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Recommended Citation

Althabhawe, Ameer Ali and Zaidan, Taghreed Fadhil (2023) "Evaluation of burning mouth syndrome and salivary chromogranin A in major depressive disorder patients," *Maaen Journal for Medical Sciences*: Vol. 2 : Iss. 1 , Article 4. Available at: <https://doi.org/10.55810/2789-9136.1015>

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Evaluation of Burning Mouth Syndrome and Salivary Chromogranin A in Major Depressive Disorder Patients

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Abstract

Major depressive disorder represents a growing concern as its prevalence keeps rising worldwide; with this rising, there is also an increased demand in the field of oral medicine in developed countries, and since many disorders and orofacial pain have been linked to be associated with psychiatric disorders and conditions, this study was aimed to evaluate burning mouth syndrome and salivary chromogranin A in major depressive disorder patients.

The study sample included 49 patients who received a diagnosis of major depressive disorder, being under treatment for at least two weeks. The control group consists of 34 healthy subjects with no signs & symptoms of systemic disease. The study group received the diagnosis according to The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM5), in Najaf city. The results showed that for the study sample, 23 (46.9%) patients had Burning Mouth Syndrome (BMS), while 26 (53.1%) patients did not have BMS for the study group. As for the control group, 5 (14.7%) individuals reported having BMS, and 29 (85.3%) didn't. The findings of the present study revealed a significant difference in salivary chromogranin A levels between the study and control groups ($p < 0.05$) using a t-test. We found salivary chromogranin A is an excellent salivary biomarker for MDD., and MDD patients have much higher incidents of reporting BMS, indicating the importance of psychological factors in this condition.

Keywords: Depression, Chromogranin A, Major depression, Burning mouth syndrome

1. Introduction

One in five people will experience major depressive disorder (MDD), a non-homogeneous disorder that is the leading cause of disability worldwide [1].

Deficits in the corticolimbic regions of the brain's structure and neurochemistry are related to MDD symptoms [2].

Anhedonia, aberrant reward-associated perception, memory deficits, and other emotional, motivational, cognitive, and physiological domains are just a handful of the behavioral symptoms of depression [3].

Patients from Baghdad exhibit depression similarly to patients worldwide [4].

The depression rate in Iraq is high [5–7]. A recent study conducted in Iraq found that depression is a critical missed criterion that may help in the early diagnosis of Bechet's disease [8].

Although it varies greatly among nations, the global prevalence of the major depressive disorder is roughly 6% [9].

With a lifetime risk of depression of 15–18% [10], major depressive disorder is common, with one episode arising in about one in five people [11].

The prevalence of depression peaks in both genders in the second and third decades of life, with a subsequent, more subdued peak occurring in the fifth and sixth decades of life; throughout a lifetime, depression is almost twice as common in women as in men [12].

Received 3 September 2022; accepted 4 March 2023.
Available online 25 April 2023

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<https://doi.org/10.55810/2789-9136.1015>

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Saliva also contains chromogranin A (CgA), an acidic glycoprotein that is released from sympathetic nerve endings and the adrenal medulla [13].

According to earlier research, pigs under stress from isolation or immobilization had high concentrations of chromogranin A in their saliva; this suggests that salivary chromogranin A can be used as a sensitive and specific biomarker of acute stress in pigs [14].

Numerous studies have suggested that salivary CgA is a sensitive as well as promising salivary biomarker of psychosomatic stress in people [15].

Although the mucosa's clinical appearance is normal, BMS is distinguished by a burning sensation or dysesthesia [16].

This study is aimed to evaluate certain oral diseases, such as burning mouth syndrome in major depressive disorder patients, and it also aimed to study the levels of specific salivary biomarker (chromogranin A) in major depressive disorder patients.

2. Materials and methods

This cross-sectional study was carried out at Al-Hakim Hospital in Najaf City, Iraq, and was authorized by the Ethical Committee of the College of Dentistry, Baghdad University (Project No: 458722).

2.1. Data collection

A total of 49 patients with MDD were included in the study, being under treatment for at least two weeks.

The control group consists of 34 healthy subjects with no signs & symptoms of systemic disease.

The study group received a diagnosis in accordance with the Fifth Edition of The Diagnostic and Statistical Manual of Mental Disorders (DSM5) at Al-Hakim hospital by psychiatric specialists in Najaf city.

2.2. Inclusion & exclusion criteria

To be included in this study, Patients of 18 years or older who have been diagnosed with depression by a psychiatrist. Exclusion criteria included Patients who consult for emergencies, unable to self-complete the questionnaire, pregnant women, subjects on corticosteroid treatment, and history of radio or chemotherapy. All patients were examined to detect any oral manifestations, oral manifestations and asked about burning mouth syndrome (BMS). Sample collection was examined from the period 30/1/2021 to 29/4/2022.

2.3. Sample collection

Mouth washing with pure water was carried out right before sampling. All participants were instructed to collect saliva in their mouths for 10 min without swallowing and to spit into a clean plastic container. Saliva samples were kept in ice during the collection. In order to reduce bubble and foam, samples were centrifuged at speed of (3000–3500 RPM), the supernatant was aspirated and stored at -20°C freezer.

2.4. Measurement kit

A human CHGA (Chromogranin A) ELISA Kit was used to measuring salivary chromogranin A levels Catalog No: E-EL-H073.

2.5. Statistical analysis

Microsoft Excel and the statistical package for the social sciences (SPSS) version 23 were both utilized for the data entry and analysis.

Firstly, the distribution of variables of the study were tested, as the data were both descriptive and quantitative, a crossover for the data was done to find any important findings in the study, also χ^2 test was used to determine the association [if any] among the study variables, charts were used in our study too [Kolmogorov–Smirnov] test was used in our study to determine the normal distribution of the quantitative data.

3. Results and discussion

The study showed that the age range of patients with MDD was between (23–66) years, for the control subjects was (20–57) years.

The mean age of MDD patients was 44.3 years with standard deviation of ± 10.19 years.

For the control group, the mean age was 41.26 years, and the standard deviation was ± 10.98 years, with no significant difference, [Table 1](#).

The study showed that for the group of patients with MDD, the number of males was 26 (53.1%), the number of females was 23 (46.9%), and for the group of healthy subjects (control group), the number of males was 19 (55.9%), while the numbering of females was 15 (44.1%). With no significant difference, [Table 1](#).

3.1. Burning mouth syndrome

The results showed that for the study group there were 23 (46.9%) patients had BMS, while 26 (53.1%) patients of the study samples did not have BMS.

Table 1. Age and gender profile of major depressive disorder (MDD) patients in comparison to healthy controls: A demographic analysis.

Covariates	MDD patients		Control		P-value
Age(years)					
Range	23–66		20–57		0.133
Mean + -SDD	44.30 ± 10.19		41.26 ± 10.98		Ns
Gender	No.	%	No.	%	0.8
Male	26	53.1	19	55.9	Ns
Female	23	46.9	15	44.1	
Total	49		34		

*Ns: non-significant ($p > 0.05$).

As for the control group 5 (14.7%) individuals reported to have BMS, while 29 (85.3%) individuals didn't have BMS, as shown in Table 2.

Chronic pain and discomfort in the mouth are the hallmarks of burning mouth syndrome (BMS), a condition that lacks any visible lesions that would indicate its cause in a clinical setting [17].

The pathogenesis of BMS is multifaceted and elusive, and 85% of individuals with BMS report having psychosocial comorbidities. In contrast to aetiological initiating triggers, it is yet unknown if the psychological disorders are a result of having BMS, separate comorbidities, or modifiers of the BMS symptoms [17–20].

The current study's findings revealed a statistically significant rise in BMS in major depressive patients compared to healthy volunteers. As a result, our findings suggest that BMS and psychological disorders are related. This study's findings are consistent with those of earlier investigations [20,21].

Mental illnesses like depression and anxiety are crucial in the modulation of pain perception because they alter individual pain perception by affecting the pain threshold, affecting nerve transmission from the peripheral pain receptors, and increasing or decreasing individual pain perception [22].

3.2. Salivary chromogranin A

The mean and standard deviation of salivary chromogranin A was 31.46 ± 10.93 pg/ml, the range was from 12 to 57 pg/ml for patients in the study group, while for control group, the mean and

Table 2. The number, percentage and p-value of subjects with Burning mouth syndrome.

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

*S: Significant ($p < 0.05$).

Table 3. The mean, standard deviation, and range of salivary chromogranin A in MDD patients and control subjects.

Groups	No.	Mean Pg/mL	SDD	Range	P-value
MDD patients	49	31.46	10.93	12–57	0.003
Control	34	24.96	7.16	12–41.5	*S

S:- Significant ($p < 0.05$).

standard deviation was 24.96 ± 7.16 , the range was 12–41.5 pg/ml.

The results of this study showed that there was a significant difference of salivary chromogranin A levels between study and control groups, ($p < 0.05$) using t-test. So salivary chromogranin A was significantly higher in MDD patients ($p < 0.05$) than in control subjects, as shown in Table 3. The results also showed that there was no correlation between salivary chromogranin A and other parameters except for Gender, as shown in Table 4.

Initially identified as the primary soluble protein of adrenal medullary chromaffin granules, salivary chromogranin A is an acidic glycoprotein. Since then, it has been found to associate with catecholamines in the secretory granules of a variety of endocrine structures and neurons [23,24].

It has been shown that CgA is stored in the submandibular gland's granular convoluted tubule and released into the saliva in response to norepinephrine and acetylcholine stimulation [25,26]. As a result, the submandibular gland releases salivary CgA when stimulated [27].

There are no reports on the level of salivary chromogranin A in people with depression or anxiety, despite previous research showing that a rapid and specific increase in CgA in human saliva occurs in response to various stress factors. The fact that salivary CgA levels are not influenced by the time of day is a significant benefit of this method of measurement [28].

No previous studies assessed salivary chromogranin A levels in major depressive disorder; however, it was found that significantly increased

Table 4. The correlation and p-value between salivary Chromogranin A and clinical findings of MDD patients.

Correlation coefficient	Chromogranin A
Age	$r = -0.16$ $p = 0.26$
Gender	$r = -0.33$ $p = 0.01$ *S
Duration of disease	$r = 0.27$ $p = 0.05$
Burning mouth syndrome	$r = 0.1$ $p = 0.49$

S:- Significant ($p < 0.05$).

salivary chromogranin A levels in subjects under psychological stress [29].

According to Matsumoto et al., women who were premenstrually exhibiting a cluster of extremely distressing negative emotional symptoms had significantly higher salivary CgA levels in the late-luteal phase [30].

4. Conclusions

In conclusion, we found MDD patients have much higher incidents of reporting burning mouth syndrome, indicating the importance of psychological factors in this condition, finally, salivary chromogranin A as a good salivary biomarker for MDD; however, we suggest more research to be done with larger sample size.

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