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Research Article

Oral Findings and Salivary Alpha-Amylase in Major Depressive Disorder Patients

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Abstract

Background: The increasing global prevalence of major depressive disorder (MDD) has become an important challenge, leading to a heightened demand for oral medicine in developed nations. This demand arises from the recognition of the association between psychiatric disorders and other conditions, including various orofacial pain disorders.

Objective: This study are to evaluate oral conditions such as recurrent aphthous ulcers, burning mouth syndrome, and altered taste and to assess salivary alpha-amylase in individuals diagnosed with major depressive disorder.

Methods: This research uses a cross-sectional study design that includes a sample of 49 patients who have been diagnosed with major depressive disorder and who have undergone treatment for at least two weeks. The control group consists of 34 healthy subjects with no signs or symptoms of systemic disease. The study group received the diagnosis in Najaf City according to the criteria in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). With respect to recurrent aphthous ulcers, the results of this study show the percentage of patients with oral ulcers is significantly higher than in the control group.

Results: The results also show that the prevalence of burning mouth syndrome is significantly higher in patients with major depressive disorder than in healthy controls. A highly statistically significant difference was found between the study group and the control group regarding altered taste. There is also a significant difference in salivary alpha-amylase levels between the study and control groups ($p = 0.009$).

Conclusion: Major depressive disorder patients have much higher incidences of reported recurrent aphthous ulcers, burning mouth syndrome, and altered taste than healthy subjects, indicating the importance of psychological factors in these conditions. Additionally, salivary alpha-amylase levels were higher in patients with major depressive disorder than in the control group.

Keywords: Altered taste; Burning Mouth syndrome; Major depressive disorder; Recurrent Oral ulcerations; Salivary Alpha-amylase.

Introduction:

Major depressive disorder is a highly prevalent and incapacitating condition that has significant global implications for individuals and public health (). Several studies indicate that the prevalence of depression in Iraq is notably high and that rates of depression are particularly high in medical students (2-7). A recent study conducted in Iraq identified depression as a significant criterion that had previously been overlooked; this study suggested that the consideration of depression as a diagnostic factor may contribute to the early detection of individuals with Behcet's disease (8). The occurrence of depression has been observed to have adverse effects on oral health, specifically in relation to the development of dental caries (9,10). Recurrent aphthous stomatitis (RAS) is widely recognized as the prevailing ulcerative condition affecting the oral mucosa. The observed condition manifests as either solitary or multiple instances of recurring shallow ulcers. These ulcers typically exhibit a circular morphology and are accompanied by distinct erythematous borders. Additionally, they present yellow or grey pseudomembranous surfaces (1). Recurrent aphthous stomatitis (RAS) is characterized by a prodromal burning sensation that persists for 2–48 hours before the manifestation of an ulcer. This condition can occur in individuals who are in good health. Typically, it is found on the buccal or labial mucosa, as well as on the tongue. However, it is uncommon to find it on the gingiva or the heavily keratinized palatal mucosa. On average, RAS affects approximately 20% of the worldwide population (2). Various factors have been suggested as potential etiological agents for recurrent aphthous stomatitis (RAS). The factors contributing to this condition encompass genetic factors, local factors such as trauma, nutritional factors such as deficiencies in vitamin B complex or folate, hematologic and immunologic factors, food allergies, the influence of drugs, and psychological problems such as stress, anxiety, and depression (2,13,14) Burning mouth syndrome (BMS) frequently presents as sensations of burning, prickling, tingling, itching, or numbness that specifically affect the tongue, lips, palate, gums, and other mucous membranes within the oral cavity (5). The level of pain experienced by individuals tends to

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escalate progressively during the day, reaching its maximum intensity during the late evening hours (6). Frequently, patients express dissatisfaction with dysgeusia, xerostomia, and altered sensation in the oral mucosa, as well as psychological problems such as anxiety and depression. The etiology of burning mouth syndrome (BMS) is postulated to be linked to psychological disorders as well as peripheral and central neuropathy (7,21). Taste dysfunction can arise from various factors, including upper respiratory tract infections (URIs), head trauma, medication usage, and idiopathic origin (22,23,24). The primary enzyme responsible for digestion in the oral cavity is known as alpha-amylase. Alpha-amylase fulfills a dual function, encompassing roles in both digestive and immunological functions (e.g., it protects the oral cavity against microbial pathogens). Alpha-amylase serves multiple purposes and offers various advantages; it is involved in the digestive process, which initiates in the mouth, and has the capacity to bind to oral bacteria and teeth (25,27). Moreover, prior research has suggested that salivary alpha-amylase serves as a reliable indicator of the sympathetic nervous system's response to various stimuli, such as adrenaline (27,31). Salivary alpha-amylase (sAA) is released in response to neurotransmitter stimulation, and its secretion is regulated by both sympathetic and parasympathetic innervation of the salivary glands. Consequently, salivary alpha-amylase has been acknowledged as a significant biomarker for assessing autonomic activity (32). The secretion of salivary alpha-amylase (sAA) by the parotid gland is influenced by adrenergic activity, which is inhibited by beta-blockers (33). The objectives of this study are to assess oral findings and salivary alpha-amylase in patients with major depressive disorder (MDD) and to compare these patients with a group of healthy control subjects.

Subjects and Methods:

This cross-sectional study was conducted at Al-Hakim Hospital in Najaf City, Iraq. Ethical approval for the study was obtained from the Ethical Committee of the College of Dentistry, Baghdad University, under assigned project number 458722.

A total of 49 patients who had been diagnosed with major depressive disorder (MDD) and who had received treatment for a minimum of two weeks were included in the study. The control group comprised 34 healthy individuals without any indications or symptoms of systemic disease. The study group was diagnosed by psychiatric specialists at Al-Hakim Hospital in Najaf City in accordance with the criteria outlined in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5).

Individuals aged 18 years or older who had received a depression diagnosis from a qualified psychiatrist were considered for participation in this research. Exclusion criteria encompassed individuals seeking emergency medical attention, those unable to independently complete the questionnaire, pregnant individuals, individuals undergoing corticosteroid treatment, and individuals with a history of radiotherapy or chemotherapy. The examination of all patients involved the identification of oral manifestations, such as aphthous ulcers. Furthermore, patients were queried regarding the presence of burning mouth syndrome (BMS) and any alterations in taste perception. The data collection period spanned January 30th, 2021 to April 29th, 2022. Prior to the collection of samples, participants underwent a mouth rinse using distilled water. Detailed instructions were provided to all participants, directing them to hold saliva in their oral cavities for a period of 10 minutes without swallowing. After the designated time, participants expelled the accumulated saliva into a sterile plastic receptacle. During the collection process, the saliva samples were stored in a refrigerated environment to maintain their integrity. To minimize the formation of bubbles and foam, the samples underwent centrifugation at a rotational speed ranging from 3000 to 3500 revolutions per minute (RPM). Salivary alpha-amylase was assessed using the human AMY1 (Amylase Alpha 1, Salivary) ELISA kit, catalog number E-EL-H0320. The Statistical Package for the Social Sciences (SPSS), version 23, was utilized alongside Microsoft Excel for data insertion and analysis. Given that the data set encompasses both descriptive and quantitative data, it was imperative to assess the distribution of the variables in the research. The Chi-squared test and *t*-test were conducted to ascertain the presence of any correlations between the variables under investigation in this study. During the course of the investigation, the Kolmogorov-Smirnov test and correlation analysis emerged as two pivotal methodologies for determining the conformity of the quantitative data to a normal distribution.

Results

Age:

This study found that the individuals diagnosed with major depressive disorder (MDD) exhibited a broad age range of 23 to 66 years, while the control group, composed of individuals without MDD, ranged in age from 20 to 57 years. The mean age of individuals diagnosed with MDD was 44.3 years, with a standard deviation of ±10.19 years. In the control group, the mean age was 41.26 years, with a standard deviation of ±10.98 years. However, no statistically significant difference was observed between the two groups in terms of age. The group of patients diagnosed with MDD consisted of 26 males (53.1%) and 23 females (46.9%). In comparison, the control group, which consisted of healthy individuals, comprised 19 males (55.9%) and 15 females (44.1%), as shown in Table (1).

Table (1): Mean, range, and percentage of MDD patients and control subjects in different age groups

Age/year	Study Group		Age/ year	Control Group		*P*-value
	Freq.	%		Freq.	%	
35–23	12	24.5	26–20	9	26.5	
36–47	14	28.6	31–26.1	8	23.5	
48–50	13	26.5	41–31.1	10	29.4	0.133 (Ns)
51–66	10	20.4	57–41.1	7	20.6	
Total	49	100	Total	34	100	
Age range year	20–57		23–66			
Mean±SD	44.30±10.19		41.26±10.98			

NS: Non-significant.

Gender

In this study, among the individuals diagnosed with major depressive disorder (MDD), there were 26 males (53.1%) and 23 females (46.9%). In the control group comprising healthy subjects, there were 19 males (55.9%) and 15 females (44.1%). However, no significant difference was observed between the two groups in terms of gender distribution, as shown in Table (2) and Figure (1).

Table (2): The numbers and percentages of males and females in the MDD patient and control groups

Gender	Study Group		Control Group		*P*-value
	No.	%	No.	%	
Male	26	53.1	19	55.9	0.803 (NS)
Female	23	46.9	15	44.1	
Total	49	100	34	100	

NS: Non-significant

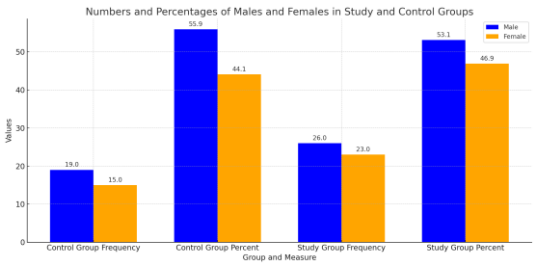

Figure (1): The numbers and percentages of males and females in the MDD patient and control subject groups.

1- Oral findings

1-Recurrent oral ulcerations

A total of 21 (42.9%) MDD patients reported that they do not have frequent oral ulcers, while 28 (57.1%) MDD patients confirmed that they have oral ulcers. In the control group, 28 (82.4%) individuals reported that they do not have a history of recurrent oral ulcers, while 6 (17.6%) reported a history of oral ulcers, as shown in Table (3). Statistical analysis showed a highly significant difference between MDD patients and control subjects ($P < 0.001$; Table 3).

Table (3): The numbers and percentages of subjects with oral ulceration in the MDD patient and control groups

Oral Ulceration	Study Group		Control Group		*P*-value
	No.	%	No.	%	
No	21	42.9	28	82.4	0.000 ** (Hs)
Yes	28	57.1	6	17.6	
Total	49	100	34	100	

****HS: Highly significant, p < 0.001**

Burning mouth syndrome

Within the study group, a total of 26 individuals (53.1%) did not exhibit symptoms of burning mouth syndrome (BMS), whereas 23 individuals (46.9%) had BMS.

In the control group, 29 (85.3%) individuals did not have BMS, while 5 (14.7%) individuals reported having BMS. A statistical analysis showed a significant difference between the study and control groups, as shown in Table (4).

A statistical analysis showed a highly significant difference between the MDD patients and control subjects ($P < 0.001$).

Table (4): The numbers and percentages of patients with BMS in the study and control groups

BMS	Study Group		Control Group		
No	No.	%	No.	%	*0.002 S
Yes	26	53.1	29	85.3	
	23	46.9	5	14.7	
Total	49	100	34	100	

***S: Significant, *P* < 0.05**

Altered taste

The results showed that 20 (40.8%) MDD patients did not have altered taste, while 29 (59.2%) patients had altered taste.

In the control group, 33 (97.1%) individuals did not have altered taste, while 1 (2.9%) individual reported having altered taste. A highly statistically significant difference was found between the study and control groups, as shown in Table (5).

Table (5): The numbers and percentages of subjects with altered taste in the MDD patient and control groups

Altered taste	Study Group		Control Group		P-value
No	No.	%	No.	%	
Yes	20	40.8	33	97.1	**0.000
Total	29	59.2	1	2.9	
No	49	100	34	100	(Hs)

**Hs: Highly significant, $P < 0.001$

Salivary alpha-amylase

\In the MDD patient group, the mean and standard deviation of salivary alpha-amylase was 1.37 ± 0.35 ng/ml, and the range was 0.5–2.25 ng/ml. In the control group, the mean±standard deviation was 1.19± 0.2 ng/ml, and the range was 0.76–1.83 ng/ml.

A *t*-test indicated a statistically significant difference in salivary alpha-amylase concentrations between the MDD patient group and the control group (p = 0.009), as shown in Table (6).

Salivary alpha-amylase was significantly higher ($P < 0.05$) in the MDD patients than in the control subjects.

Table (6): The mean, standard deviation and range of salivary alpha-amylase in the MDD patient and control groups

Group	No.	Mean ng/ ml	SD	Range (ng/ml)	*P*-value
MDD patients	49	1.37	0.35	0.5-2.25	*0.009 S
Control	34	1.19	0.20	0.76-1.83	

***S: Significant. *P* < 0.05).**

Discussion:

Oral findings

Recurrent oral ulcerations

The results of this study indicate that the number of MDD patients who have reported frequent oral ulceration is highly significant. The oral cavity is widely regarded as a reflection of overall systemic health, given that various physical and psychological disorders and systemic diseases can manifest in the oral mucosa (34,36). It is widely acknowledged that psychological factors, including anxiety, depression, and psychological stress, may influence a variety of oral lesions (37,40). Recurrent aphthous stomatitis (RAS) consists of painful ulcerations that typically manifest on non-keratinized mucosa of the oral cavity, exhibit a yellowish-white appearance, and are encircled by an erythematous halo. The prevalence of RAS in the overall populace ranges from 5% to 20%, with higher incidence rates observed in females than males. RAS is frequently observed in pediatric and young adult age groups. The exact etiology of recurrent aphthous stomatitis (RAS) remains unclear (41). Psychological stress, anxiety, and depression are regarded as common triggers in the occurrence and progression of RAS (42, 45). It is suggested that psychological disorders contribute to the onset and progression of oral health conditions. Several researchers have noticed that oral disorders commonly experience cycles of remission and exacerbation, which are often closely linked to the emotional state of the patients (46).

Given the great reactivity of oral tissues to psychological factors, it is typical for oral problems to emerge as psychosomatic symptoms. Psychological variables lead to changes in the markers of the neurological system. The oral disease is initiated and progresses due to the presence of catecholamines (adrenaline, noradrenaline, and dopamine), markers of the endocrine system (cortisol and aldosterone), and components of the immune system (T cells, B cells, natural killer cells, and immunoglobulins) (47).

Burning Mouth Syndrome

This study found a significant difference between the MDD and control groups in terms of the number of patients who reported burning mouth syndrome. This finding is consistent with previous studies (39,40,49,50). Multiple possible causative or precipitating factors of BMS have been suggested, including psychiatric disorders; these psychological factors could be a possible etiology of BMS (48,53).

Mental disorders like depression and anxiety play a critical role in the modulation of pain perception through various mechanisms that can alter the pain threshold, influence nerve transmission from peripheral pain receptors, and increase or decrease individual pain perception (54).

Altered taste

Studies investigating the association of major depression with altered taste are limited. This study found that 59.2% of patients with major depression report altered taste, which is higher than the results reported by an earlier study (55). The relatively high number of patients reporting altered taste could be explained by the recent Covid-19 outbreak, which can also cause altered taste in patients (56). A similar study using a questionnaire found a strong relationship between major depression and altered taste and smell dysfunction in adults in certain age groups in the general American population (57). One case-control study examining the correlation between taste perception and depression was identified in the existing literature. In a study conducted in 1969, it was observed that depressed patients exhibited a notably elevated threshold concentration in perceiving fundamental taste modalities (sweet, salty, sour, and bitter) compared to non-depressed patients. The study had a sample size of 39 individuals (58). Altered taste sensation could be a result of increased spontaneous firing rates of afferent taste fibers or efferent inhibition of other taste fibers. A change in salivary composition may also account for altered taste perception (59).

The link between taste irregularities and depression may be explained by the development of anhedonia, a key hallmark of depressive disorder. This can be observed in rat models through a reduced reaction to tasty food. A study showed that rats with anhedonia have lower levels of 5-HT1A receptors for serotonin in their taste cells. This suggests that changes in taste cells could play a role in the development of depressed symptoms (60).

Biochemical findings

Salivary alpha amylase

The findings of this study indicate that the levels of salivary alpha-amylase (sAA) among individuals diagnosed with major depressive disorder (MDD) are elevated to a statistically significant degree ($p < 0.05$) compared to the control group. Recent studies have found higher sAA levels in depressed patients and subjects with negative emotional states (61,62).

This finding is consistent with previous research that found that individuals diagnosed with major depressive disorder (MDD) exhibited significantly higher levels of alpha amylase compared to control subjects, both prior to and following electrical stimulation (63) Similarly, other researchers observed elevated levels of salivary alpha-amylase and cortisol in both unremitted and remitted depressed patients (64). It has been postulated that α-amylase could serve as an indicator of the activity of the sympathoadrenal medullary system (SAM) (65).

Elevated sAA levels have been observed in individuals diagnosed with major depressive disorder (MDD). Moreover, the administration of medications has the potential to decrease salivary alpha-amylase (sAA) levels and mitigate symptoms of depression. Other studies have concluded that the activation of the parasympathetic nervous system can also lead to the release of sAA (66).

Conclusions

MDD patients have much higher incidences of reported recurrent ulcerations, burning mouth syndrome, and altered taste than subjects without MDD, indicating the importance of psychological factors in these conditions. Salivary alpha-amylase levels are also higher in patients with MDD, suggesting that this is essential for the evaluation of MDD.

Authors' declaration:

We confirm that all the Figures and Tables in the manuscript belong to the current study. Besides, the Figures and images, which do not belong to the current study, have been given permission for re-publication attached to the manuscript.

Authors sign on ethical consideration's approval-Ethical Clearance: The project was approved by the local ethical committee in was conducted at Al Hakim Hospital in Najaf City, Iraq. Ethical approval for the study was obtained from the Ethical Committee of the College of Dentistry, Baghdad University, according to the code number 458722. The data collection period spanned January 30th, 2021 to April 29th, 2022.

Conflicts of Interest: None.

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Authors' Contributions

The manuscript should mention the contribution of each author to the research done:

Study conception & design: Taghreed F. Zaidan. Literature search: Ameer A. Althabhawee, Mohammed Ali. Data acquisition: Ameer A. Althabhawee. Data analysis & interpretation: Taghreed F. Zaidan, Ameer A. Althabhawee. Manuscript preparation: Ameer A. Althabhawee Manuscript editing & review: Taghreed F. Zaidan

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النتائج الفموية وألفا الأميليز اللعابية في مرضى اضطراب الاكتئاب الشديد

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الخلاصة:
الخلفية: أصبح الانتشار العالمي المتزايد لاضطراب الاكتئاب الشديد (MDD) تحديًا مهمًا، مما أدى إلى زيادة الطلب على طب الفم في الدول المتقدمة. ينشأ هذا الطلب من الاعتراف بالارتباط بين الاضطرابات النفسية وغيرها من الحالات، بما في ذلك اضطرابات الألم الفموي الوجهي المختلفة.
الأهداف: أهداف هذه الدراسة هي تقييم حالات الفم مثل القرح القلاعية المتكررة، ومتلازمة الفم الحارق، وتغير الذوق وتقييم ألفا الأميليز اللعابي لدى الأفراد الذين تم تشخيص إصابتهم باضطراب اكتئابي كبير.
الطرق: يستخدم هذا البحث تصميم دراسة مقطعية يتضمن عينة من 49 مريضا تم تشخيص إصابتهم باضطراب اكتئابي كبير والذين خضعوا للعلاج لمدة أسبوعين على الأقل. تتكون المجموعة الضابطة من 34 شخصًا يتمتعون بصحة جيدة ولا تظهر عليهم أي علامات أو أعراض لأمراض جهازية. تم تشخيص مجموعة الدراسة في مدينة النجف وفق معايير الدليل التشخيصي والإحصائي للاضطرابات النفسية، الطبعة الخامسة .(DSM-5) وفيما يتعلق بالقرح القلاعية المتكررة، أظهرت نتائج هذه الدراسة أن نسبة المرضى الذين يعانون من تقرحات الفم أعلى بكثير من المجموعة الضابطة.
النتائج: أظهرت النتائج أيضا أن معدل انتشار متلازمة الفم الحارق (BMS) أعلى بكثير في المرضى الذين يعانون من MDD مقارنة بالأشخاص الأصحاء. تم العثور على فرق ذو دلالة إحصائية عالية بين مجموعة الدراسة والمجموعة الضابطة فيما يتعلق بتغير الذوق. هناك أيضًا اختلاف كبير في مستويات ألفا الأميليز اللعابية بين مجموعتي الدراسة والسيطرة (ع = 0.009). الاستنتاج: في الختام، مرضى MDD لديهم حالات أعلى بكثير من القرحات القلاعية المتكررة، ومتلازمة حرق الفم، وتغير الذوق من الأشخاص الأصحاء، مما يشير إلى أهمية العوامل النفسية في هذه الحالات. بالإضافة إلى ذلك، كانت مستويات ألفا الأميليز اللعابية أعلى في المرضى الذين يعانون من MDD مقارنة بالمجموعة الضابطة.
الكلمات المفتاحية: تغير الذوق، متلازمة الفم الحارق، اضطراب الاكتئاب الشديد، تقرحات الفم المتكررة، ألفا الأميليز اللعابي