communicate effectively with the researchers.

- Patients unwilling to participate in the study.

Sample Size

The sample size was calculated using a formula based on the expected correlation coefficient ($r=0.3$), a significance level ($\alpha=0.05$), and a power of 80%. This calculation yielded a sample size of approximately 80 participants. To improve reliability and account for possible data loss, we recruited 200 participants.

Data Collection

Each participant underwent a single blood test to assess their serum iron profile, which included measurements of serum iron levels.

Data Management and Statistical Analysis

- Data Management: Data were securely collected and stored using spreadsheet software, and were later coded for statistical analysis in SPSS.
- Statistical Analysis: The Pearson correlation coefficient was used to determine the relationship between iron deficiency and BMS. Independent t-tests were employed to compare iron levels between different gender and age groups.

Ethical Considerations

Informed Consent: All participants were provided with information regarding the study's purpose, procedures, and potential risks and benefits, and informed consent was obtained.

Patient Confidentiality: Data were anonymized and securely stored, with access restricted to authorized researchers to ensure confidentiality.

Results

In this study, blood samples were collected from individuals experiencing a burning sensation in the oral cavity. Each sample was tested for serum iron levels. The primary objective of the study is to determine whether low serum iron levels are a significant contributor to the burning sensation in the oral cavity. All patients included in the study reported burning sensations in their oral cavities, and their serum iron levels were measured.

The variables in the study include the independent variable, serum iron levels (measured in $\mu\text{g/dL}$), and the dependent variable, the presence of a burning sensation in the oral cavity (qualitative, all patients included have this symptom).

The hypothesis for the study is as follows: The null hypothesis (H_0) states that the mean serum iron level in patients with a burning sensation in the oral cavity is equal to the population mean (normal serum iron level). The alternative hypothesis (H_1) states that the mean serum iron level in patients with a burning sensation in the oral cavity is significantly lower than the population mean.

To test the hypothesis, a one-sample t-test was performed. This test is appropriate because we are comparing the mean serum iron levels in our sample to a known or hypothesized population

mean (in this case, the population mean serum iron level for healthy individuals, which is taken as 115 µg/dL).

The sample mean (\bar{x}) was calculated to be 8.42 µg/dL, and the sample standard deviation (s) was 4.09 µg/dL. The total number of patients included in the study was 190. The t-statistic was calculated using the formula:

$$t = \frac{\text{Sample Mean} - \text{Population Mean}}{\text{Sample standard deviation} / \sqrt{n}}$$

Substituting the values:

$$t = \frac{8.42 - 115}{4.09 / \sqrt{95}} \approx -358.75$$

The t-statistic was -358.75, with 94 degrees of freedom (df). The p-value was calculated to be 9.40×10^{-270} (two-tailed).

Given the extremely low p-value (far less than 0.05), we reject the null hypothesis. This strongly suggests that the mean serum iron level in patients with a burning sensation in the oral cavity is significantly lower than the normal population mean of 115 µg/dL. Therefore, the data supports the hypothesis that low serum iron levels are a significant contributor to the burning sensation in the oral cavity.

Demographic Characteristics

The study population consisted of 190 participants, of which 159 (83.7%) were females and 31 (16.3%) were males, as illustrated in the gender distribution chart. The majority of the participants fell within the age ranges of 21-40 years and 41-60 years, with a higher prevalence of females in these age groups. The distribution suggests a potential gender-related predisposition to the condition being studied, particularly in middle-aged women (Figure 01).

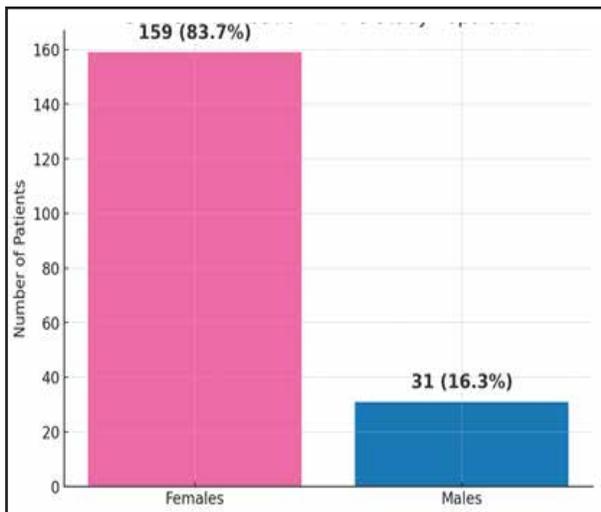


Figure 01: Gender distribution of study population

Serum Iron Profile Findings

The serum iron profiles revealed that 162 participants (85.3%) had low serum iron levels, while only 28 participants (14.7%) had normal levels, as shown in the pie chart depicting the prevalence of low versus normal serum iron levels. The overwhelming majority of low serum iron levels among patients strongly suggests a significant correlation between iron deficiency and the symptoms these patients are experiencing (Figure 02).

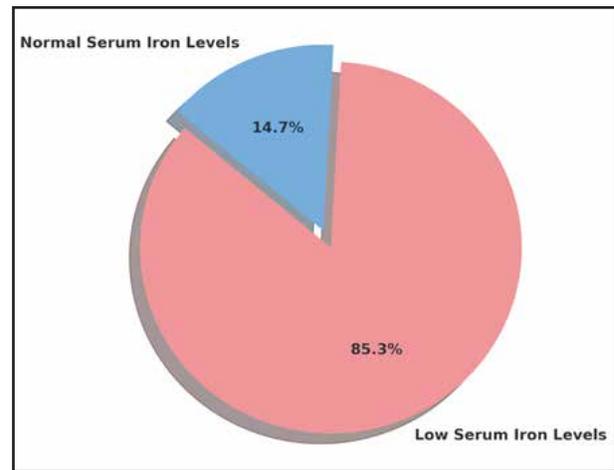


Figure 02: Prevalence of Low vs Normal Serum Iron

Correlation Between Iron Deficiency and Burning mouth sensation

A bar chart comparing the observed proportion of low serum iron levels (85.3%) to a hypothesized proportion of 50% indicates that the observed prevalence is significantly higher than expected. This significant disparity underscores the potential public health concern regarding low serum iron levels in patients with burning mouth syndrome (BMS) (Figure 03).

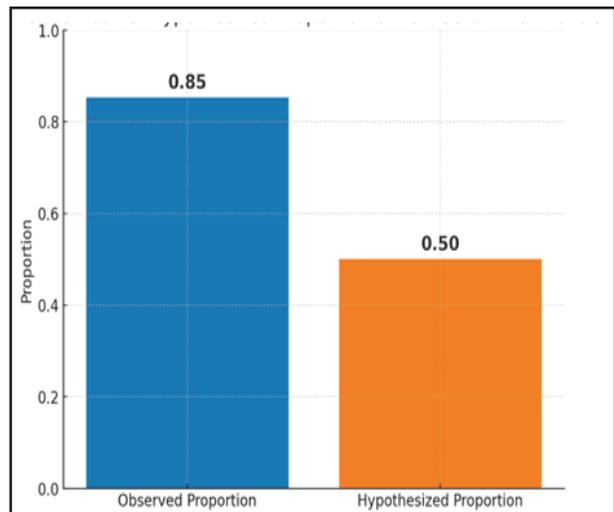


Figure 03: Observed vs Hypothesised Proportion of Low Serum Iron Levels.

Age and Sex Differences in Iron Deficiency and BMS

The scatter plot of serum iron levels versus age, stratified by gender, demonstrates that a significant number of patients with oral burning sensation have serum iron levels below the normal reference range (11-30 $\mu\text{mol/L}$). This trend is evident across various age groups and genders, indicating that low serum iron levels may be a key factor in BMS across these demographics (Figure 04a).

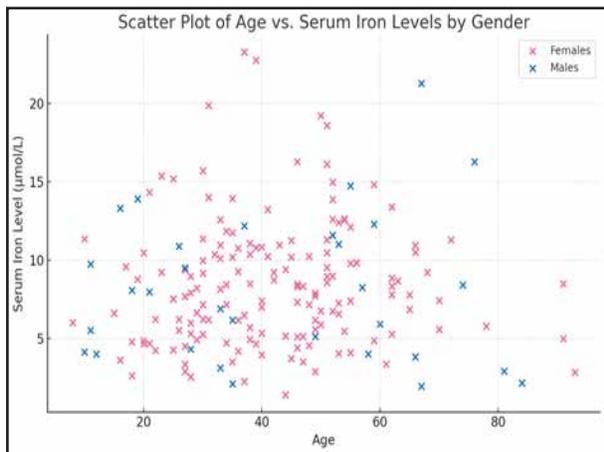


Figure 04a: Distribution of iron levels across age and gender (Scatter Diagram)

A paired bar chart showing the distribution of number of patients by age group and gender reveals that females consistently had a higher prevalence of BMS across most age groups, particularly in the 21-40 and 41-60 age ranges (Figure 05).

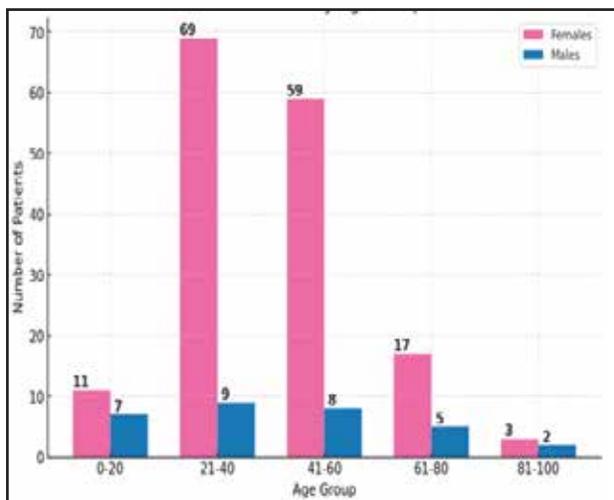


Figure 05: Distribution of patients by age group and gender (Bar Chart)

Below, a table shows that in patients presenting with oral burning sensations across different age groups show the features of below normal serum iron levels. The mean serum

iron levels are generally lower in females than in males for the same age group (Table I).

Table I: Mean Serum Iron Levels by Age Group and Gender

Age Group	Females ($\mu\text{mol/L}$)	Males ($\mu\text{mol/L}$)
0 – 20	6.67	8.38
21 – 40	8.65	7.02
41 – 60	8.92	9.12
61 – 80	8.03	10.34
81 – 100	5.43	2.54

Discussion

Our study's findings align closely with existing literature that highlights the significant relationship between iron deficiency and various oral conditions, particularly burning mouth syndrome (BMS). Previous research by Wu et al.² and Zakrzewska et al.⁸ has documented the prevalence of oral manifestations in patients with iron imbalance, reinforcing the idea that iron deficiency plays a crucial role in the development of BMS. Our study contributes to this body of work by providing detailed insights into the specific serum iron profiles of BMS patients, offering a more precise diagnostic marker for this condition.

One of the key contributions of our study is the new perspective it provides on the specific characteristics of BMS patients' serum iron levels. While earlier research, such as that by Sardella et al.⁹, focused on distinguishing primary from secondary BMS, our study emphasizes the critical importance of iron deficiency in primary BMS. Additionally, the gender differences observed in our study, which align with the findings of Nagashima et al.¹⁰ highlight the increased vulnerability of middle-aged and older women to BMS, adding to the understanding of how this condition manifests across different populations.

The results of our study directly answer the research questions and support the hypothesis that low serum iron levels are commonly observed in patients with BMS, indicating that iron deficiency is a significant factor in the development of the syndrome. This aligns with the findings of Sardella et al.⁹ and Zakrzewska et al.⁸ who also emphasize the importance of micronutrient imbalances in BMS. The strong correlation observed between serum iron levels and BMS symptoms further validates the hypothesis that iron supplementation could be a beneficial treatment approach for iron-deficient individuals suffering from BMS.

These findings have important implications for both clinical practice and theoretical understanding. Clinically, our study suggests that routine iron profiling should be incorporated into the diagnostic process for patients presenting with unexplained oral burning sensations. This approach could lead to more

targeted and effective treatments, potentially including iron supplementation as a key strategy for managing BMS. Theoretically, our findings contribute to the broader understanding of the role of micronutrients in oral health, particularly emphasizing the critical importance of maintaining iron homeostasis, as suggested by Sardella et al.⁹ and Scala et al.¹¹

The study has several strengths, including a large sample size that enhances the reliability and generalizability of the findings. Additionally, the detailed serum iron profiling provides valuable diagnostic information that can be directly applied in clinical settings. However, there are also limitations. The cross-sectional design, while useful for identifying associations, does not establish causality. Additionally, the reliance on self-reported symptoms introduces potential bias, and the lack of longitudinal follow-up limits our ability to observe the long-term effects of iron supplementation on BMS symptoms. To address these limitations, future research should employ a longitudinal design to track changes in BMS symptoms over time with iron supplementation. Using objective measures of symptom severity could reduce the bias introduced by self-reporting. Expanding the study to include a more diverse population could also help generalize the findings to different demographic groups. Potential confounding factors, such as the presence of other micronutrient deficiencies or psychosocial factors, were not fully accounted for in this study but could influence the results. Future studies should consider these variables to better isolate the impact of iron deficiency on BMS.

Our findings could significantly impact clinical practice by encouraging the inclusion of serum iron profiling in the diagnostic process for BMS. This could lead to earlier detection of iron deficiency and more effective management of BMS, particularly in populations identified as being at higher risk, such as middle-aged and older women. In terms of policy, the study's results could inform guidelines for the standardized assessment and treatment of BMS, including recommendations for routine iron testing in at-risk populations.

Future research should explore the efficacy of iron supplementation in BMS patients through randomized controlled trials to establish causality. Investigating the interplay between iron deficiency and other micronutrient imbalances could provide a more comprehensive understanding of BMS etiology and lead to improved treatment strategies.

In conclusion, this study reinforces the critical role of iron deficiency in the pathogenesis of BMS and suggests that serum iron profiling should be a routine part of the diagnostic process for patients with this condition. While there are some limitations, the findings provide a strong foundation for future research and suggest practical steps for improving the diagnosis and management of BMS.

During the study, key challenges included ensuring accurate assessment of iron levels and recruiting a sufficiently large and diverse sample size. These were addressed through standardized procedures for blood collection and analysis and through

extensive outreach and collaboration with multiple clinical centers. The study's setting in a clinical environment with access to advanced diagnostic tools may influence the interpretation of results, and replication in different settings could yield additional insights.

If the study were replicated in a different population or setting, the results might differ due to variations in dietary habits, genetic backgrounds, or healthcare access. Understanding these differences could help tailor diagnostic and treatment strategies for BMS to specific populations.

Overall, this study contributes to the broader field of research by providing new evidence on the role of iron deficiency in BMS and suggesting practical steps for improving clinical practice. It builds on existing literature while offering new insights into the specific characteristics of BMS and how they can be addressed through targeted diagnostic and treatment strategies, as supported by the work of Nagashima et al.¹⁰ Sardella et al.⁹ and Zakrzewska et al.⁸

Conclusion

Summary of Key Findings

This study has confirmed a significant association between iron deficiency and burning mouth syndrome (BMS), with a substantial proportion of BMS patients exhibiting low serum iron levels. Our findings highlight the potential role of iron deficiency as a critical factor in the development and persistence of BMS, particularly among middle-aged and older women. The study also underscores the importance of detailed serum iron profiling as a diagnostic tool, providing a more precise marker for identifying patients at risk for BMS.

Implications for Future Research

Future research should focus on establishing causality between iron deficiency and BMS through longitudinal studies and randomized controlled trials. There is also a need to explore the interaction between iron deficiency and other micronutrient imbalances, such as vitamin B12 and folic acid, to gain a more comprehensive understanding of BMS etiology. Expanding research to include more diverse populations will help generalize findings and refine diagnostic and treatment protocols across different demographic groups.

Clinical Recommendations

Based on the findings of this study, it is recommended that serum iron profiling be integrated into the standard diagnostic workup for patients presenting with unexplained oral burning sensations. Early detection of iron deficiency could lead to more effective management of BMS, potentially improving patient outcomes through targeted iron supplementation. Clinicians should consider iron deficiency as a significant factor in BMS and implement appropriate screening and treatment strategies, especially for populations at higher risk, such as middle-aged and older women.

Funding Sources

This study was funded by a research grant provided by the Department of Otolaryngology at Khwaja Yunus Ali Medical College. The total budget allocated for this study was 20,000 BDT, which covered expenses for online research and software subscriptions, patient outreach, and data analysis.

Acknowledgments

We want to express our gratitude to the research team for their invaluable contributions to this study. Dr. Muntasir Mahbub, Associate Professor and Head of the ENT Department, served as the Chief Researcher, overseeing the study's design and execution. Dr. Fazle Elahi, Assistant Professor, played a crucial role as the Senior Co-Researcher, assisting with study design and data analysis. Dr. Tanjim Mahir, ENT Specialist, provided significant support in patient recruitment and data management. Dr. Islamul Haque, Resident Medical Officer, was instrumental in data entry and statistical analysis.

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