Sultan Qaboos University Med J, November 2015, Vol. 15, Iss. 4, pp. e507–511, Epub. 23 Nov 15
Submitted 28 Dec 14
Revisions Req. 10 Mar & 6 May 15; Revisions Recd. 13 Apr & 19 May 15
Accepted 24 May 15
doi: 10.18295/squmj.2015.15.04.011

CLINICAL & BASIC RESEARCH

Evaluation of Salivary Secretory Immunoglobulin A Levels in Diabetic Patients and Association with Oral and Dental Manifestations

Shahla Kakoei,[1,2] *Bahareh Hosseini,[1,3] Ali-Akbar Haghdoost,[4] Mojgan Sanjari,[5]
Ahmad Gholamhosseinian,[6] Vahid F. N. Afshar[2]

تقييم مستويات جلوبيولين المناعي A المفرز في اللعاب لدى مرضى السكري وعلاقته مع أعراض الفم والأسنان

شهلا كاكوي، بهاره حسيني، علي أكبر حاجدوست، مويجن سنجاري، أحمد غلام حسينيان ، وحيد افشار

ABSTRACT: ***Objectives:*** Oral and dental manifestations in diabetic patients can arise due to numerous factors, including elevated salivary secretory immunoglobulin A (s-IgA) levels. This study aimed to evaluate s-IgA concentrations in patients with type 2 diabetes mellitus (T2DM) and to investigate the association between s-IgA levels and oral and dental manifestations of T2DM. ***Methods:*** This cross-sectional descriptive study was carried out between October 2011 and September 2012 in Kerman, Iran, and included 260 subjects (128 patients with T2DM and 132 healthy controls). Unstimulated salivary samples were collected from all subjects and s-IgA levels were determined using the immunoturbidimetric method. The oral cavities and teeth of T2DM patients were evaluated for oral and dental manifestations. ***Results:*** Both diabetic and control subjects with higher concentrations of s-IgA had significantly higher numbers of decayed, missing or filled teeth (DMFT) and periodontal index (PDI) scores (P <0.050). s-IgA levels were significantly higher in subjects with oral candidiasis (P <0.050). Among diabetic patients, significantly higher s-IgA levels were concomitant with xerostomia and denture stomatitis (P ≤0.050). There were no significant differences between s-IgA concentrations and other oral or dental manifestations in either group. ***Conclusion:*** Individuals with a greater number of DMFT, a higher PDI score and oral candidiasis had significantly higher s-IgA levels. s-IgA levels were not significantly higher among diabetic patients in comparison to the control group. However, significantly higher s-IgA levels occurred with xerostomia and denture stomatitis in diabetic patients. In addition, s-IgA was significantly higher in patients with uncontrolled diabetes compared to those with controlled diabetes.

Keywords: Diabetes Mellitus; Saliva; Secretory Immunoglobulin A; Oral Manifestations; Iran.

الملخص: الهدف: أعراض الفم والأسنان في مرضى السكري يمكن أن تنشأ نتيجة لعوامل عديدة، بما في ذلك ارتفاع مستويات جلوبيولين المناعي A المفرز في اللعاب. هدفت هذه الدراسة إلى تقييم تركيز جلوبيولين المناعي A المفرز في لعاب المرضى الذين يعانون من النوع 2 من داء السكري ولتقييم ارتباط مستويات جلوبيولين المناعي A المفرز وأعراض الفم والأسنان. **الطريقة:** أجريت هذه الدراسة الوصفية المستعرضة بين أكتوبر 2011 وسبتمبر 2012 في كرمان، إيران، وشملت 260 شخصا (128 من مرضى السكري من النوع 2 و 132 من الاصحاء). تم جمع عينات اللعاب غيرالمحفز من جميع المشاركين وتم تحديد مستويات جلوبيولين المناعي A باستخدام طريقة قياس التعكر المناعي. تم تقييم تجاويف الأسنان والفم لمرضى السكري. **النتائج:** كان الاصحاء ومرضى السكري الذين لديهم تركيزات أعلى من مستويات جلوبيولين المناعي A لديهم نسبة أعلى إحصائيا من الأسنان النخرة والمفقودة أو بها حشو أسنان ودرجات مؤشر اللثة أعلى (P <0.050). وكانت مستويات جلوبيولين المناعي A أعلى بكثير في المشاركين الذين لديهم داء المبيضات الفموي (P <0.050). وفي مرضى السكري، كانت مستويات جلوبيولين المناعي A المرتفعة إحصائيا مصاحبة لجفاف الفم والتهاب الفم المصاحب لطقم الأسنان (P ≤0.050). لم توجد فروق اخرى ذات دلالة إحصائية بين مستويات جلوبيولين المناعي A و أعراض الفم أو الأسنان في أي من المجموعتين (السكري والأصحاء). **الخلاصة:** الاشخاص الذين لديهم أسنان نخرة أومفقودة أو بها حشو أسنان ودرجات مؤشر اللثة مرتفعة ولديهم داء المبيضات الفموي لديهم نسبة أعلى بكثير في مستويات جلوبيولين المناعي A. ولكن ليس هناك فرق إحصائي في مستويات جلوبيولين المناعي A لدى مرضى السكري مقارنة مع مجموعة التحكم الأصحاء. ومع ذلك، فهناك زيادة إحصائية في مستويات جلوبيولين المناعي A عند الأشخاص المصابين بجفاف الفم والتهاب الفم المصاحب لطقم الأسنان في مرضى السكري. بالإضافة إلى ذلك، فإن التهاب الفم المصاحب لطقم الأسنان أعلى بكثير في المرضى الذين يعانون من مرض السكري غير المنضبط مقارنة مع أولئك المصابين بداء السكري المنضبط بالعلاج.

مفتاح الكلمات: مرض السكري؛ اللعاب؛ جلوبيولين المناعي A؛ أعراض الفم؛ إيران.

Departments of [1]Oral Medicine and [6]Biochemistry and Centers for [2]Oral & Dental Diseases Research, [3]Endontology Research, [4]Modeling in Health Research and [5]Endocrinology & Metabolism Diseases Research, Institute of Basic & Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran

**Corresponding Author e-mail: bhd_1362@yahoo.com*

Advances in Knowledge

- *To the best of the authors' knowledge, little information exists regarding the probable association between salivary secretory immunoglobulin A (s-IgA) levels and oral and dental manifestations in patients with type 2 diabetes (T2DM).*

Advances in Patient Care

- *Determination of the salivary components of patients with T2DM could play a fundamental role in predicting, detecting and managing oral and dental manifestations of the disease. Based on the results of this study, it is recommended that patients exhibiting a change or decrease in their s-IgA levels undergo periodic oral health evaluations.*

Type 2 diabetes mellitus (T2DM) is one of the most prevalent metabolic disorders worldwide; by 2025, approximately 320 million people will have the disease.[1] The disease has a wide range of signs and symptoms and manifests differently in various organs. In the oral cavity, manifestations of diabetes can include a dry or burning mouth, periodontal diseases, bone loss, dental abscesses, fungal and bacterial infections, oral lichen *planus* and delayed wound healing.[1,2]

Immunoglobulin A (IgA) and immunoglobulin G affect oral cavity microorganisms in the saliva, gingival sulcular fluid and plasma.[3] These antibodies prevent bacterial metabolism and adhesion of microorganisms to the oral tissue.[3] Although there are many non-specific defensive elements in the saliva, such as lactoferrin and lysozymes, salivary secretory IgA (s-IgA) is the foremost protective mechanism against bacterial colonisation of the oral mucous membranes. As s-IgA plays an important role in protecting against these pathogens, the antibody might also protect against periodontal diseases.[4] Changes in salivary IgA concentrations in diabetic patients could have an effect on their oral health. Several studies have sought to determine salivary flow rates and components that can affect the progression, symptoms and varieties of oral changes in diabetic patients.[1,2,5] Overall, determining the salivary components of diabetic patients can be useful in detecting and managing their oral manifestations.[5]

Previous research has assessed s-IgA levels and oral conditions among diabetic patients. A Brazilian study reported that diabetic patients with lower s-IgA levels had more severe and frequent periodontal disease.[4] However, two Iranian studies yielded different results: Mohiti-Ardekani *et al*. recorded significantly higher s-IgA levels in diabetic patients while Bakianian Vaziri *et al*. found no significant differences between diabetic and non-diabetic groups.[1,5] Other studies have also reported conflicting results with regards to s-IgA levels and their relationship to various diseases.[6,7] The current study aimed to compare s-IgA levels between healthy subjects and T2DM patients and determine the association between s-IgA levels and various oral and dental manifestations in diabetic patients. This relationship could help determine the prognosis of oral diseases in diabetic patients and serve as a guide for their dental care.

Methods

This cross-sectional descriptive study was carried out between October 2011 and September 2012 in Kerman, Iran, and included 260 subjects divided into two groups. The first group consisted of 128 patients with T2DM who routinely attended follow-up appointments at the Diabetes Center of Shahid Bahonar Hospital in Kerman. The non-diabetic control group was composed of 132 healthy individuals with no history of DM who attended annual check-ups at either the Razi Laboratory or the Besat Clinical Laboratory in Kerman. Information regarding the subjects' gender, age, diabetes type and medical results (including assessments of glycated haemoglobin [HbA1C] and fasting blood sugar [FBS] levels) was compiled by a trained dental student. Smokers and subjects <20 years old were excluded from the study. Control subjects were included only if they had FBS levels of <100 mg/dL, no systemic disorders and did not take medications that affected either IgA secretion or its levels in the saliva. A diagnosis of T2DM was made with a HbA1C level of ≥6.5%, fasting plasma glucose (PG) level of ≥126 mg/dL and a two-hour PG level of ≥200 mg/dL. For patients exhibiting classic symptoms of hyperglycaemic crises, a random PG measurement of ≥200 mg/dL met the criteria for a diagnosis of T2DM.[8] Known diabetic patients who were already taking medicine for lowering blood glucose and who had a HbA1C level of ≥6.5% were determined to have uncontrolled T2DM.

The oral mucosa of all subjects was checked for abnormalities, including manifestations of oral candidiasis (erythematous candidiasis, thrush, angular cheilitis, median rhomboid glossitis and denture stomatitis), lichenoid reactions and frequent abscesses. The characteristics of any noted lesions and their locations were recorded. In addition, a tongue blade test was performed on all participants to detect xerostomia. The guidelines of the World Health Organization for assessing dental cavities were used to calculate the number of decayed, missing or filled teeth (DMFT).[9] The periodontal disease index (PDI) were used to evaluate the effect of any periodontal disease on the supporting tissues of the oral mucosa. Xerostomia was assessed using Fox *et al*.'s standardised questionnaire.[10]

Table 1: Correlation between salivary secretory immunoglobulin A concentrations and other variables among control and diabetic subjects in Kerman, Iran (N = 260)

Variable	Correlation with s-IgA concentration r (*P* value)		
	Control group (n = 132)	Diabetic group (n = 128)	Total
Age	0.05 (0.520)	0.15 (0.070)	0.10 (0.080)
HbA1C	-	0.30 (0.009)*	-
FBS	-0.07 (0.370)	-0.06 (0.460)	-0.01 (0.830)
DMFT	0.06 (0.510)	0.22 (0.040)†	0.14 (0.04)†
PDI	0.40 (0.001)*	0.50 (0.004)*	0.12 (0.001)*

*s-IgA = salivary secretory immunoglobulin A; HbA1C = glycated haemoglobin; FBS = fasting blood sugar; DMFT = decayed, missing or filled teeth; PDI = periodontal index. *Highly statistically significant at P <0.001. †Statistically significant at P <0.050.*

Unstimulated salivary samples were collected from all subjects in the morning (between 7:30 and 9:30 a.m.) after fasting for eight hours and having cleaned their mouths and teeth 90 minutes beforehand.[1] Participants were requested to keep their mouths closed for a few moments in order for saliva to pool and then hold their heads over a container and release, resulting in a sample of 1–2 mL of saliva.[3] Samples were then frozen to -20 °C and sent to a laboratory for testing.[11] Concentrations of s-IgA were determined using the immunoturbidimetric method with measurements obtained from a commercial kit (Pars Azmoon Co., Tehran, Iran) and an automated continuous flow analyser (AutoAnalyzer, TechniCon Systems Inc., Oakland, California, USA).[12]

Data were analysed using the Statistical Package for the Social Sciences (SPSS), Version 17 (IBM Corp., Chicago, Illinois, USA). Pearson's correlation coefficient test was used to determine the relationship between s-IgA levels and age, HbA1C and FBS. The independent t-test was used to compare DMFT and PDI indices between the groups.

This study was approved by the Ethics Committee of Kerman University of Medical Sciences (#K/91/05). All subjects gave informed consent before participating in the study.

Results

A total of 128 T2DM patients and 132 healthy adults were included in the study. The mean age of the subjects was 47.96 years (range: 20–83 years old). Mean s-IgA levels in the diabetic and control groups were 45.40 ± 6.87 mg/dL and 41.17 ± 7.66 mg/dL, respectively; this difference between the two groups was not significant (*P* >0.050). There was no significant difference in s-IgA levels between genders or with age. However, there was a significant increase in s-IgA levels among patients with uncontrolled T2DM compared to those with controlled disease (*P* <0.050). Both the DMFT and PDI indices showed significant increases among the diabetic patients in comparison with the control group (*P* <0.050). Between the two groups, s-IgA levels were significantly higher among subjects with a higher PDI index. Correlations between s-IgA levels and other variables are shown in Table 1.

Table 2: Comparison between salivary secretory immunoglobulin A levels and oral and dental manifestations among control and diabetic subjects in Kerman, Iran (N = 260)

Oral/dental manifestation	Control group		Diabetic group	
	Mean IgA in mg/dL ± SE	*P* value	Mean IgA in mg/dL ± SE	*P* value
Oral candidiasis	79.5 ± 16.5	0.010*	67.5 ± 10.6	0.006*
Erythematous candidiasis	-	-	74.0 ± 16.8	0.160
Thrush	-	-	49.0 ± 11.7	0.630
Median rhomboid glossitis	-	-	35.7 ± 15.9	0.810
Denture stomatitis	64.1 ± 22.9	0.280	71.4 ± 14.7	0.002
Angular cheilitis	95.0 ± 25.0	0.010*	89.2 ± 27.9	0.110
Lichenoid reactions	34.6 ± 6.6	0.880	126.5 ± 76.5	0.460
Frequent abscesses	-	-	35.0 ± 6.5	0.650
Xerostomia	35.0 ± 15.0	0.890	51.8 ± 7.5	0.050*

*IgA = immunoglobulin A; SE = standard error. *Statistically significant at P ≤0.05.*

Table 2 shows the distribution of various oral and dental manifestations among the two groups. s-IgA levels were significantly higher in subjects with oral candidiasis in both the diabetic and control groups. Tongue blade signs were positive for two subjects in the control group and 38 patients in the diabetic group. s-IgA levels were significantly higher for diabetic patients with xerostomia in comparison to the control subjects (*P* = 0.050). Diabetic patients also suffered from denture stomatitis more frequently than control subjects with significantly higher s-IgA levels (*P* ≤0.050).

Discussion

As patients with systemic diseases such as DM become better educated regarding self-management

and beneficial lifestyle choices, they are increasingly seeking to address their oral health issues.[13] While various research has focused on diabetic subjects, few studies have evaluated salivary immunoglobulin levels among this patient population. Unlike other body fluids, saliva is easily accessible and there is therefore no need for aggressive sampling techniques in order to make a diagnosis or determine the prognosis of a disease. As such, many researchers prefer to use saliva instead of blood for sampling purposes.[14,15] Saliva is a complex biological fluid and conditions which affect saliva production—such as xerostomia and saliva excretion dysfunction—decrease its buffering and cleansing capacity. In addition, neuropathic disturbances in diabetic patients can influence the development of dental caries and periodontal diseases.[16]

Within the oral cavity, s-IgA can act as the first line of defence against pathogens that affect mucous membranes by preventing the aggregation and adhesion of bacteria to the mucosa and neutralising enzymes, toxins and viruses.[10] The concentrations of various salivary elements, such as s-IgA, have been investigated in a number of systemic diseases as well as many oral conditions, including periodontitis, xerostomia, lichen *planus* and smoking-induced oral diseases.[14,17–21] Immune suppression or disturbances have been observed in diabetic patients;[2] it is possible that T2DM affects the secretion of IgA in the saliva and, consequently, the defence reaction of the mucosa.

In the present study, s-IgA levels in diabetic patients were not significantly higher in comparison with non-diabetic individuals. This result is similar to those seen in previous studies.[5–7,9,22] In contrast, Mohiti-Ardekani *et al.* demonstrated that s-IgA levels in diabetic patients were higher than in non-diabetics.[1] Other studies have also found higher s-IgA levels in diabetic patients.[1,22] Discrepancies between these results could be attributed to differences in study designs and sampling and measuring techniques (e.g. the use of stimulated versus unstimulated saliva or immunoturbidimetric versus immunonephelometric methods).[5] s-IgA levels were considerably higher in patients with uncontrolled T2DM in the current study. Harrison *et al.* and Malicka *et al.* found similarly high s-IgA levels in patients with poorly controlled diabetes.[10,24]

In the current research, there was a significant positive relationship between s-IgA and PDI and DMFT indices in both groups, suggesting that the innate immune system tries to synthesise high levels of IgA to reduce periodontal tissue infections.[10] In addition, Kakoei *et al.* also noted a positive association between high salivary glucose levels and DMFT and PDI indices in diabetic patients.[25] This is compatible with other findings showing that s-IgA levels were significantly higher in diabetic patients with periodontitis.[10,18,26] Using the gingival and modified sulcus bleeding indices, Malicka *et al.* reported that the periodontal status of diabetic patients was significantly worse than that of healthy subjects.[12] Ranadheer *et al.* showed that s-IgA levels were significantly higher among individuals with more than three DMFT.[15] In studies by Bakianian Vaziri *et al.* and Lopez *et al.*, diabetic patients had significantly increased numbers of DMFT in comparison with healthy subjects.[5,27]

In the current study, the prevalence of oral candidiasis was significantly higher in the subjects with higher s-IgA levels in both groups; this is consistent with the results observed by Jaganathan *et al.*[28] However, no significant relationship between s-IgA and oral lichen *planus* was found. This correlates with previous research by Divya *et al.*, who did not report any significant association between s-IgA levels and pre-cancerous lesions like lichen *planus*.[20] In contrast, Ghalayani *et al.* found higher s-IgA levels in patients with oral lichen *planus* in comparison with normal individuals.[21] In the present study, a significant increase in s-IgA levels was found in diabetic patients with denture stomatitis. A study by Papova *et al.* also showed that s-IgA levels in patients with denture stomatitis were significantly higher in comparison to a control group.[29] The results of the current study differed from those observed in a study by Wilson *et al.*, who found that that s-IgA levels were significantly lower in denture wearers with denture stomatitis in comparison to healthy subjects.[30]

Changes in the function and components of saliva as a result of different conditions among diabetic patients (e.g. dental caries, periodontitis, burning mouth and sensory problems) are not yet fully understood. Previous investigations have shown the efficacy of the buffering capacity and cleansing effect of saliva in negating some of these changes.[16] However, the differences in s-IgA levels in different studies could be attributed to different sampling techniques or detection methods. One of the limitations of the current study was an inability to assess oral hygiene among the subjects. Further investigations are recommended to detect salivary immunoglobulins among diabetic patients in order to determine a precise and more reliable technique to predict and manage oral manifestations of the disease.

Conclusion

The s-IgA levels of the diabetic patients were not significantly higher than those of the control group among the studied population. In both groups, subjects with a higher number of DMFT, greater PDI scores and oral candidiasis were found to have significantly

higher s-IgA levels. Among diabetic patients, significantly higher s-IgA levels were concomitant with xerostomia and denture stomatitis. Furthermore, s-IgA levels were found to be significantly elevated in patients with uncontrolled T2DM compared to those with controlled T2DM. Further research is needed to investigate s-IgA concentrations among diabetic patients in order to aid in the prediction and management of oral manifestations.

ACKNOWLEDGEMENTS

This article was based on a thesis submitted to the Kerman Dental School (no. 753). The authors wish to thank the Research Committee of the Kerman University of Medical Sciences for their financial support.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

References

1. Mohiti-Ardekani A, Karbassi MH, Mohiti-Ardekani J, Akhondinasab F, Mohammad MH. Evaluation of salivary IgA in diabetic and non-diabetic patients: A case-control study. Iran J Diabetes Obes 2012; 4:167–71.
2. Petrou-Amerikanou C, Markopoulos AK, Belazi M, Karamitsos D, Papanayotou P. Prevalence of oral lichen planus in diabetes mellitus according to the type of diabetes. Oral Dis 1998; 4:37–40. doi: 10.1111/j.1601-0825.1998.tb00253.x.
3. Marcotte H, Lavoie MC. Oral microbial ecology and the role of salivary immunoglobulin A. Microbiol Mol Biol Rev 1998; 62:71–109.
4. Branco-de-Almeida LS, Alves CM, Lopes FF, Pereira Ade F, Guerra RN, Pereira AL. Salivary IgA and periodontal treatment needs in diabetic patients. Braz Oral Res 2011; 25:550–5. doi: 10.1590/S1806-83242011000600013.
5. Bakianian Vaziri P, Vahedi M, Mortazavi H, Abdollahzade SH, Hajilooi M. Evaluation of salivary glucose, IgA and flow rate in diabetic patients: A case-control study. J Dent (Tehran) 2010; 7:13–18.
6. Bonamico M, Nenna R, Luparia RP, Perricone C, Montuori M, Lucantoni F, et al. Radioimmunological detection of anti-transglutaminase autoantibodies in human saliva: A useful test to monitor coeliac disease follow-up. Aliment Pharmacol Ther 2008; 28:364–70. doi: 10.1111/j.1365-2036.2008.03720.x.
7. Yap G, Sil BK, Ng LC. Use of saliva for early dengue diagnosis. PLoS Negl Trop Dis 2011; 5:e1046. doi: 10.1371/journal.pntd.0001046.
8. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2010; 33:S62–9. doi: 10.2337/dc10-S062.
9. World Health Organization. Oral health surveys: Basic methods. 3rd ed. Geneva, Switzerland: WHO Press, 1987.
10. Fox PC, Busch KA, Baum BJ. Subjective reports of xerostomia and objective measures of salivary gland performance. J Am Dent Assoc 1987; 115:581–4. doi: 10.1016/S0002-8177(87)54012-0.
11. Belazi MA, Galli-Tsinopoulou A, Drakoulakos D, Fleva A, Papanayiotou PH. Salivary alterations in insulin-dependent diabetes mellitus. Int J Paediatr Dent 1998; 8:29–33. doi: 10.1046/j.1365-263X.1998.00057.x.
12. Malicka B, Kaczmarek U, Skośkiewicz-Malinowska K. Selected antibacterial factors in the saliva of diabetic patients. Arch Oral Biol 2015; 60:425–31. doi: 10.1016/j.archoralbio.2014.07.010.
13. Parirokh M, Eghbal MJ, Ghoddusi J, Kakoei S, Haghdoost AA, Kakooei S. The frequency of medically compromised patients in endodontic offices in Iran. Iran Endod J 2013; 8:48–51. doi: 10.7508/10.7508/iej.
14. Castagnola M, Picciotti PM, Messana I, Fanali C, Fiorita A, Cabras T, et al. Potential applications of human saliva as diagnostic fluid. Acta Otorhinolaryngol Ital 2011; 31:347–57.
15. Ranadheer E, Nayak UA, Reddy NV, Rao VA. The relationship between salivary IgA levels and dental caries in children. J Indian Soc Pedod Prev Dent 2011; 29:106–12. doi: 10.4103/0970-4388.84681.
16. Al-Maskari A, Al-Maskari M, Al-Sudairy A. Oral manifestations and complications of diabetes mellitus: A review. Sultan Qaboos Univ Med J 2011; 11:179–86.
17. Ohyama K, Moriyama M, Hayashida JN, Tanaka A, Maehara T, Ieda S, et al. Saliva as a potential tool for diagnosis of dry mouth including Sjögren's syndrome. Oral Dis 2015; 21:224–31. doi: 10.1111/odi.12252.
18. Brito e Cabral P, Júnior JE, de Macedo AC, Alves AR, Gonçalves TB, Brito e Cabral TC, et al. Anti-PGL1 salivary IgA/IgM, serum IgG/IgM, and nasal Mycobacterium leprae DNA in individuals with household contact with leprosy. Int J Infect Dis 2013; 17:e1005–10. doi: 10.1016/j.ijid.2013.05.011.
19. Olayanju OA, Rahamon SK, Joseph IO, Arinola OG. Salivary immunoglobulin classes in Nigerians with periodontitis. J Contemp Dent Pract 2012; 13:163–6. doi: 10.5005/jp-journals-10024-1114.
20. Divya VC, Sathasivasubramanian S. Estimation of serum and salivary immunoglobulin G and immunoglobulin A in oral pre-cancer: A study in oral submucous fibrosis and oral lichen planus. J Nat Sci Biol Med 2014; 5:90–4. doi: 10.4103/0976-9668.127294.
21. Ghaleyani P, Sardari F, Akbari M. Salivary IgA and IgG in oral lichen planus and oral lichenoid reactions diseases. Adv Biomed Res 2012; 1:73. doi: 10.4103/2277-9175.102977.
22. Ben-Aryeh H, Cohen M, Kanter Y, Szargel R, Laufer D. Salivary composition in diabetic patients. J Diabet Complications 1988; 2:96–9. doi: 10.1016/0891-6632(88)90011-6.
23. Dodds MW, Yeh CK, Johnson DA. Salivary alterations in type 2 (non-insulin-dependent) diabetes mellitus and hypertension. Community Dent Oral Epidemiol 2000; 28:373–81. doi: 10.1034/j.1600-0528.2000.028005373.x.
24. Harrison R, Bowen WH. Flow rate and organic constituents of whole saliva in insulin-dependent diabetic children and adolescents. Pediatr Dent 1987; 9:287–91.
25. Kakoei S, Hosseini B, Haghdoost AA, Sanjari M, Hashemipour MA, Gholamhosseinian A. The detection of salivary glucose, caries and periodontal status in diabetes mellitus patients. J Oral Health Oral Epidemiol 2014; 3:79–84.
26. Bachrach G, Muster Z, Raz I, Chaushu G, Stabholz A, Nussbaum G, et al. Assessing the levels of immunoglobulins in the saliva of diabetic individuals with periodontitis using checkerboard immunodetection. Oral Dis 2008; 14:51–9. doi: 10.1111/j.1601-0825.2006.01345.x.
27. López ME, Colloca ME, Páez RG, Schallmach JN, Koss MA, Chervonagura A. Salivary characteristics of diabetic children. Braz Dent J 2003; 14:26–31. doi: 10.1590/S0103-64402003000100005.
28. Jeganathan S, Ufomata D, Hobkirk JA, Ivanyi L. Immunoglobulin A1 and A2 subclass of salivary antibodies to Candida albicans in patients with oral candidosis. Clin Exp Immunol 1987; 70:316–21.
29. Popova E, Stankova G, Dermendzieva S. [Quantitative determination of immunoglobulins in serum and saliva of patients with denture stomatitis]. Stomatologiia (Sofiia) 1989; 71:23–7.
30. Wilson J, Wilton JM, Sterne JA. Comparison of secretory IgA and IgG isotype levels in palatal secretions of denture stomatitis patients with denture wearers having clinically healthy palates. Eur J Prosthodont Restor Dent 2007; 15:50–4.