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RESEARCH ARTICLE
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CORRELATION BETWEEN CLINICAL AND HISTOLOGICAL CHARACTERISTICS OF BURNING MOUTH SYNDROME

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Abstract:
This study looked into the relationship between the histology and clinical characteristics of burning mouth syndrome (BMS). Individuals who experienced BMS symptoms for a minimum of six months underwent clinical and histological evaluations. Preliminary assessments included recording mean age, diabetes mellitus, menopausal status, length of non-irritable and irritative salivation or symptoms, and oral hygiene. Clinical trials were conducted on the following conditions: headache, pain, non-specific health issues, taste, thirst, dry mouth, and severe menopausal symptoms. Blood tests for HBS Ag, CBC and S. Iron, S. Ferritin, S. Folic acid as well as testing for female hormones including iron, folic acid, TSH, FT3, T4, and estrogen, were among the laboratory tests. The tongue is subjected to a prospective, blind histological examination, and mucosal samples are prepared for light microscopy. The Statistical Package of Social Science (SPSS) version 23 computer statistical program (SPSS Inc. Chicago, USA) was used to compile the data that had been gathered. The tongue and oral mucosa were examined for variations in their histological and clinical characteristics using the Chi Squire and Student's t-tests; *p*-values less than 0.05 are regarded as statistically significant. In summary, BMS is linked to xerostomia, altered taste on laboratory examination, physical and psychological stress, and histological characteristics that may indicate a source of neuropathy.

Key words: burning mouth syndrome, histology, tongue, oral mucosa

Introduction

Burning Mouth Syndrome (BMS) is a chronic pain condition that mainly affects middle-aged and older women who have mental health difficulties and hormonal abnormalities.[1,2] Because of the psychological disorders it exacerbates, the prognosis for this condition is poor and it impairs the patient's quality of life and lifestyle.[3,4] BMS sufferers thus continue to be heavy users of healthcare resources.[5,6] It is typified by an ongoing burning or comparable discomfort in the mouth that is not associated with any noticeable alterations to the oral mucosa.[7,8]

There have been publications on the causes of BMS and patient complaints[8,9], and there have been a number of recent selective studies that concentrate on particular BMS concerns.[10,11] Nonetheless, there are still certain contentious BMS concerns that present difficulties for physicians and researchers alike. It can also be identified by the symptoms that result from different systemic or local illnesses. While some of them avoid diagnosis and pose a risk to treatment, others can be positively recognized and treated.

A number of writers have proposed dietary and hormonal adjustments as selection factors for BMS that are thought to affect concentration.[12, 13] Moreover, all other forms of chronic BMS associated with different illnesses and the lack of local/systemic causes ought to be regarded as symptoms within the clinical spectrum of these pathology groups.[14, 15] More recently, more sensitive diagnostic tools have identified a neuropathic basis for BMS. Burning pain without mucosal or cutaneous involvement is also a characteristic indication of persistent neuropathic pain states resulting from nerve injury.[16-18]

This new data from a growing number of BMS patients points to a shared neuropathy-related history in the pathophysiology of the illness. As a result, a relationship seems to exist between the histological characteristics and clinical manifestations of BMS. Histologically, spongy, follicular, flat, or elevated papillae linked to alterations in papillary morphology characterize the burning or painful feeling as a chronic neuropathic sequel to nerve injury.[19-22] Histological examination is one sensitive diagnostic approach that has improved in recent years for the identification of BMS.[16,17] It is therefore necessary to show links between clinical and histological characteristics. This study looked into the relationship between the histopathological and clinical characteristics of burning mouth syndrome.

Materials and methods

The Department of Conservative Dentistry and Endodontics and Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka jointly conducted this cross-sectional study. The study population consist of female subjects who reported experiencing oral cavity burning sensations. The age range of 40 to 70 years old and the presence of burning mouth in the oral cavity for at least six months were the inclusion criteria. Oral candidiasis precluded any participant from the research.

Pre-assessment of the participants:

Participants having burning mouth syndrome will be subjected to assessment of age, duration of symptom, diabetes mellitus, menopausal condition, unstimulated and stimulated salivary flow rates, or duration of symptoms, sleep disturbance as well as dental procedure.

Clinical evaluations:

The clinical evaluation will be performed as follows: dry mouth, thirst, taste and sleep disturbance, headache, pain severity, site, whitish margin, and menopausal symptoms.

Laboratory investigation: Blood examination for HBS Ag, CBC, S. Iron, S. Ferritin, S. Folic acid, HIV, FT3, T4, TSH, Female hormone such as Estrogen and Progesterone.

Histological features of tongue and oral buccal mucosa: A prospective blinded evaluation of tongue and mucosal specimens were processed for light microscopy.

Data Collection and analysis:

Pre-assessment, clinical, laboratory, and histological examination data were gathered. The data collecting sheet contained a record of the pertinent findings. Once finished, the information was displayed as needed using tables, figures, and graphs. A liner regression line analysis was used to determine the relationship between the histological and clinical features of the tongue and oral mucosa. The Statistical Package of Social Science (SPSS) version 23 computer-based statistical program was used to analyze the collected data (SPSS Inc. Chicago, USA). To evaluate the distinction between clinical and histological features, the chi-square and student t tests were used. The testing level of significance was determined by observing the 95% confidence interval (*p* value <0.05).

Results

The clinical and histologic characteristics of 72 female individuals with BMS were compared in this study.

In Table 1, among them 60 patients were considered as nor BMS and the remaining 12 as pathological BMS.

Table-2 shows the prevalence of clinical findings among 72 subjects with burning mouth syndrome. The data indicates that majority proportion of patients experience dry mouth (66.7%), thirst (70.8%), taste alteration (72.2%), sleep disturbance (83.3%), headache (69.4%), low salivary flow rate (72.2%), and identify hot and spicy foods as aggravating factors (79.2%). Furthermore, over half of the patients have dental prosthesis or restoration (52.8%).

Table-3 shows hematologic evidence comparing normal and pathological burning mouth syndrome (BMS) subjects. In the normal BMS group, the mean hemoglobin level was 12.3±1.3 g/dl, while in the pathological BMS group, it was 11.8±1.20 g/dl (p=0.223). The RBS (random blood sugar) levels were 6.5±1.5 mmol/L for the normal BMS group and 6.8±1.50 mmol/L for the pathological BMS group (p=0.529). The ESR (erythrocyte sedimentation rate) was significantly different, with a mean of 25±4 mm/hr in the normal BMS group and 48±8.0 mm/hr in the pathological BMS group (p<0.001). Similarly, significant differences were observed in the serum ferritin (p=0.015), serum folic acid (p<0.001), and postmenopausal estrogen levels (p=0.169) between the two groups. Other factors such as TSH, FT3 and T4 did not show significant differences between the normal and pathological BMS subjects. There is a markedly increased incidence of dry mouth, thirst and dysgeusia in patients with BMS. Severe menopausal symptoms, headache, pain complaints, and general health issues are observed. Furthermore, pathological BMS subjects had immunological abnormalities and erythrocyte sedimentation. On the other hand, nor BMS subjects evaluated showed no hematologic indications of malnutrition. There was an increase in velocity. These results validate many general hypothesized etiologic factors in BMS, but they also show traits that set BMS patients apart from age- and sex-matched controls.

The buccal mucosa exhibits modest hyperkeratosis, parakeratosis, hypergranulosis, and vascular degeneration of the basal layer according to a histological examination of oral leucoplakia. Along the dermoepidermal junction, a substantial infiltration of chronic inflammatory cells is observed. Additionally, there appears to be an artificial gap-like region between the epidermis and dermis. Oral leukoplakia of the buccal mucosa presents histologically as areas of moderate dysplastic alteration, hyperplastic lining epithelium, and epidermal hypertrophy. Chronic inflammatory cells are densely infused into the subepithelial stroma (Figure 1).

Based on a histological examination of oral lichen planus, there is modest hyperkeratosis, parakeratosis, hypergranulosis, and basal layer vascular degeneration in the buccal mucosa. The dermoepidermal junction has a significant infiltration of chronic inflammatory cells. The area between the dermis and epidermis also appears to be artificial, like a gap. Areas of epithelial hyperplasia, epidermal hyperplasia, and mild dysplastic alterations are visible in the histological appearance of oral lichen planus of the buccal mucosa. A substantial infiltration of chronic inflammatory cells is visible in the subepithelial stroma (Figure 2). On the other hand, oral mucosa

of a patient with burning mouth syndrome. There were no pathological changes seen in the histology (Figure 3).

Table 1. Number of subjects with normal and pathological BMS

Clinical findings	Number of subject	Pathology
White patch of Tongue & oral mucosa	60	Normal 52 Leucoplakia 3 Lichen planus 5
Red appearance of tongue & oral mucosa	12	Normal 0 Leucoplakia 7 Lichen planus 5

Table 2. Prevalence of clinical findings among the subjects with burning mouth syndrome (n=72)

	Number of patients	**Percentage**
Dry mouth	48	66.7
Thirst	51	70.8
Taste alteration	52	72.2
Sleep disturbance	60	83.3
Headache	50	69.4
Low Salivary flow rate	52	72.2
Aggravating factor (hot and spicy)	57	79.2
Dental prosthesis/restoration	34	52.8

Table-2 shows the prevalence of clinical findings among 72 subjects with burning mouth syndrome. The data indicates that majority proportion of patients experience dry mouth (66.7%), thirst (70.8%), taste alteration (72.2%), sleep disturbance (83.3%), headaches (69.4%), low salivary flow rate (72.2%), and identify hot and spicy foods as aggravating factors (79.2%). Furthermore, over half of the patients have dental prosthesis or restoration (52.8%).

Table 3. Hematologic evidence of the normal & pathological BMS subjects tested

Factors	Normal value	Normal BMS (n=60) Mean±SD	Pathological BMS (n=12) Mean±SD	p-value
Hemoglobin (g/dl)	(M: 15±2 F: 13.5±1.3)	12.3±1.3	11.8±1.20	0.223
RBS (mmol/L)	7.8	6.5±1.5	6.8± 1.50	0.529
ESR (mm/hr)	(M: 0-22 F: 0-29)	25±4	48±8.0	<0.001*
S. Ferritin (ng/ml)	(M: 20-250 F: 10-120)	130± 8.1	136.3±7.80	0.015*
S. Folic acid(ng/ml)	4.97-19.96	10.3±1.5	12.6±1.80	<0.001*
FT3 (pmol/L)	3.5-6.5	4.89±0.67	5.04±0.70	0.484
T4 (nmol/L)	58-140	137.6±11.70	135.6±9.67	0.581
THS (ml/UL)	0.55-4.78	0.39±0.40	0.37±0.56	0.883
Postmenopausal Estrogen (pg/ml):	<28	12±3.7	13.7±4.7	0.169

p-value obtained by Unpaired t-test, *significant

Table-3 shows hematologic evidence comparing normal and pathological burning mouth syndrome (BMS) subjects. Significant differences were observed in the serum ferritin (p=0.015), serum folic acid (p<0.001), and postmenopausal estrogen levels (p=0.169) between the two groups. Other factors such as FT3, T4, and TSH did not show significant differences between the normal and pathological BMS subjects.

Figure 1: Buccal mucosa is visible in leucoplakia slices. These show areas of moderate dysplastic alterations, acanthosis, and hyperplastic lining epithelium. There is a significant infiltration of chronic inflammatory cells in the subepithelial stroma.

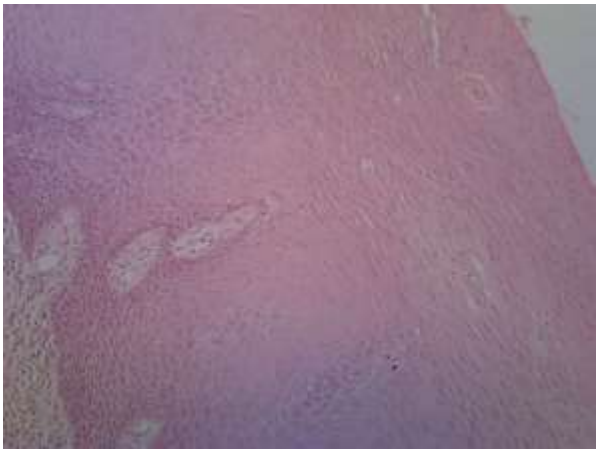

Figure 2: A lichen planus instance. There is wedge-shaped hypergranulosis and uneven epidermal hyperplasia that provide the appearance of a saw tooth. Vacuolar degeneration is seen in the basal layer of the epidermis, usually accompanied by noticeable necrosis of individual keratinocytes.

Figure 3: Representative photograph of oral mucosa of a patient with normal burning mouth syndrome. There were no pathological changes seen in the histology.

Discussion

Many studies have examined a range of risk variables related to BMS patients.[23, 24] In this study, 72 female BMS individuals' pathological and clinical data were correlated. The organs most commonly affected in our study were the tongue and the oral mucosa, particularly the tip and front two-thirds.

The anterior palate, gingiva, and oral mucosa were the next most often affected sites, with the tongue accounting for around half of the cases, according to a previous study.[25, 26] Research revealed that individuals who additionally reported headache, nonspecific health problems, dry mouth, thirst, taste changes, disturbed sleep, pain complaints, and severe menopausal symptoms were significantly more likely to experience constipation. However, no significant differences were seen in other areas of the mouth or teeth. Every participant in the perimenopausal research anticipated a negative outcome and thought it would only grow worse. It is probable that compared to men, people with monoposis have a significantly higher psychosocial burden and a lower quality of life. Furthermore, research has shown that the stress of being unmarried for an extended period of time increases the risk of hypertension.

Psychological stress is likely to play a role in the development of burning mouth syndrome. Participants in our study were more likely than non-stressed participants to report pain complaints, severe menopausal symptoms, dry mouth, thirst, taste abnormalities, sleep disturbances, migraines, and general health problems. It showed signs of being vulnerable to BMS. These results are in line with a study by Dahiya et al.[27] that highlights the significance of raising public awareness of BMS, especially in relation to symptoms associated with perimenopausal women. This may facilitate a speedy diagnosis and allay some of the patients' fears. On the other hand, there are contradicting results on sleep issues in BMS. While some research found that pain did not interfere with up to 70% of patients' attempts to fall asleep,[11,18] other studies found that BMS patients frequently experienced pain-sleep interactions.[27-28] Nonetheless, BMS's common vulnerability to discomfort, anxiety, or melancholy might also be connected to BMS's sleep problems.[29] Additionally, consistent with other studies, a small number of patients in this study experienced burning sensations triggered by certain foods, especially those that were spicy or hot. This has also been identified as an increasing factor. Cold drinks can help some individuals feel less pain. In order to activate the thick fibers and often lessen discomfort, the patient can consume, chew gum, or sucke dried fruit. Xerostomia is a common problem; the incidence of BMS varies from 46% to 70%.[30]

Several studies have focused on a number of risk factors for an individual with BMS. The association between pathological and clinical data in 72 patients with burning mouth syndrome was examined in this study. The most often impacted sites in our study were the tongue's mucosal membrane and the oral cavity, specifically the tip and the front two-thirds. An earlier study found that the anterior palate, gums, and oral mucosa are the areas most damaged in nearly half of the patients.[3] Moreover, the study found that while the stuffy-feeling patients did not significantly differ in any oral or dental features, they did experience significantly higher rates of dry mouth, thirst, taste and sleep disturbances, headaches, non-specific health concerns, pain complaints, and severe menopausal symptoms. This stress may be caused by a variety of circumstances, such as the participant's age, gender, and menopausal status. Every one of the study's peri- and postmenopausal participants thought a terrible thing was about to happen. Menopausal stress may occur depending on how a person responds to and manages the menopausal stage.

It is realistic to expect that subjects with monoposis will generally report higher levels of psychosocial stress and worse levels of life satisfaction when compared to men. Furthermore, studies have shown a connection between a prolonged period of single stress and a higher risk of hypertension. In a different study, Rabiei et al.[31] discovered that age and gender were the main factors influencing BMS. psychiatric disorders and were discovered to be closely associated with the emergence of BMS. This study included BMS subjects with normal blood counts who had burning sensations in their mouths for at least six months without any clinical signs.

The results of this study also suggested that mental stress may have an impact on the development of burning mouth syndrome (BMS). Patients with headache, non-specific health problems, dry mouth, thirst, taste disturbances, sleep disturbances, pain complaints, and severe menopausal symptoms were more likely to develop BMS than those who did not experience stress. Women who are peri- and postmenopausal in particular need to be made more aware of the symptoms linked to BMS, according to Riordian et al. [32] This should speed up a diagnosis and help individuals feel less

apprehensive. On the other hand, there are contradicting results on sleep issues in BMS. There is a high prevalence of sleep interaction between BMS pain and sleep, despite some studies finding that up to 70% of patients do not experience pain when they go asleep.[11, 18] While sleep disruption is occasionally noted as a coexisting condition, it is rare for pain to be the direct cause of sleep loss in the absence of a causal relationship. But insomnia in BMS patients may also be connected to a shared susceptibility to BMS discomfort, depression, or anxiety.[33] Additionally, consistent with previous studies, some patients in this study experienced burning sensations triggered by specific foods, especially spicy or hot foods. As a result, it has also been observed that stress and fatigue are contributing factors. Some people may find that drinking anything cool and stimulating their large fibers with food, gum, or dried fruit sucking will both help them feel less pain.[34]

Conclusion

BMS is linked to xerostomia, altered taste on laboratory examination, physical and psychological stress, and histological characteristics that may indicate a source of neuropathy.

Ethical Issue

This study was approved by Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University (BSMMU/2019/13624).

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Conflict of Interest

Authors declare no conflict of interest.

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