

IgA	493.21	0.479	0.24	0.208	0.063	0.179	0.288	0
								5
								3
								7

(*) HS: Highly Sig. at P<0.01; (*) S: Sig. at P<0.05; Non-Sig. at P>0.05; The positive actual state is Positive.

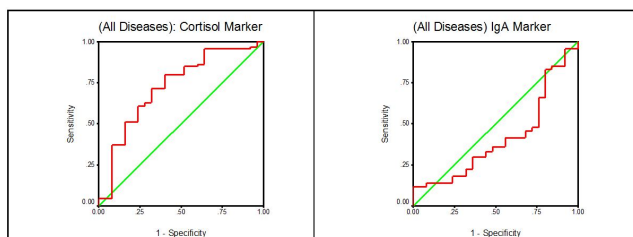


Figure 1: ROC curve plots of all disease's groups in admixture formed regarding studied markers.

DISCUSSION

Numerous studies on stress have pointed on several salivary stress biomarkers as indicators of stress reactions. So, salivary cortisol level is brought into relation by the hypothalamic pituitary-adrenal (HPA) axis activation [21]. In addition, because the immunosuppressive effect shown by stress, the level of secretory IgA [22] in saliva is used as a stress reactive biomarker. Estimation the levels of these salivary stress biomarkers (cortisol and IgA) in stressed individuals will aid to know that the stress as a one of the probable causes that explains the change in the levels of these salivary biomarkers. The salivary samples were collected from individuals; aged 15 years and over. The case group was stressed individuals with stress related oro-facial conditions and arranged into five subgroups (cheek biting, RAS, herpes labialis, tongue indentation, and TMJDs), their mean age was 23.94 years. The control group comprised of volunteers without stress, their mean age was 30.10 years. This study showed that there was a non-significant difference between the studied groups regarding gender. This result parallels other study done previously by Kania [23] who revealed that the difference in stress levels between males and females was insignificant.

Salivary cortisol is usually used as a biomarker of stress and related physical or mental diseases [15]. That agrees with the results of this study which show salivary cortisol is a useful biomarker for evaluating psychological stress. The results showed a high reading of salivary cortisol level was registered in comparison with that of the control group. There was a highly significant difference (Asymp. Sig.=0.001) between the study group and control group as shown in table II.

Cheek biting as a linea alba or traumatic ulcer may be Psychological related [24]. The results of this study

showed a highly significant difference (P= 0.000) was present between the case group of cheek biting and control group. The trimmed mean of salivary cortisol in control group was (83.17ng/ml) while in cheek biting group was (317.72 ng/ml).

Recurrent aphthous stomatitis (RAS) is a usual condition in which ovoid or round painful ulcers occur on the oral mucosa repeatedly. It is considered that psychological disturbances, for example stress and anxiety play an important role in the incidence of RAS [25]. In this study, the association between the salivary cortisol level and RAS was analyzed. The results showed a highly significant difference was accounted in at least at P<0.05 between control group and RAS group. This agrees with a previous study by Karthikeyan et al. [26] who found a high significant cortisol level in the RAS group in comparison with the control group and they suggested that a higher psychological stress level was present in the study group in comparison with the control group indicating that the psychological stress can play a role in the RAS manifestation.

Tongue indentation is a term for the appearance of tongue when indentations are present along the sides (the lateral borders), because of compression of the tongue opposing the adjacent teeth [27]. The results of this study showed (P=0.06) that can be reported as a significant difference between the case group of tongue indentation and the control group in correlation with the salivary cortisol level. As far as we know, there are no studies considering salivary cortisol level in stressed individuals to compare with the results of the current study.

Recurrent herpes labialis: a form of infection by herpes simplex virus (HSV-1). The reactivation occurs in the presence of aggravating factors and one of these factors is the emotional stress [28]. This result showed that there was a non-significant difference reported between the study group of recurrent herpes labialis and the control group according to the salivary cortisol level. This result disagrees with a previous study by Mehta et al [29] who confirmed that astronaut undertaking a long-duration spaceflight experience both increased latent viral reactivation and changes in diurnal trajectory of salivary cortisol concentrations. The statistical difference between this current study and the previous study may be attributed to a more stress level that the astronauts subjected in comparison with the participants of this study.

The factors that can prolong the symptoms of the temporo-mandibular joint disorders are stress and parafunction [30]. The results of this study showed that there was no significant difference reported between the study group of TMJ disorder and control group in relation with salivary cortisol level. This result is in agreement with Takatsuji et al [31] who observed no significant differences in the concentration of salivary cortisol before and after the student's examination, so these findings suggested that the acute stress because of the examination is not associated with salivary cortisol elevation. While this result disagrees with a previous result by Ali & Hadi [32] who studied salivary cortisol levels in 80 stressor students with a temporo-mandibular disorder and found significantly higher salivary cortisol levels than the controls. The cause of the non-significant difference of the result of this study may be due to the lower number of participants with TMD in comparison.

Considering IgA: There was a non-significant difference (Asy. Sig.= 0.179) in salivary IgA level between the general group of stress and control. This result agrees with a study by Lambert et al [33]. The authors indicated a normal SigA profile in stressed women who are breast cancer survivors in comparison with women without history of cancer. But, the result of the present study showed that there was a highly significant difference in salivary IgA level between study group of herpes labialis and control group and this is in agreement with a study by Shirtcliff et al [34]. The authors found higher significant HSV-sIgA levels in the physically abused and post institutionalized adolescents than in participants who had a normal rearing background.

In this study, the result showed that there was a non-significant difference in salivary IgA level between recurrent aphthous stomatitis group and control group and this disagrees with a previous study by Brozović et al [35] who noted that IgA values in saliva differed significantly in individuals with minor RAU (recurrent aphthous ulceration) during the acute stage in comparison with controls. The cause of the statistical difference with the present study may be because of the collection of all salivary samples was in the acute stage of RAS in the previous study in comparison.

The result of this study showed that there was a non-significant difference in salivary IgA level between study group of tongue indentation and control group. Also, the result of this study showed a non-significant difference in salivary IgA level between study subgroups of both of (cheek biting and tongue indentation) and control group. We did not find a study considering salivary IgA level in stressed patients with cheek biting or tongue indentation. The results of this study showed that there was a non-significant difference in salivary IgA level between TMD group and control group and this agrees with a study by Doepel et al [36] who found no significant changes when comparing salivary IgA levels before and after treatment TMD (temporo-mandibular disorder) patients.

REFERENCES

1. Maheswari T, Gnanasundaram N. Stress related oral diseases-A research study. *Int J Pharm Bio Sci* 2010; 1:1-10.
2. Bhushan K, Sandhu, PK, Sandhu S. Psychological stress related oral health problems-Dental perspective. *IJRID* 2014; 4:43-47.
3. Kandagal, VS, Shenai P, Chatra L, et al. Effect of stress on oral mucosa. *Biol Biomed Rep* 2012; 1:13-16.
4. Nagabhushana D, Rao BB, Mamatha GP, et al. Stress related oral disorders-A review. *J Indian Acad Oral Med Radiol* 2004; 16:197.
5. Sanadi RM, Vandana, KL. Stress and its implications in periodontics: A review. *J Indian Acad Oral Med Radiol* 2005; 17:8.
6. Makino M, Masaki C, Tomoeda K, et al. The relationship between sleep bruxism behavior and salivary stress biomarker level. *Int J Prosthodont* 2009; 22.
7. Preeti L, Magesh KT, Rajkumar K, et al. Recurrent aphthous stomatitis. *J Oral Maxillofac Pathol* 2011; 15:252.
8. Esguep A. Association between psychological disorders and the presence of Oral lichen planus, burning mouth syndrome and recurrent aphthous stomatitis. *Oral Med* 2004; 9:1-7.
9. Scully C. Oral and maxillofacial medicine: The basis of diagnosis and treatment. E- Book 2008.
10. Scott E. Cortisol and stress: How to stay healthy. About. com. Retrieved. 2011; 29.
11. Hoehn K, Marieb EN. Human anatomy & physiology. San Francisco: Benjamin Cummings 2010.
12. Debono M, Ghobadi C, Rostami-Hodjegan A, et al. Modified-release hydrocortisone to provide circadian cortisol profiles. *J Clin Endocrinol Metab* 2009; 94:1548-1554.
13. Dickerson SS, Kemeny ME. Acute stressors and cortisol responses: A theoretical integration and synthesis of laboratory research. *Psychol Bull* 2004; 130:355.
14. Gröschl, Michael. Current status of salivary hormone analysis. *Clin chem* 2008; 54:1759-1769.
15. Hellhammer DH, Wüst S, Kudielka BM. Salivary cortisol as a biomarker in stress research. *Psychoneuroendocrinol* 2009; 34:163-171.
16. Fagarasan S, Honjo T. Intestinal IgA synthesis: regulation of front-line body defences. *Nat Rev Immunol* 2003;3(1):63.
17. Cohen S, Miller GE, Rabin BS. Psychological stress and antibody response to immunization: A critical review of the human literature. *Psychosomatic Med* 2001; 63:7-18.
18. Junqueira LCU, Carneiro J. Basic histology. McGraw-Hill 2003.
19. Holmgren J, Czerkinsky C. Mucosal immunity and vaccines. *Nat Med* 2005; 11:S45-53.
20. Ng V, Koh D, Mok BY, et al. Salivary biomarkers associated with academic assessment stress among

- dental undergraduates. *J Dent Educ* 2003; 67): 1091-1094.
21. Clow A, Hucklebridge F, Thorn L. The cortisol awakening response in context. In: *International review of neurobiology*. Acad Press 2010; 153-175.
 22. Lee KM, Kang D, Yoon K, et al. A pilot study on the association between job stress and repeated measures of immunological biomarkers in female nurses. *Int Arch Occup Environ Health* 2010; 83:779-789.
 23. Kania SK. The relationship between gender differences and stress. *The Huron Univ Coll J Learn Motiv* 2014; 52:7.
 24. Dilsiz A, Aydin T. Self-inflicted gingival injury due to habitual fingernail scratching: a case report with a 1-year follow up. *Eur J Dent* 2009; 3:150.
 25. Ślebioda Z, Szponar E, Kowalska A. Etiopathogenesis of recurrent aphthous stomatitis and the role of immunologic aspects: Literature review. *Arch Immunol Ther Exp* 2014; 62:205-215.
 26. Karthikeyan P, Aswath N. Stress as an etiologic cofactor in recurrent aphthous ulcers and oral lichen planus. *J Oral Sci* 2016; 58:237-240.
 27. Ghom A. *Textbook of oral medicine and oral radiology* 2005.
 28. Woo SB, Challacombe S J. Management of recurrent oral herpes simplex infections. *Oral Surg Oral Med Oral Pathol Oral Radiol Endodontol* 2007; 103:S12-e1.
 29. Mehta SK, Laudenslager ML, Stowe RP, et al. Latent virus reactivation in astronauts on the international space station. *Npj Micrograv* 2017; 3:11.
 30. Wassell RW, Naru A, Steele J, et al. *Applied occlusion*. Quintessentials Dent Pract 2008.
 31. Takatsuji K, Sugimoto Y, Ishizaki S, et al. The effects of examination stress on salivary cortisol, immunoglobulin A, and chromogranin A in nursing students. *Biomed Res* 2008; 29:221-224.
 32. Ali SQ, Hadi R. Assessment of cortisol as salivary psychological stress marker in relation to temporomandibular disorders among a sample of dental students. *J Baghdad Coll Dent* 2015; 325:1-14.
 33. Lambert M, Couture-Lalande MÈ, Brennan K, et al. Salivary secretory immunoglobulin a reactivity: A comparison to cortisol and α -amylase patterns in the same breast cancer survivors. *Contemp Oncol* 2018; 22:191.
 34. Shirtcliff, EA. Coe CL, Pollak SD. Early childhood stress is associated with elevated antibody levels to herpes simplex virus type 1. *Proc Natl Acad Sci* 2009; 106:2963-2967.
 35. Brozović S, Vučićević-Boras V, Buković D. Serum Iga, Igg, Igm and salivary IgA in recurrent aphthous ulceration. *Coll Antropol* 2001; 25:633-637.
 36. Doepel M, Söderling E, Ekberg EL, et al. Salivary cortisol and Iga levels in patients with myofascial pain treated with occlusal appliances in the short term. *J Oral Rehabil* 2009; 36:210-216.