ECRONICON OPEN ACCESS

EC DENTAL SCIENCE
Research Article

Exploring the Relationship between Periodontal Health and Salivary Status in Children with Type 1 Diabetes Mellitus: A Systematic Review

Salah A Yousief[1,2]*, Maha Abdullah A Almalki[3], Sahar Ayman Sabahani[3], Amjad Mohammed Aljohani[4], Ahmed Nasser M Muharraq[4] and Gyhaida Abdallah Alshehry[3]

[1]Department of Restorative and Prosthetic Dental Sciences, College of Dentistry, Dar Al Uloom University, Riyadh, Saudi Arabia

[2]Department of Crown and Bridge, Faculty of Oral and Dental Medicine, Al Azhar University, Assiut, Egypt

[3]General Dentist, Saudi Arabia

[4]General Dentist -KSA

***Corresponding Author:** Salah A Yousief, Department of Restorative and Prosthetic Dental Sciences, College of Dentistry, Dar Al Uloom University, Riyadh, Saudi Arabia and Department of Crown and Bridge, Faculty of Oral and Dental Medicine, Al Azhar University, Assiut, Egypt.

Received: December 02, 2023; **Published:** December 08, 2023

Abstract

Background: Saliva, gingival crevicular fluid (GCF), and serum have all been used frequently to identify different periodontal disease markers; however, for children, saliva sampling is the most recommended method because it is much more convenient and tolerable for the patient. Furthermore, since entire saliva is a collection of samples containing contributions from every periodontal locations, evaluation of indicators in saliva may provide a comprehensive evaluation of an illness status as compared with site-specific GCF analysis. With this background the aim of our study was to investigate the association between salivary contents and dental caries in children with uncontrolled type-1 Diabetes Mellitus (T1DM).

Methods: We searched 4 different electronic databases (PubMed, Web of Science, Scopus, and EBSCO from inception till June 2023. The following search strategy was used for all the databases "Saliva OR Salivary" AND "type 1 Diabetes Mellitus" OR "T1DM" OR "Diabetes Mellitus type 1" AND "Child" OR "Children" OR "pediatric". Our search strategy was comprehensive, with no restrictions on settings, design, or publication date.

Results: Six studies were included in our systematic review after screening. A study reported that there was decreased levels of salivary lipids, and total proteins in diabetic individuals without association between them and the periodontal health, but there was increased gingival inflammation. However, one study found that people with T1DM had considerably higher salivary triglycerides and cholesterol. In these kids, there was a noteworthy correlation between salivary triglycerides and dental caries. According to a report, the diabetic subjects' glycemic status has an impact on their salivary pH, periodontal probing depths, buffering ability, and peroxidase production.

Levels of salivary alkaline phosphatase have been shown to be a helpful indicator of children with uncontrolled T1DMwhen it comes to their periodontal health.

Conclusion: This study shows that salivary contents can be used as biomarkers of periodontal health status in T1DM children which includes lipids, alkaline phosphatase, protein content and the characteristics of this saliva such as pH, buffering capacity, and antioxidant activity. However, further studies are required to validate our findings.

Keywords: *Diabetes Mellitus; Saliva; Biomarkers; Children*

Introduction

Type 1 diabetes mellitus (T1DM), which is most commonly diagnosed in children and young adults, is characterised by the autoimmune destruction of pancreatic islet cells, resulting in the loss of insulin production [1]. Adult-onset type 2 diabetes mellitus (T2DM) is distinguished by an increase in insulin resistance as well as an irregular inability of pancreatic b-cells to make enough insulin to compensate. Diabetes mellitus (DM) is a major independent risk factor for gingivitis and periodontitis, as well as a contributory factor in several organ adverse consequences [2].

Diabetes and periodontal disease, two chronic disorders, have long been thought to have a biological link. Diabetes has been linked to the onset, progression, and severity of periodontal disease in several case reports, cross-sectional studies, longitudinal studies, and reviews [3,4].

The sixth most frequent complication of diabetes was reported to be periodontal diseases and gingivitis, which are typically related to the severity of the disease [5]. Studies comparing the healthy population to children and adolescents with type-1 diabetes revealed a higher prevalence of gingival inflammation [6,7].

Insulin hormone deficiency in diabetics alters the amount and composition of saliva, leading to hyposalivation and elevated salivary glucose levels, which raise the risk of dental caries [8]. A systematic review and meta-analysis involving 10 publications and 538 patients was conducted by Wang., *et al*. to ascertain the prevalence of dental caries in children and adolescents with T1DM. In overall, dental caries was present in 67% of children and adolescents with T1DM. Interestingly, the prevalence was lower (47%) among diabetic patients who had proper metabolic regulation. Geographically speaking, Europe had the lowest prevalence (57%) and South America had the highest (84%) [9].

There are multiple variables which contribute to elevated inflammation in the periodontal tissue of diabetics, such as oxidative stress, reactive oxygen species accumulation, and connections to advanced glycation end products (AGEs) and their receptor (RAGE) in the periodontal tissues [10]. Patients with diabetes also have abnormalities in their lipid metabolism as a result of altered insulin secretion and activity, as well as poor glucose metabolism. Patients with systemic lipid disorders have demonstrated elevated lipid concentrations in their saliva and blood. Lipids act as nuclei in the mineralization of dental plaque and hasten the activity of the glucosyltransferase enzyme, which gives rise to oral microorganisms' carcinogenic potential. Elevated levels of cholesterol and triglycerides within the plaque impede its lactic acid release. Salivary lipids influence the hydrophobic surfaces of bacteria, which aids in their attachment to dental surfaces [10,11].

Serum, gingival crevicular fluid (GCF), and saliva have all been used extensively to identify various markers of periodontal disease; however, saliva sample is the most recommended approach for children due to its greater patient convenience and tolerability. Additionally, as saliva is a collection of samples from all periodontal areas, evaluating indications in saliva, as opposed to site-specific GCF analysis, may offer a holistic evaluation of a disease condition [12]. In light of this, our study's objective was to determine whether salivary contents and dental caries are related in kids with uncontrolled type 1 diabetes.

Methods

This systematic review and meta-analysis was conducted in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) criteria [13].

Search strategy

We searched 4 different electronic databases (PubMed, Web of Science, Scopus, and EBSCO from inception till June 2023. The following search strategy was used for all the databases "Saliva OR Salivary" AND "type 1 Diabetes Mellitus" OR "T1DM" OR "Diabetes Mellitus

type 1" AND "Child" OR "Children" OR "pediatric". Our search strategy was comprehensive, with no restrictions on settings, design, or publication date.

Inclusion and exclusion criteria

Studies examining the relationship between periodontal health and dental caries in children with type 1 diabetes and salivary contents were considered. All observational study types (cross-sectional, cohort, and case-control) were included; narrative and systematic reviews, meta-analyses, case reports, and case series were not.

Study selection and data extraction

Four authors independently did the screening process which was done in two steps: title and abstract screening and full-text screening to determine the finally included studies. Any disagreements between the authors during the screening process were resolved by discussion with a senior author. Data were extracted in a preformed Microsoft Excel spreadsheet, which included study information (study design, year, country, sample size, inclusion and exclusion criteria), participant characteristics (gender, age, and salivary biomarkers) and lastly the summary of findings in each of the included studies.

Quality assessment

We used the Newcastle Ottawa scale to conduct the quality assessment of the included studies [14]. Four researchers conducted this assessment, and any disagreement was resolved with a senior reviewer. Scores of 0 - 3 were considered as low quality, 4 - 6 as moderate quality, and 7 - 9 as high quality.

Results

Literature search results

Our literature databases search yielded 352 records. After the removal of duplicates, 273 studies remained to the title and abstract screening. Eleven articles were eligible for full-text screening. From these, six studies [12,15-19] were included in the meta-analysis. The PRSMA flow diagram of the study is shown in figure 1.

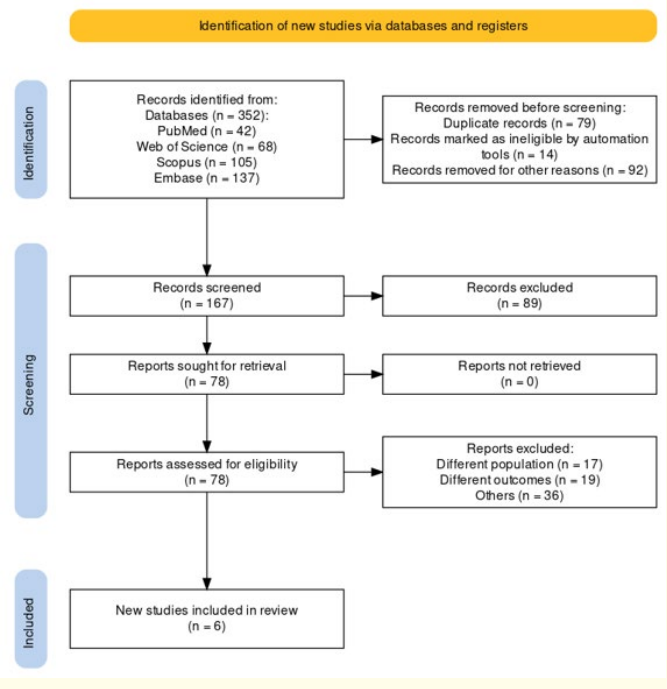

Figure 1: *PRISMA flow diagram of the selection process.*

Baseline characteristics

The six included studies were of cross-sectional study design and conducted in five different countries: Iran, Mexico, Turkey, Iraq, and two were conducted in India. The age of the included participants ranged from 6 to 18 years old. Two of the included studies investigated the effect of salivary triglycerides and cholesterol [18,19], two investigated the pH and buffer capacity [15,16], one investigated the antioxidant capacity, and protein carbonyl [17] and the last one investigated the effect of alkaline phosphatase [12] (Table 1).

According to Tabatabaei., *et al*. [19], diabetic individuals had lower levels of albumin, total proteins, and salivary lipids; there was no correlation between these parameters and periodontal health, but there was an increase in gingival inflammation. However, Subramaniam., *et al*. [18] found that people with T1DM had considerably greater amounts of cholesterol and salivary triglycerides. In these kids, there was a noteworthy correlation between salivary triglycerides and dental caries (Table 1).

Rosas., *et al*. [16] demonstrated a substantial correlation between DM and a higher incidence of disorders affecting the mouth in children. Also, According to Aren., *et al*. [15], a person's glycemic condition affects their salivary pH, periodontal probing depths, buffering capacity, and peroxidase activity. However, Obaid., *et al*. [17] found that salivary levels of protein carbonyl and total antioxidant capacity were significantly impacted by diabetes, but there was no significant effect on the occurrence of dental caries.

Moreover, Sridharan., *et al*. [12] found that the signs and symptoms of periodontal disease are influenced by the children's glycemic status. When examining the periodontal health of kids with uncontrolled T1DM, salivary alkaline phosphatase levels may be a helpful tool (Table 1).

Study ID	Study Design	Country	Total sample	Age	Gender	Salivary biomarkers	Inclusion criteria	Exclusion criteria	Key findings
Tabatabaei 2021	Cross-sectional study	Iran	120 subjects aged 6-16 years (60 well-controlled and poorly-controlled diabetics and 60 healthy individuals)	6-16 years	NA	Salivary triglyceride, cholesterol, albumin, α-amylase, and total protein levels.	Children aged 6-16 years with type-1 diabetes mellitus and healthy individuals.	Children with other diseases (asthma, cardiovascular disease, epilepsy, and renal deficiency)	More gingival inflammation and salivary α-amylase activity and lower level of salivary lipids, albumin, and total proteins were found in diabetic patients, but there was no association between the level of lipids, proteins, and the total antioxidant capacity of saliva with periodontal health indicators in patients with DM and healthy individuals.

Rosas 2018	Cross-sectional study	Mexico	60 pediatric patients with both types of diabetes mellitus	2-16 years	NA	Stimulated flow, pH (using pH indicator strips), buffer capacity and Snyder's Test.	Pediatric patients with both types of diabetes mellitus	Patients who were under orthodontic/orthopaedic procedures, who had received periodontal treatment in the previous 6 months and/or did not have the required information in their medical records were excluded.	There was a significant relationship between diabetes mellitus and an increased prevalence of oral cavity related diseases in the paediatric population. These are also associated with a poor adherence to the nutritional plan.
Aren 2023	Cross-sectional study	Turkey.	48 (Sixteen newly diagnosed children with DM (group1), 16 children with type 1 DM of long duration (group 2), and 16 healthy children (group 3) participated in the study)	Group 1 (12.8 ± 5.8), Group 2 (12.7 ± 3.8) and Group 3 (12.4 ± 1.9)	NA	Salivary Buffering Capacity, pH, Flow Rate, and Peroxidase Activity.	Newly diagnosed children and children with diabetes of long duration.	NA	The glycemic status of the diabetic subjects affects the periodontal probing depths, salivary pH, buffering capacity, and peroxidase activity.

Obaid 2023	Cross-sectional study	Iraq	90 (45 diagnosed children with type 1 diabetes mellitus and 45 healthy children without any systemic disease)	11.2 ± 0.81 years (10-12 years)	NA	Salivary Levels of Protein Carbonyl and Total Antioxidant Capacity	Children with type 1 diabetes mellitus (the quality of disease control is determined by the level of HbA1c with more than 7.5 considered non-control diabetes) with normal body mass index (BMI=5 percentile to less than 85 percentile) and without any other systemic problem from different geographical areas in the city.	NA	The diabetic status had a significant effect on salivary levels of TAOC and PC, but no significant effect on the prevalence of dental caries.
Subramaniam 2015	Cross-sectional study	India	60 (30 children with DM1, 30 healthy children)	12–16 years	NA	Salivary triglycerides and cholesterol	Children with DM1, only cooperative children having their complete medical records were included.	NA	Both salivary cholesterol and triglycerides levels were significantly higher in children with type 1 diabetes mellitus. Salivary triglycerides showed a significant association with dental caries in these children.

Sridharan 2017	Cross-sectional study (Pilot study)	India	30 (10 non diabetic patients, 10 patients diagnosed as type 1 diabetes mellitus a year back and 10 children diagnosed as type 1 diabetes mellitus for greater than 4 years.	12- 18 years	NA	Salivary alkaline phosphatase	1- diagnosis of Type 1DM 12 months prior to the study; 2- presence of at least 20 teeth;	1- Presence of any important disease except for DM; 2- smoking; 3-having taken antibiotics, corticosteroids or nonsteroidal anti-inflammatory drugs within the 6 months prior to examination; 4-and having undergone periodontal treatment within the previous 2 years.	The glycemic status of the children affects the periodontal disease parameters. Salivary alkaline phosphatase levels could be a useful tool in analyzing periodontal status of children with uncontrolled type I diabetes mellitus.

Table 1: *The baseline characteristics of the included studies.*

Quality assessment

According to NOS for quality assessment of the included studies, five [12,15,17-19] of them were of moderate quality with a score of six stars and only one [16] was of low quality with a score of three stars as shown in table 2.

Study ID	**NOS (Cross-sectional) (non-coded)**							
	Selection				**Comparability**	**Outcome**		**Outcome score**
	Representativeness of the sample	**Sample size**	**Non-respondents**	**Ascertainment of the exposure (risk factor)**	**The subjects in different outcome groups are comparable, based on the study design and analysis. Confounding factors are controlled**	**Assessment of outcome**	**Statistical test**	

Tabatabaei 2021	*	*	*	0	*	*	*	6 stars
Rosas 2018	*	0	*	0	_ (Single arm cross sectional)	*	0	3 stars
Aren 2023	*	0	*	*	*	*	*	6 stars
Obaid 2023	*	0	*	*	*	*	*	6 stars
Subramaniam 2015	*	0	*	*	*	*	*	6 stars
Sridharan 2017	*	0	*	*	*	*	*	6 stars

Table 2: *NOS for quality assessment of the included studies.*

Discussion

Due to an absolute or relative lack of insulin, DM1 is a syndrome characterized by abnormal metabolism of proteins, fats, and carbohydrates that can lead to both acute and long-term complications. Diabetes and its related complications have been linked to a multitude of oral health conditions. The connection between diabetes and periodontal disease has attracted the most interest, while other conditions like caries, salivary dysfunction, soft tissue illnesses, oral infections, and other sensory problems are getting much fewer spotlights overall-and considerably less in the paediatric DM1 population [16].

The current study showed that there was an association between salivary lipids (cholesterol and triglycerides) with gingival inflammation and dental caries. However, there was no association between them and periodontal health. The study also showed an association between DM and an increased prevalence of oral cavity related diseases in the pediatric population. Also, Aren., *et al*. [15] revealed that the periodontal probing depths, salivary pH, buffering capacity, and peroxidase activity of the diabetic subjects are influenced by their glycemic status. The current study also demonstrated that measuring salivary alkaline phosphatase levels may be a helpful method for determining a child's periodontal health if their T1DM is uncontrolled.

Numerous factors contribute to the pathogenesis of diabetes mellitus in gingivitis and periodontitis, such as the involvement of small vessels, modifications to the composition of gingival fluid and an increase in inflammatory mediators [20], changes in collagen metabolism, a reduction in defence responses, an increase in oxidative stress and periodontal pathogenic infections [21] and a genetic predisposition to non-enzymatic glycosylation [22,23]. As demonstrated by Daković and Pavlović [22] gingival bleeding, dental biofilm, and periodontitis have all been positively associated. It was proposed that these things could be used as periodontitis prognostic markers.

Tabatabaei., *et al*. [19] revealed that DM patients had greater salivary α-amylase levels than individuals in good health. However, healthy people had higher levels of albumin and total proteins in their saliva. Patients with DM had higher levels of salivary total proteins and α-amylase, according to Lakshmi., *et al* [23]. In their study, Panchbhai., *et al*. [24] studied total proteins and α-amylase in saliva from patients with well-controlled and poorly-controlled DM compared to healthy people. Their findings revealed that patients with well-controlled DM had significantly lower salivary α-amylase levels than healthy subjects. Nevertheless, no noteworthy distinctions were discovered between the other variables and groups.

Aren., *et al*. [15] demonstrated that compared to normal controls, diabetic patients had more substantial plaque index values. This finding makes sense because patients with marginal metabolic control excrete excess glucose into their saliva and gingival crevicular fluid, and plaque growth is generally promoted by a sugar-rich biofilm. Higher plaque index values may be related to factors such as ignorance about oral health and proper hygiene management. Long-term diabetic patients had a higher prevalence of gingivitis-affected sites than did short-term patients. While some epidemiologic studies have found no correlation between managing DM and periodontal disease, there is evidence that, in certain cases of diabetes, prolonged periods of hyperglycemia increase the risk of periodontal tissue destruction. Consequently, poorly controlled diabetic subjects have a higher long-term incidence of periodontal disease [15]. However, certain clinical epidemiologic data indicate that diabetes may lower the chance of acquiring gingivitis and periodontitis if the condition is managed well metabolically, or if there are no associated complications [13]. Researchers have found that compared to non-diabetic controls, adults and children with T1DM had increased incidence and severity of periodontal disease. Research indicates that kids with diabetes who experience inadequate control of their metabolism are more likely than kids without diabetes to develop gingivitis. Compared to their age-matched non-diabetic peers, children with diabetes who have poor metabolic control typically have higher gingival index scores. The current study found that the median HbA1c levels for newly diagnosed and long-term diabetic patients were 8.1% and 8.3%, respectively. These values suggest that the patients had marginal metabolic control at the time of examination [15].

Aren., *et al*. [15] also revealed that the salivary pH and buffering capacity of the diabetic children were different from those of the healthy subjects. It's probable that people with diabetes have lower pH levels and a reduced ability to buffer because their saliva contains more glucose, which plaque metabolizes into lactic acid. This could account for the vulnerability to periodontal infections. Gingival index values and blood glucose levels were highly correlated. It can be clarified that elevated microangiopathy, a consequence of poor metabolic control, may be the source of high gingival index values in diabetic complications. The finding that the periodontal indexes of the diabetic subjects were significantly different from the ones in the healthy controls suggests that those with diabetes will likely have an increased risk toward severe periodontitis starting in early childhood due to variables like the beginning of puberty and reduced host immunity against infections [18].

Sridharan., *et al*. [12] found that the signs and symptoms of periodontal disease are influenced by the children's glycemic status. When examining the periodontal health of kids with uncontrolled T1DM, salivary alkaline phosphatase levels may be a helpful tool. This could be explained by the fact that alkaline phosphatase is a crucial enzyme in the periodontium because it aids in bone homeostasis, normal periodontal ligament turnover, and root cementum maintenance. Twenty It is thought that alkaline phosphatase is a crucial marker of osteoblastic activity. Alkaline phosphatase is found in bacteria from dental plaque, desquamated epithelial cells, leukocytes, and the parotid, submandibular, and minor salivary glands. Salivary alkaline phosphatase levels are typically a sign of periodontal tissue inflammation and degradation. The degree of periodontal disease is positively connected with alkaline phosphatase levels [15]. Studies have shown that during the acute stage of periodontal disease, alkaline phosphatase activity is notably enhanced. These enzymes' activity reverted to that seen in healthy individuals after receiving periodontal treatment [12].

Limitation of the Study

There exist some limitations in the present study including small number of included studies, and the cross-sectional design that doesn't allow to draw causal relationships. Therefore, future randomized controlled trials are recommended with large sample size in order to allow the investigation of a causal relationship between salivary contents and periodontal health in T1DM children.

Conclusion

This study shows that salivary contents can be used as biomarkers of periodontal health status in T1DM children which includes lipids, alkaline phosphatase, protein content and the characteristics of this saliva such as pH, buffering capacity, and antioxidant activity. However, further studies are required to validate our findings.

Bibliography

1. Mealey BL and Oates TW. "Diabetes mellitus and periodontal diseases". *Journal of Periodontology* 77.8 (2006): 1289-1303.
2. Nathan DM., *et al*. "Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes". *New England Journal of Medicine* 353.25 (2005): 2643-2653.
3. Mealey BL and Rose LF. "Diabetes mellitus and inflammatory periodontal diseases". *Current Opinion in Endocrinology, Diabetes and Obesity* 15.2 (2008): 135-141.
4. Taylor GW and Borgnakke WS. "Periodontal disease: associations with diabetes, glycemic control and complications". *Oral Diseases* 14.3 (2008): 191-203.
5. Saini R., *et al*. "Periodontal disease: The sixth complication of diabetes". *Journal of Family and Community Medicine* 18.1 (2011): 31.
6. Lalla E., *et al*. "Periodontal changes in children and adolescents with diabetes: a case-control study". *Diabetes Care* 29.2 (2006): 295-299.
7. Jenkins WM and Papapanou PN. "Epidemiology of periodontal disease in children and adolescents". *Periodontology 2000* 26 (2001): 16-32.
8. Assiri SA., *et al*. "Assessment of dental caries and salivary characteristics among type 1 diabetic Saudi children". *Journal of Dental Sciences* 17.4 (2022): 1634-1639.
9. Wang Y., *et al*. "Prevalence of dental caries in children and adolescents with type 1 diabetes: a systematic review and meta-analysis". *BMC Oral Health* 19.1 (2019): 213.
10. Casanova L., *et al*. "Diabetes and periodontal disease: a two-way relationship". *British Dental Journal* 217.8 (2014): 433-437.
11. Lasisi TJ and Fasanmade AA. "Salivary flow and composition in diabetic and non-diabetic subjects". *Nigerian Journal of Physiological Sciences* 27.1 (2012): 79-82.
12. Sridharan S., *et al*. "Salivary alkaline phosphatase as a noninvasive marker for periodontal disease in children with uncontrolled type 1 diabetes mellitus". *Journal of Clinical Pediatric Dentistry* 41.1 (2017): 70-74.
13. Moher D., *et al*. "Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement". *British Medical Journal* 339 (2009): b2535.
14. Wells GA., *et al*. "The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses" (2014).
15. Aren G., *et al*. "Periodontal health, salivary status, and metabolic control in children with type 1 diabetes mellitus". *Journal of Periodontology* 74.12 (2003): 1789-1795.
16. Díaz Rosas CY., *et al*. "Dental, periodontal and salivary conditions in diabetic children associated with metabolic control variables and nutritional plan adherence". *European Journal of Paediatric Dentistry* 19.2 (2018): 119-126.
17. Obaid SF., *et al*. "Relationship between salivary levels of protein carbonyl and total antioxidant capacity and prevalence of dental caries among type 1 diabetic children: an analytical cross-sectional study". *Dental Hypotheses* 14.2 (2023): 59-61.
18. Subramaniam P., *et al*. "Association of salivary triglycerides and cholesterol with dental caries in children with type 1 diabetes mellitus". *Special Care in Dentistry* 35.3 (2015): 120-122.

19. Tabatabaei F., *et al*. "Evaluation of the relationship between salivary lipids, proteins and total antioxidant capacity with gingival health status in type-1 diabetic children". *Journal of Dentistry (Shiraz)* 22.2 (2021): 82-89.

20. Sanz M., *et al*. "Scientific evidence on the links between periodontal diseases and diabetes: Consensus report and guidelines of the joint workshop on periodontal diseases and diabetes by the International diabetes Federation and the European Federation of Periodontology". *Diabetes Research and Clinical Practice* 137 (2018): 231-241.

21. Buczko P., *et al*. "Saliva and oxidative stress in oral cavity and in some systemic disorders". *Journal of Physiology and Pharmacology* 66.1 (2015): 3-9.

22. Daković D., *et al*. "Gingivitis and periodontitis in children and adolescents suffering from type 1 diabetes mellitus". *Vojnosanitetski Pregled* 72.3 (2015): 265-273.

23. Lakshmi PV., *et al*. "Diagnostic perspective of saliva in insulin dependent diabetes mellitus children: An *in vivo* study". *Contemporary Clinical Dentistry* 6.4 (2015): 443-447.

24. Panchbhai AS., *et al*. "Estimation of salivary glucose, salivary amylase, salivary total protein and salivary flow rate in diabetics in India". *Journal of Oral Science* 52.3 (2010): 359-368.

Volume 23 Issue 1 January 2024