Evaluation salivary level of Glutathion reductase, Catalase and Free thiol in patients with temporomandibular joint disorder

Fahimeh Rezazadeh (rezazadehf@sums.ac.ir)
Shiraz University of Medical Sciences
Nima Fassihi
Shiraz University of Medical Sciences
Dorsa Mahdavi
Shiraz University of Medical Sciences
Amir Tabesh
Shiraz University of Medical Sciences
Elham Tayebi Khorami
Shiraz University of Medical Sciences
hossein sedarat
Jahrom University of Medical Sciences

Research Article

Keywords: Temporomandibular joint disorder, saliva, Glutathion reductase, catalase, free thiol

Posted Date: April 19th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1552798/v1

Abstract

Introduction:

Temporomandibular joint disorders (TMD) are characterized by jaw pain combined with dysfunction of the muscles and joints. Extreme fabrication of oxidative stress in the TMJ thus results in tissue injury, which advances to TMD.The aim of this study was to evaluate the Glutathion reductase, catalase, and free thiol in saliva of TMD patients and compare it with people without TMD.

Materials and Methods

In this cross sectional study 35 patients with temporomandibular joint and 20 people without TMD were participated in the study. Five mL of each unstimulated saliva sample was collected in the morning and salivary level of antioxidants was assessed by ELISA (Enzyme Linked Immunosorbent Assay) technique. Helkimo index and visual analogue scale (VAS) also were measured during this experiment.

Results

There was significantly decrease in salivary level of Glutathion reductase and catalase in patients but there were no differences among two groups in free-thiol level.There was also correlation between antioxidant status and presence of click, pain and severity of disease; however, there was no correlation between age and gender with antioxidants contents.

Conclusion

The mean salivary levels of Glutathion reductase and Catalase in TMD patients were lower than that in the control group, which means these antioxidants were affected by TMD and also related with severity of it, but no significant difference was detected in salivary Free thiol between groups. So salivary Glutathion reductase and Catalase level may be used as a biomarker for TMD monitoring and treatment.

Introduction

Temporomandibular joint (TMJ) disorders are a pathologic state describing a sort of indicators of modified arrangement or presentation of articular and periarticular tissues(1). The aetiology of Temporomandibular muscle and joint disorder (TMD) is poorly comprehended but is possible to be multifactorial and comprises,, anatomical, psychosocial and pathophysiological features. Successful administration of the disorder involves recognising and management of these disposing and causative features(2). Musculoskeletal dysfunction is the most prevalent source of TMD(3). Parafunctional behaviors such as, teeth grinding, bruxism, clenching and stress and anxiety, may all conduct to masticatory muscle spasm and ache. Perceptive and psychiatric disruption, such as anxiety and

depression, autoimmune disorders, and other chronic pain situations also commonly comply with TMD(4). Intra-articular reasons of TMD include internal joint derangement, capsular inflammation, osteoarthritis, hypermobility and traumatic harm. Articular disc displaceme is the most common intra-articular etiologic factor of TMD(5). Temporomandibular muscle and joint disorders (TMD) are the second most prevalent musculoskeletal conditions culminating in ache and disability, succeeding to chronic low back pain. TMD prevails among 5 to 12% of the population, with an annual cost estimated at 4 billion dollars. One half to two-thirds of people with TMD complaints will chase treatment. Among this group, about 15% will prosper chronic TMD(6). Therefore, there is a prerequisite to advance enhanced plans for handling musculoskeletal ache. These efforts are blocked by the statement that ache is mainly a subjective sensation for which objective conditions do not at present exist. Identification of biomarkers as an objective portion for musculoskeletal ache would resolve this problem and produce metrics to measure the validity of clinical inquiry(7). Levels of biomarkers have been assessed in patients with TMD to describe the pain mechanism and enable early detection of joint pain and destruction with the aim of avoiding the progression of pain and disability(8, 9). Oxidative stress (OS) appears due to the discharge of free radicals in high strengths, over-whelming the natural scavenging mechanisms of antioxidant defense resulting in subsequent initiation of inflammatory processes(9, 10). Physiologically, antioxidants neutralize the toxicity of free radicals and cytokines, and reduction in antioxidant levels induces to OS(11). In the TMJ, mechanical stress, trauma, degenerative changes and disk derangements, can provoke the release of free radicals resulting in OS and an inequality in resulting biomarkers(12). To balance the oxidative stress, animals and plants preserve compound structures of overlapping antioxidants, such as glutathione and enzymes (e.g., superoxide dismutase and catalase), manufactured internally, or the dietary antioxidants vitamin E and C (13). Catalase is a usual enzyme detected in almost all living creatures exposed to oxygen. Catalase is a very significant enzyme in defending the cell from oxidative harm by reactive oxygen species (ROS). Also, catalase has one of the highest turnover records of all enzymes; one catalase molecule can transform millions of hydrogen peroxide molecules to oxygen and water per second(14). Glutathione reductase catalyzes the reduction of glutathione disulfide (GSSG) to the sulfhydryl form glutathione (GSH), which is an important molecule in resisting oxidative stress and preserving the reducing situation of the cell. The ratio of GSSG/GSH existing in the cell is a key cause in accurately maintaining the oxidative stability of the cell, it is significant that the cell preserves great stages of the reduced glutathione and a small stage of the oxidized glutathione disulfide. This slight balance is preserved by glutathione reductase, which catalyzes the reduction of GSSG to GSH(15).; Thiol collections are significant players of the antioxidant team and have been displayed to annihilate ROS and other free radicals by enzymatic and non-enzymatic appliances(9). Total thiol groups of proteins are chiefly in charge for their antioxidant reply, and they can serve as a delicate pointer of oxidative stress (16). Intracellular thiols such as glutathione act a significant role in preserving the extremely reduced surroundings inside the cell (9). Extracellular thiols are protein bounds and are chiefly disulfide proteins due to the oxidative surroundings. Total thiol position in the body, exclusively thiol groups existing on protein are studied as major plasma antioxidants in vivo and most of them are existing over albumin, and they are the main reducing groups existent in our body fluids (10). When the cells are revealed to oxidative stress, thiol groups are the first antioxidants that are expended. Thiol oxidase is an enzyme that

catalyse the chemical feedback among the reduced form of the thiol (free thiol) and the oxidize form of the thiol(disulfide form)(16). Saliva is a protecting fluid of the oral cavity and has been suggested as a probable diagnostic medium for numerous conditions. Salivary assays ,unlike blood, are less disturbing, and can be self-administered without distinctive tools or personnel, and cost. Combined of both enzymatic and non-enzymatic antioxidants, saliva acts a remarkable role as portion of the antioxidant structure (17, 18). Its non-aggressive collection produces saliva the biological fluid of preference to regulate stages of biomarkers associated with OS and can verify to be a brilliant diagnostic approach to perceive primary TMJ degenerative alterations. To neutralize the toxic outcomes of oxidants, saliva has developed a sequences of low molecular weight antioxidants (LMWA) (e.g. uric acid, reduced glutathione and ascorbate) and antioxidant albumin from plasma is transported to saliva via the crevicular fluid(19).

With regards to previous studies ,considering the fact that no similar studies have evaluated these biologic markers, we aimed to find out the salivary level of catalase, glutathione reductase and free thiol in patients with TMDs and the relation between these values and severity of disease.

Materials And Method

In this cross sectional study (during 2019–2020) 35 patients with temporomandibular joint disorder ,who referred to oral and maxillofacial disease department of Shiraz dental faculty, were enrolled based on RDC criteria. 20 cases without TMD were chosen as control group (age and sex matched). Clinical examination including pain severity of TMJ, muscle tenderness, jaw movement, click sound, deviation and Helkimo-Index(20) was taken. Pain severity was evaluated based on visual analogue scale (VAS). The inclusion criteria for the patients was having one or more of RDC criterias of TMD (ache in the TMJ and/or in the masticatory muscles; muscle spasm or clicking) and signing the written consent form. The exclusion criteria were the following: other inflammatory diseases; the use of anti-inflammatory drugs during 2 months ago, muscle relaxants and/or analgesics, vitamin E and/or vitamin C; smoking, which rises the levels of oxidants; and individuals who had been formerly treated for TMD.

This study was approved by ethical committee of Shiraz University of Medical Science (number = IR.SUMS.DENTAL.REC.1398.108).

Subjects were appealed to not using chewing gum, lipstick, drinking or eating any liquids excepting water for one hours before sampling saliva. They rinsed their oral cavity for 30 s with clean water, and the water was removed. Subjects were trained not to attempt to produce saliva, think, or talk about foods.

Five mL of unstimulated saliva sample was collected in a sterile container in the morning, and frozen at -20 c and stored until the start of analysis. Salivary level of antioxidants was measured by ELISA (Enzyme Linked Immunosorbent Assay) technique using Kiazist kit (Kiazist, Iran).

Data analyzed by SPSS version 25.0 (SPSS Inc., IL, USA), applying mean ± SD and frequency (%). Independent t-test and chi square were used to compare all data such as age, sex, pain severity, Helkimo

index between groups. A repeated measure ANOVA (RM-ANOVA) was used to assess the changes in some measurement during times. $P < 0.05$ was significant.

Result

In this experiment, we evaluated 35 patients with TMD problems and 20 healthy people. Total mean age of the patients and healthy participants was 31.38 ± 10.55 (age range: between 19–65). The mean age of patients was 33.77 ± 11.88 and healthy participants' was 31.85 ± 5.98 which there was no significant differences between them ($p = 0.43$).

We had 36 females and 19 males in total. In control group we had 11 females and 9 males, versus 25 females and 10 males in TMD group. Regarding to Chi-square test, both groups were similar in sex distribution ($p = 0.21$).

In patients with TMD based on Click examination we had 11 patients with left click (31.4%), 7 with right click (20%), 11with bilateral click (31.4%) and 6 patients with no sign of click (17.1%).

Based on having pain, we had 16 patients with pain (45.7%) and 19 patients without pain (54.3%).

Also we had 9 patients with left deviation (25.7%), 9 patients with right deviation (25.7%) and 17 patients with no sign of deviation (48.6%).

Statistical analyses of data showed that the mean Glutathion reductase was 0.2536 (± 0.1610) mU/ml in TMD patients and 0.3901 (± 0.1060) mU/ml in control group. The mean saliva level of catalase was 0.1590 (± 0.0711) mU/ml in TMD patients and 0.2700 (± 0.0563) mU/ml in control group. Salivary level of free thiol was 0.0604 (± 0.0497) mU/ml in TMD patients and 0.0569 (± 0.0155) mU/ml in control group.(Fig. 1)

According to Independent T-test, there was a significant decrease in salivary level of Glutathion reductase and catalase in patients ($p = 0.001$) but there were no differences between two groups in free-thiol level($p = 0.75$).

Based On One Way ANOVA test, there was no relation on Glutathion reductase, Ctalase and Free thiol level with age and sex and main relation was on differences between Groups in Glutathion reductase and Catalase.(Table 1).

Table 1: Comparison of, age and sex in different antioxidants

		p-value
Glutathion reductase	Group	0.007
	Age	0.543
	Sex	0.142
Catalase	Group	0.000
	Age	0.952
	Sex	0.489
Free thiol	Group	0.665
	Age	0.257
	Sex	0.201

Generally there was significantly decrease in glutathione reductase (p = 0.001) and catalase level(p = 0.020) in TMD patients suffering pain.(Table 2)

Table 2
Comparison of pain in different antioxidants

	Pain	Number	Mean	St.Deviation	P-value
glutathion_reductase (mU/ml)	Yes	16	0.1544	0.1282	0.000
	No	19	0.3371	0.1385	
Catalase	Yes	16	0.1296	0.0546	0.020
(mU/ml)	No	19	0.1837	0.0752	
free_thiol	Yes	16	0.0578	0.0209	0.782
(mU/ml)	No	19	0.0626	0.0655	

In total, there was a significant decrease in glutathione reductase (p = 0.001) and catalase level(p = 0.001) in patients with click.(Table 3)

Table 3
Comparison of Click in different antioxidants

	Click	Number	Mean	St.Deviation	P-value
glutathion_reductase	**Yes**	30	0.2243	0.1543	0.000
(mU/ml)	**No**	5	0.4290	0.0538	
Catalase	**Yes**	30	0.1391	0.0534	0.000
(mU/ml)	**No**	5	0.2783	0.0390	
free_thiol	**Yes**	30	0.0633	0.0529	0.419
(mU/ml)	**No**	5	0.0435	0.0169	

There was no significant difference, in three antioxidants level between patients with or without deviation. (Table 4)

Table 4
Comparison of Deviation in different antioxidants

	Deviation	Number	Mean	St.Deviation	P-value
glutathion_reductase	**Yes**	18	0.2167	0.1552	0.167
(mU/ml)	**No**	17	0.2926	0.1624	
Catalase	**Yes**	18	0.1425	0.0554	0.162
(mU/ml)	**No**	17	0.1764	0.0828	
free_thiol	**Yes**	18	0.0750	0.0655	0.075
(mU/ml)	**No**	17	0.0450	0.0142	

In total there was a significant decrease in glutathione reductase ($p = 0.001$) and catalase level($p = 0.011$) in patients with Helkimo more than ten points.(Table 5)

Table 5
Comparison of Helkimo index in different antioxidants

	Helkimo	Number	Mean	St.Deviation	P-value
glutathion_reductase (mU/ml)	< 10	18	0.3785	0.1146	0.000
	> 10	17	0.1213	0.0711	
Catalase	< 10	18	0.1879	0.0719	0.011
(mU/ml)	> 10	17	0.1283	0.0575	
free_thiol	< 10	18	0.0671	0.0674	0.425
(mU/ml)	> 10	17	0.0534	0.0181	

Discussion

It is noted that reactive oxygen species (ROS), comprising free radicals such as hydroxyl radical and superoxide anion, are extremely reactive molecules normally, produced through normal metabolism and cellular breathing. Below usual physiological state, free radicals can also behave as triggering molecules included in cellular mechanism, for example signal transmission of numerous gene expressions. Gathering of extra free radicals in a tissue results in a pathologic state by injuring intracellular and extracellular molecules as well as extreme activation of cellular procedures, such as DNA injury, lipid oxidation or denaturation of protein. To manage free radical facilitated reaction, antioxidant enzymes [e.g. superoxide dismutase (SOD),] presented in the body that function to transform extremely reactive free radicals to a smaller amount of active molecular types(21). Furthermore, low-molecular-weight antioxidant, such as, glutathione, ascorbate scavenge free radicals as they are generated in metabolically active tissues. Free radical responses and oxidative destruction are in the majority of situations detained in check by aforesaid antioxidant defence tools, but where an extreme quantity of ROS are generated or defence methods are harmed, oxidative damage such as lipid peroxidation can emerge. Such type of disturb among composition of ROS and antioxidant defence structure was accomplished certain as oxidative stress. It has furthermore been claimed that mechanical stresses may cause to ROS-induced oxidative stress of the temporomandibular joint (TMJ). Extreme generation of oxidative stress in the TMJ then results in tissue harm, which advance promotes to TMD(22).

In this study the relationship between mean salivary level of some of antioxidants (Glutathione reductase, Catalase and Free thiol) and TMD were analyzed. There was a significant reduction in Glutathione reductase and Catalase level in TMD patients in comparison with healthy people; due to the click, pain mechanisms, and severity of TMD (Helkimo index), which means these antioxidants were affected by TMD. To the best of our knowledge there was not found any similar study that assessed salivary level of these antioxidants in TMD. (However, various researches assessed other antioxidants level in TMD patients that we compared them with our study. in accordance with present study) Orhan et al discovered that the action of SOD appeared to be increasingly declined as the stage of the temporomandibular joint

internal derangement increased. However, they evaluated synovial fluid of patients with temporomandibular joint internal derangement and proved the association between the action of SOD and the stage of the disease. (23).

Confirming the finding of the present study, Lawaf et al measured the total antioxidant capacity(TAC) of saliva and serum of TMD patients. They assumed that the mean plasma TAC in TMD patients with/without pain was meaningfully lower than control group but no significant distinction was detected in salivary TAC between their groups(24).

Suma et al, proved in their experiments on brain tumor patients whose salivary protein thiol levels were significantly raised(25), although the condition of their patients was different from our patients, maybe with the reduction of free thiol in reduced form of intracellular glutathione, there was another compensating way with another form of extracellular free thiol protein and the final measurable free thiol remained constant in our results.

According to this study, age and gender have no relationship with antioxidants level. So the level of antioxidants is not affected by age and gender of the patients.

In accordance with our result, Demir et al also surveyed relation between expressive features (gender and age) and serum stages of malondialdehyde (MDA), an oxidative stress indicator, and antioxidant enzymes glutathione (GSH), catalase (CAT), and superoxide dismutase (SOD) in TMD patients. They discovered that there were no changes among the groups for gender and age. There was no relationship among gender and age and SOD, MDA, GSH and CAT levels in the TMJ disorders or control group. They finally decided oxidative stress indicators might have promising capacity as biomarkers in the diagnostic approach and therapeutic goals of TMJ disorders(26).

As we found in this study, Ishimaru et al, surveyed the relationship among the antioxidant volume of synovial fluid and radiological outcomes of intra-articular structures in patients with disorders of the temporomandibular joint (TMJ), they clarified that there is a relationship among the oxidative stress of the synovial fluid and closed-lock in disorders of the TMJ(27). They perceived that there is a significant decrease in antioxidant volume of synovial fluid of patients with close lock, as we showed there is decrease in antioxidant capacity of saliva in patients with click and the relation between click and decreasing antioxidants values.

In contrast, Almedia et al perceived as a result, the oxidative stress index (OSI) was meaningfully greater in the TMD and pain group. There was no relationship among Visual Analogue Scale (VAS), total antioxidant capacity (TAC), and total oxidant status (TOS) values. They discovered, oxidative changes appear to effect the pathogenesis of pain in TMDs (28). Our results are in according to their results which there is decrease in antioxidants values in those patients with pain and there is significant relationship in having pain and decreasing antioxidants.

Ahmed Fleifel et al revealed Oxidative stress of SOD and MDA was raised while GSH was declined. Based on these outcomes they decided that Oxidative stress is related in the pathogenesis of the temporomandibular joint disorders. The antioxidant agents might be deemed in managing of TMJ pain and dysfunction to inhibit probable elevated oxidative stress(29).

Tomida et al researched the redox status of albumin in the synovial fluid from patients with temporomandibular joint (TMJ) disorders (TMD).They discovered that the TMJ is marked by intra-articular oxidative stress, and the seriousness of TMD relates closely with the amount of oxidative elements(30). We also perceived decrease in GSH in our results and the relationship between oxidative stress, click and TMD; that decreasing antioxidants or increasing oxidative stress affects TMD situation. Although Tomida analysed on albumin in synovial fluid but their results is in accordance to our findings.

Ege et al investigated on serum prolidase action and oxidative stress in patients with temporomandibular joint internal derangement (TMJ-ID). They assumed meaningfully elevated prolidase action and oxidative stress in patients with TMJ-ID; they also found there was no important difference in GSH among groups(31). Our results were different from their result in GSH content which may be because of measuring serum instead of saliva or measuring only patients with internal derangement.

Limitation of this study: the sample size was small, another limitation of our study was discovering an approved laboratory to obtain reliable saliva test results. different labs and several kits were assessed and the reliability and validity of the one, used in our study, were proved.

Conclusion

In this study we found salivary level of Glutathion reductase and Catalase were lower in TMD group patients than the group without TMD. there was also correlation between presence of click, pain and severity of TMD (Helkimo index) with antioxidant status; however, there was no correlation between age and gender with antioxidants contents. our findings show these antioxidants were affected by TMD and also related to severity of it. So salivary Glutathion reductase and Catalase level may be used as a biomarker for TMD monitoring and treating.

Declarations

Acknowledgment:

The authors would like to thank the Vice-Chancellery of research, Shiraz University of Medical Sciences for supporting this research (Grant#17801). This article is based on the thesis by nima fasihi. The authors of would also like to thank Dental Research Development Center, for help in statistical analyses.

Compliance with ethical standards

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Contribution:

Fahimeh Rezazadeh: study design and concept, data interpretation, drafting, Final approval, Agreement to be accountable for all aspects of the work

Nima Fassihi , Dorsa Mahdavi : study design and concept, data collection , drafting, Final approval, Agreement to be accountable for all aspects of the work

Hossein sedarat, Amir Tabesh , Elham Tayebi Khorami : data interpretation, drafting, Final approval, Agreement to be accountable for all aspects of the work

Funder:

Shiraz University of medical science

Data Availability Statement:

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

1. Singh RK. Temporomandibular joint disorders. National journal of maxillofacial surgery. 2016;7(1):1-2.
2. Sharma S, Gupta DS, Pal U, Jurel SK. Etiological factors of temporomandibular joint disorders. National journal of maxillofacial surgery. 2011;2(2):116.
3. Reiter S, Goldsmith C, Emodi-Perlman A, Friedman-Rubin P, Winocur E. Masticatory muscle disorders diagnostic criteria: the American Academy of Orofacial Pain versus the research diagnostic criteria/temporomandibular disorders (RDC/TMD). Journal of oral rehabilitation. 2012;39(12):941-7.
4. Scrivani SJ, Keith DA, Kaban LB. Temporomandibular disorders. New England Journal of Medicine. 2008;359(25):2693-705.

5. De Leeuw R, Klasser GD. Orofacial pain: guidelines for assessment, diagnosis, and management: Quintessence Chicago; 2008.
6. Available at:http://www.nidcr.nih.gov/DataStatistics/FindDataByTopic/FacialPain/. . National Institute of Dental and Craniofacial Research Facial pain. Accessed March 7, 2014.
7. Dl B. AV, El Schiffman,Pa Lenton,Da Besspiata,Am Rankin,Pj Hughes,Jq Swift,Lj Kehl. Human Temporomandibular Joint and Myofascial Pain Biochemical Profiles: A Case-Control study. . J Oral Rehabil 2012 May 39(5): 326–337. doi:10.1111/j.1365-2842.2011.02271.x.
8. Richards RS RT, McGregor NR, Dustan RH, Butt HL. Blood parameters indic-ative stress are associated with symptom ex-pression in chronic fatigue syndrome. . Redox Rep 2000;5(1):35-41. .
9. Jones DP CJ, Mody VC, et al. Redox state of glutathione in human plasma. . Free Radic Biol Med. 2000 Feb 15; 28: 625-35.
10. Schafer FQ BG. Redox environment of the cell as viewed through the redox state of the glutathione disulfide/glutathione couple. . Free Radic Biol Med 2001; 30: 1191-212.
11. Draper HH HM. Malondialdehyde determination as index of lipid peroxidation. . . Methods Enzymol. 1990;186:421-31.
12. HA. G. Multidisciplinary diagnosis and management of orofacial pain. . Gen Dent [PubMed: 12004713]. 2002; 50:178–186.[PubMed: 12004713].
13. Dabelstein W, Reglitzky A, Schütze A, Reders K, Brunner A. Automotive fuels. Ullmann's Encyclopedia of Industrial Chemistry. 2000:1-41.
14. DS G. "Catalase". . Molecule of the Month RCSB Protein Data Bank. (2004-09-01),Retrieved 2016-08-23.
15. M D. "Glutathione catalysis and the reaction mechanisms of glutathione-dependent enzymes". . Biochim Biophys Acta. (May 2013). 1830 (5): 3217–66. doi:10.1016/j.bbagen.2012.09.018. PMID 23036594.
16. Halliwell B GJ. The antioxidants of human extracellular fluids. . Arch Biochem Biophys. 1990; 280: 1-8.
17. Moore S CK, Miller NJ, Rice-Evans CA. Antioxidant activity of saliva and periodontal disease. . Free Radic Res. 1994; 21:417–425. [PubMed: 7834056].
18. Nagler RM KI, Zarzhevsky N, Drigues N, Reznick AZ. Characterization of the differentiated antioxidant profile of human saliva. . Free Radic Biol Med. 2002; 32:268–277. [PubMed: 11827752].
19. Sculley DV, Langley-Evans SC. Salivary antioxidants and periodontal disease status. Proceedings of the Nutrition Society. 2002;61(1):137-43.
20. Rani S, Pawah S, Gola S, Bakshi M. Analysis of Helkimo index for temporomandibular disorder diagnosis in the dental students of Faridabad city: A cross-sectional study. The Journal of the Indian Prosthodontic Society. 2017;17(1):48.
21. Halliwell B, Gutteridge JM. Free radicals in biology and medicine: Oxford University Press, USA; 2015.

22. Milam SB, Zardeneta G, Schmitz JP. Oxidative stress and degenerative temporomandibular joint disease: a proposed hypothesis. Journal of oral and maxillofacial surgery. 1998;56(2):214-23.
23. Orban G UST, Ilker D,Eugene E K, Murat H. . Superoxide Dismutase Activity in Synovial Fluids in Patients With Temporomandibular Joint Internal Derangement. . American Association of Oral and Maxillofacial Surgeons J Oral Maxillofac Surg. 65:1940-1943, 2007.
24. Lawaf S, Azizi A, Tabarestani T. Comparison of serum and salivary antioxidants in patients with temporomandibular joint disorders and healthy subjects. Journal of dentistry (Tehran, Iran). 2015;12(4):263.
25. Suma H, Prabhu K, Shenoy RP, Annaswamy R, Rao S, Rao A. Estimation of salivary protein thiols and total antioxidant power of saliva in brain tumor patients. Journal of cancer research and therapeutics. 2010;6(3):278.
26. Demir CY, Kocak OF, Bozan N, Ersoz ME, Demir H. Is there a role for oxidative stress in temporomandibular joint disorders? Journal of Oral and Maxillofacial Surgery. 2018;76(3):515-20.
27. kyoko I SO, Hitoshi Y,Shinpei M,Jun I,Kazuo S. Antioxidant capacity of synovial fluid in the temporomandibular joint correlated with radiological morphology of temporomandibular disorders. 53 British Journal of Oral and Maxillofacial Surgery. (2015) 114–120. Elsevier http://dx.doi.org/10.1016/j.bjoms.2014.10.006.
28. de Almeida C, Amenábar JM. Changes in the salivary oxidative status in individuals with temporomandibular disorders and pain. Journal of oral biology and craniofacial research. 2016;6:S1-S4.
29. Fleifel AM, Al Khiary YM. Oxidative stress biomarkers versus magnetic resonance imaging (MRI) assessment in patients with temporomandibular disorders. J Am Sci. 2013;9:649.
30. Tomida M, Ishimaru J-I, Murayama K, Kajimoto T, Kurachi M, Era S, et al. Intra-articular oxidative state correlated with the pathogenesis of disorders of the temporomandibular joint. British Journal of Oral and Maxillofacial Surgery. 2004;42(5):405-9.
31. Ege B, Kucuk AO, Koparal M, Koyuncu I, Gonel A. Evaluation of serum prolidase activity and oxidative stress in patients with temporomandibular joint internal derangement. CRANIO®. 2019:1-11.

Figures

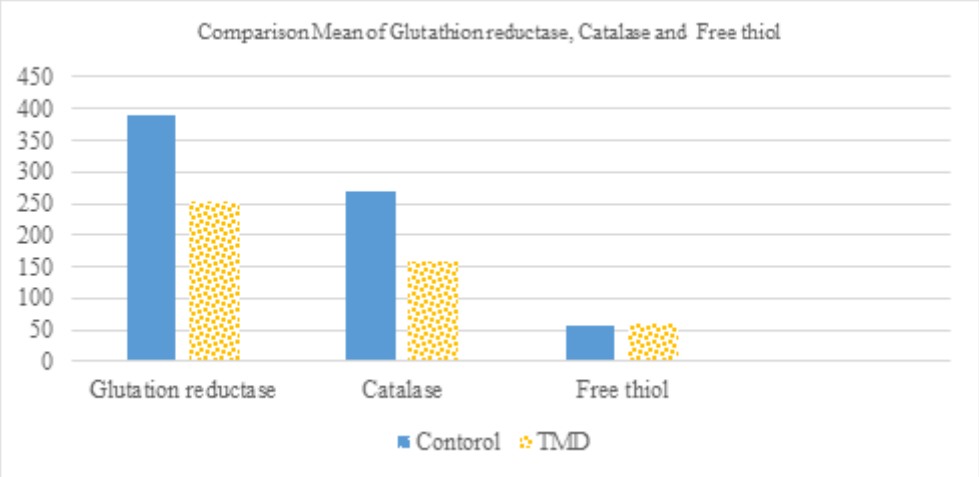

Figure 1

Comparison Mean of Glutathion reductase, Catalase and Free thiol between TMD and Control group