Research Article

The salivary redox biomarkers related to periodontal conditions among insulin resistance and controlled type 2 diabetic according 2017 classification

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Abstract: Background: Periodontal disease is highly prevalent among insulin-resistant and type 2 diabetes mellitus (T2DM) subjects. However, the pathogenesis and associated factors of periodontal disease among these subjects are not well known. Recently, it has been re-ported that oxidative stress-antioxidant (redox) imbalance may play an important role in the pathogenesis of periodontal disease. Objective: Determine the relation between three salivary redox biomarkers; total antioxidant capacity (TAC), total oxidative status (TOS), advanced glycation end products (AGEs), and periodontal disease parameters in insulin resistance (IR) and controlled T2DM (C-T2DM) subjects. Methods: An analytical observational study was conducted on 180 participants aged between 35 and 65 years; males and females were di-vided into three groups, each consisting of 60 individuals: IR group, C-T2DM, and healthy control group. Periodontal parameters were examined: dental plaque index (PLI), bleeding on probing percentage (BOP%), probing pocket depth (PPD), and clinical attachment level (CAL), according to these, three subgroups presenting (healthy periodontium, gingivitis, or periodontitis) were conducted. Un-stimulated saliva was collected, and Enzyme-linked immunosorbent assay (ELISA) was used to determine salivary AGEs, while colorimetric assays were used to determine salivary TAC and TOS. The data were analyzed using SPSS version 21. Results: A significant correlation between TOS and PLI and an inverse correlation between TAC and PLI in the periodontitis subgroup of the control subjects were found. In multiple regression analysis, salivary AGEs and CAL were inversely associated in the C-T2DM group. Conclusion: Salivary TOS and AGEs were the highest in the periodontitis subgroup of the IR and C-T2DM groups, while the salivary TAC was found the lease in the both IR and C-T2DM groups when compared to the control group. In addition, there were a relationship between salivary redox biomarkers and periodontal parameters. However, salivary AGEs were considered a significant independent predictor for CAL in C-T2DM.

Keywords: Periodontal disease, insulin resistance, type 2 diabetes mellitus, oxidative stress, antioxidant biomarkers.

Introduction

Although there have been improvements in the methods used to prevent and treat diabetes mellitus, 47.1% of cases in Iraq remain undiagnosed [1]. Furthermore, only 13.8% of individuals with type 2 diabetes mellitus (T2DM) have successfully achieved glycemic control [2]. In addition, the World Health Organization (WHO) has forecasted that diabetes mellitus will rank as the sixth most common cause of death by 2030 [1, 3]. Insulin resistance is a complicated and not fully understood condition in which all organ systems have a role in contributing to the resistance to insulin. Insulin resistance refers to the decrease in the ability of insulin-responsive tissues to take up glucose from the bloodstream [4]. If prolonged, high blood glucose levels are accompanied by malfunction of the pancreatic beta cells and a relative lack of

insulin. Insulin resistance can develop into T2DM, a multifaceted, long-term metabolic disorder that occurs when the body fails to utilize insulin efficiently [3, 4].

Dental plaque biofilm, a structured gathering of microorganisms living within a complex intercellular matrix [5], is the main cause of the beginning and advancement of periodontal disease. Nevertheless, chronic and persistent exposure to periodontal inflammation over an extended period will result in an increased proinflammatory cytokines entering the bloodstream, potentially exacerbating insulin resistance and diabetes mellitus [6, 7]. Individuals with diabetes mellitus or with resistance to insulin are more prone to experiencing more severe periodontitis compared to those with normoglycemia [8, 9]. Additional research is required to ascertain whether there is a relation between periodontal parameters, insulin resistance, and glycemic control in individuals with T2DM. Undoubtedly, the progression of periodontitis requires more than just a simple rise in dental biofilm. Recently, only a handful of researchers have concentrated on redox variables in relation to periodontitis and metabolic issues [6, 10, 11]. T2DM and periodontitis have in common an increase in reactive oxygen species (ROS) concentration in the body. In subjects affected by T2DM, the rising of ROS participates in the insulin resistance process [12]. Patients with periodontitis exhibit elevated levels of biomarkers indicative of ROS-induced tissue damage, as well as increased levels of antioxidant enzymes, suggesting a state of oxidative stress (OS) within inflamed periodontal tissue and gingival fluid [13].

The body has a vast array of oxidant and antioxidant components that support the overall oxidative equilibrium. It is important to remember that differences in these traits might not always occur in certain illnesses or situations. Understanding the oxidative balance in the body depends on understanding total antioxidant capacity (TAC) and total oxidative status (TOS), which do not focus on individual antioxidants or oxidants but rather take into account the cumulative effects and interactions of multiple components involved in the oxidative stress-antioxidant (redox) biomarkers balance. Greater TAC values show a potent capacity to neutralize ROS and preserve oxidative balance, whereas elevated TOS levels indicate increased OS and a greater risk for tissue injury [14].

Through chronic hyperglycemia, as it arises in insulin resistance and T2DM, protein, and lipids exposed to non-enzymatic glycation result in the formation of advanced glycation end products (AGEs), which may play a significant role in the pathogeneses of T2DM-associated diseases, such as periodontitis. OS and inflammation are produced when AGEs attach to the signaling receptor for advanced glycation end products (RAGE), which is present on monocytes and endothelial cells [15]. These suggest that in insulin resistance and T2DM, both OS and AGEs may be important for increased inflammatory response and periodontal degradation. For individuals exhibiting gingivitis or periodontitis, but who are systemically healthy, insulin-resistant (IR), or have well-controlled glycemia, salivary TAC, TOS, and AGEs may serve as valuable biomarkers with significant clinical implications. The current study aims to evaluate the salivary levels of TAC, TOS, and AGEs in IR, controlled-T2DM (C-T2DM), and healthy subjects, and their periodontal conditions according to the 2017 classification of periodontal health and conditions.

Materials and Methods

One hundred eighty subjects aged 35-65 years, including males and females, were recruited for this analytical observational study at the Center for Research and Treatment in Baghdad, Iraq, between July 2022 and March 2023. The study was conducted in accordance with ethical principles. Before sample collection, both written and verbal informed consent were given by the subjects. The Declaration of Helsinki's ethical guidelines were followed when conducting the study. Prior to the collection of samples, a local ethics committee examined and approved the study protocol, subject information, and consent form. (Document number no. 1563322, issued on 17/4/2022).

Participant Selection

Participants were divided into three groups: 60 IR, 60 C-T2DM, and 60 systemically healthy control subjects. Group assignment was based on the following diagnostic criteria from blood samples collected after a fast of ≥8 hours:

IR group: Subjects met the American Diabetes Association's criteria for prediabetes and the criteria of American Association of Clinical Endocrinologists [16, 17]: Glycated hemoglobin (HbA1c) between 5.7-6.4%, fasting plasma glucose (FPG) between 100-125 mg/dL and had a homeostasis model assessment of insulin resistance (HOMA-IR) value >2 [18].

C-T2DM group: Participants had a physician-diagnosed T2DM for at least five years, were on oral hypoglycemic therapy, and met two of the criteria of American Diabetes Association for diabetes (HbA1c between 6.5-8% and FPG ≥ 126 mg/dL) [16].

Control group: Systemically healthy subjects with no diagnosed systemic disease and no medication use in the previous three months. HbA1c ranged from 4% to 5.6%, FPG <100 mg/dL [16], and HOMA-IR <2 [18] as showed Figure 1. Participants were recruited through patient companions or coworkers at the study center under the following selection criteria: All subjects were Iraqi Arabs, fasted for at least 8 hours before sampling, and had at least 20 teeth. Subjects were excluded when known chronic illnesses, medication use before the study affecting outcome measures, refusal to participate or withdrawal, pregnancy, lactation, head and neck radiation therapy, chemotherapy, self-reported or physician-diagnosed type 1 diabetes, insulin administration, and poor T2DM control (HbA1c > 9) [18].

Clinical Oral Examination

Clinical periodontal parameters: dental plaque index (PLI), bleeding on probing percentage (BOP%), CAL, and probing pocket depth (PPD) were assessed using a WHO periodontal probe and measured in a logical sequence. PLI was determined using the Silness and Löe method by visually examining plaque presence on the probe inserted onto the tooth surface. Plaque at the gingival border was coded as 2 (19), extensive plaque covering the tooth surface as 3 (19), and no plaque as index (0). Using a WHO probe, six locations per tooth (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual/palatal, mid-lingual/palatal, and disto-lingual/palatal) were assessed for periodontal disease by measuring the (BOP%, CAL, and PPD parameters).

Excluding third molars. BOP% was calculated by dividing the number of sites with bleeding on probing by the number of sites examined, multiplying by 100, and applying the classification of periodontal conditions by Chapple [19]. CAL was measured from the cemento-enamel junction to the base of the clinical pocket, and PPD from the gingival margin to the base of the clinical pocket [19, 20].

Participants for all groups were classified into three sub-groups based on the 2017 classification of periodontal health and conditions: Healthy periodontium: Intact periodontium with no gingival inflammation (BOP% < 10%, PPD ≤ 3 mm, no CAL). Gingivitis: Gingival inflammation (BOP% ≥ 10%, PPD ≤ 3 mm, no CAL). Periodontitis: Interdental CAL detected on ≥ 2 non-adjacent teeth, or buccal or lingual CAL ≥ 3 mm, and PPD > 3 mm detected on ≥ 2 teeth [20].

Saliva collection

Unstimulated saliva was collected from all included subjects early in the morning after at least eight hours of fasting. Participants were instructed to sit upright with their heads tilted downward and collect saliva in the floor of their mouths for five minutes before expelling it into a sterile plastic cup, following the protocol described by Khurshid, et al [21]. The clear supernatant of 2 mL from a 15-minute centrifugation of saliva samples at 3000 rpm was then transferred to three Eppendorf tubes and stored at -20°C for subsequent biochemical analysis.

Biochemical determination

Salivary TAC and TOS were measured calorimetrically using Erel's colorimetric method [22, 23]. Specifically, TAC was determined using the kit catalog No: E-BC-K136-S (Elabscince, China), which measures the ability of antioxidants in the sample to neutralize the ABTS radical (2,2′-azino-bis-(3-ethylbenzothiazoline-6-sulfonic) acid). Changes in ABTS solution absorbance were monitored at 520 nm. Similarly, TOS was measured using the kit catalog No: E-BC-K802-M (Elabscince, China). Under acidic conditions, oxidizing substances in the sample oxidize Fe2+ to Fe3+, which forms a blue-purple complex with xylenol orange. This complex exhibits maximum absorbance at 590 nm, allowing for the indirect calculation of total oxidation status. The detection range is 2.5-100 μmol. Salivary AGEs were quantified using a sandwich enzyme-linked immunosorbent assay (ELISA). Capture antibodies were pre-coated on 96-well plates, and biotin-conjugated detection antibodies were used. Sequential additions of standards, test samples, and detection antibodies were made, and then there were washing procedures. After adding streptavidin-horse radish peroxidase (HRP), unbound conjugates were eliminated. The HRP enzymatic reaction was visualize using tetramethylbenzidine (TMB) substrates, which provide a blue colour that changes to yellow when an acidic stop solution is added. The quantity of target collected in the plate directly correlates with the intensity of the yellow color. Using a microplate reader, absorbance was measured at 450 nm, and the desired concentration was computed.

Statistical Analysis

The Statistical Package for Social Sciences (SPSS, version 21, Chicago, Illinois, USA). Results were presented as mean and standard error (SE). One-way analysis of variance [24] was used to test the difference in a quantitative variable among independent groups. A p-value < 0.05 was considered statistically significant. Pearson's correlation coefficient (r) was used to describe the correlation between two continuous quantitative variables that were bivariate and normally distributed. Multiple regression was used to test the effect of the variability of multiple independent variables on the quantitative dependent variable.

Results

Periodontal parameters and salivary redox biomarkers in the groups

When comparing the groups' age and sex distributions, there were no discernible differences. The 2017 classification of periodontal health and conditions (healthy, gingivitis, periodontitis) was applied to the periodontal metrics (PLI, BOP%, PPD, and CAL) in the IR, C-T2DM, and control groups was shown in Table 1.

Concerning PLI in the control and IR group, the highest mean value was observed in the periodontitis subgroup, followed by the gingivitis subgroup. The lowest mean of PLI was found in the healthy periodontium subgroup, with significant differences ($p < 0.05$). Conversely, among C-T2DM subjects, the mean PLI was highest in the gingivitis subgroup, followed by the healthy periodontium and periodontitis subgroups, without significant differences. However, the mean PLI in the healthy periodontium subgroup was lowest in the control group and greatest in the C-T2DM group, IR group, and so on., with significant differences ($p < 0.001$).

Regarding BOP%, the highest mean was observed in the gingivitis subgroup, followed by the periodontitis subgroup, and the lowest in the healthy periodontium subgroup among the IR, control, and C-T2DM groups, respectively, with significant differences ($p < 0.001$).

Concerning to the CAL, the highest mean was in C-T2DM, followed by IR, while the less in control group. Interestingly, in C-T2DM, the mean CAL was highest in the periodontitis subgroup, followed by the healthy periodontium and the less in gingivitis subgroups with significant differences ($p <0.05$). However, the mean CAL in gingivitis subgroups was highest in the control group, followed by the IR and C-T2DM groups, with significant differences ($p < 0.05$). Additionally, the C-T2DM group had the highest mean CAL

among the periodontitis subgroups, significantly different from the IR and control groups. Additionally, the IR group had the highest mean PPD, followed by the control group, whereas the C-T2DM group had the lowest mean PPD, a specific periodontitis measure, without significant differences, as shown in Table 1.

Table 2 shows that, in general, the highest TAC values were obtained in all three subgroups of the control group, while the lowest values were found in all three subgroups of the IR group, with a significant difference ($p<0.001$) in the healthy and periodontitis subgroups. For T*OS and AGEs, the highest values were found in all subgroups of the IR group, while the lowest values were found in all cases of the control group with significant differences ($p<0.001$).

Table 1: Periodontal parameter according to the 2017 classification of periodontal health and conditions in the IR, C-T2DM, and control groups

Periodontal parameters	Periodontal Subgroups	Control n=60		C- T2DM n=60		IR n=60		
		Mean	SE	Mean	SE	Mean	SE	P* value
PLI	Healthy	.25	.04	.93	.09	.71	.10	0.001*
	Gingivitis	.80	.06	1.12	.14	1.08	.14	0.055
	Periodontitis	.91	.07	.89	.08	1.13	.14	0.249
P# value		0.001*		0.298		0.021*		
BOP%	Healthy	2.76	.44	3.05	.57	2.20	.51	0.482
	Gingivitis	19.37	1.61	18.07	3.03	22.23	2.75	0.515
	Periodontitis	2.07	.95	5.85	2.28	8.61	3.12	0.376
P# value		0.001*		0.001*		0.001*		
PPD	Periodontitis	5.50	.33	5.15	.39	5.74	.53	0.619
CAL	Healthy	3.40	.24	3.38	.12	3.25	.08	0.697
	Gingivitis	4.20	.37	3.25	.11	4.10	.24	0.032*
	Periodontitis	3.94	.24	5.37	.35	4.09	.40	0.019*
P# value		0.208		0.003*		0.233		

C-T2DM: controlled type 2 diabetes mellitus; IR: insulin resistant; PLI: dental plaque index, BOP%: bleeding on probing; PPD: probing pocket depth: CAL: clinical attachment level; SE: standard error; *: statistical significance ($p<0.05$), P* value: the statical significant between (IR, C-T2DM, Control); P# value: the statical significant between (healthy, gingivitis, periodontitis).

Table 2: Salivary redox biomarkers according to the 2017 classification of periodontal health and conditions in the IR, C-T2DM, and control groups.

Variables	Periodontal subgroups	Control n=60		C- T2DM n=60		IR n=60		
		Mean	SE	Mean	SE	Mean	SE	P* value
TAC U/ml	Healthy	33.61	0.31	25.00	0.57	18.83	3.14	0.001*
	Gingivitis	32.58	0.45	48.15	21.84	14.26	0.93	0.152
	Periodontitis	31.80	0.41	25.18	0.61	14.54	0.33	0.001*
P# value		0.025*		0.164		0.417		
TOS µmol	Healthy	9.76	0.21	12.00	0.27	31.46	0.56	0.001*
	Gingivitis	10.04	0.26	11.64	0.18	32.77	1.10	0.001*
	Periodontitis	10.32	0.24	12.97	0.53	32.18	0.90	0.001*
P# value		0.401		0.063		0.503		
AGEs Pg/ml	Healthy	3.39	0.11	4.51	0.17	7.16	0.23	0.001*
	Gingivitis	3.42	0.09	4.32	0.13	7.25	0.59	0.001*
	Periodontitis	3.80	0.05	4.85	0.11	7.16	0.30	0.001*
P# value		0.137		0.049*		0.982		

C-T2DM: controlled type 2 diabetes mellitus; IR: insulin resistant; TAC: total antioxidant capacity; TOS: total oxidative status; AGEs: advanced glycation end products; U/ml: unit per milliliter; µmol: micromole; pg./ml: picograms per milliliter; SE: standard error; *: statistical significance ($p<0.05$) P* value: the statical significant between (IR, C-T2DM, Control); P# value: the statical significant between (healthy, gingivitis, periodontitis).

Correlations of salivary redox biomarkers with periodontal parameters in the groups

Table 3 presents the correlations between periodontal parameters according to the 2017 classification of periodontal health and conditions (healthy periodontium, gingivitis, periodontitis) and the accessed salivary redox biomarkers.

Regarding periodontitis subgroups in the control group, TAC demonstrated a positive significant correlation with BOP%, while TOS exhibited an inverse significant correlation with BOP% in the same group.

Notably, in the C-T2DM and IR groups, no significant correlations were found between periodontal parameters and salivary biomarkers in the groups.

Table 3: Correlations between periodontal parameters and salivary redox biomarkers in insulin resistant, controlled type 2 diabetes mellitus and control groups when present periodontitis

Periodontitis	Control								C-T2DM								IR							
	PLI		BOP		PPD		CAL		PLI		BOP		PPD		CAL		PLI		BOP		PPD		CAL	
	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p
TAC	-.31	.46	.88	.001*	.68	.06	.10	.81	-.24	.26	-.05	.83	-.08	.71	.11	.62	.45	.07	.22	.40	-.24	.35	.21	.43
TOS	.06	.89	-.73	.04*	-.59	.13	.08	.84	-.05	.84	.17	.44	.05	.84	-.21	.33	-.07	.78	-.36	.16	-.20	.45	-.16	.53
AGEs	-.44	.28	-.30	.47	-.29	.49	.43	.29	-.12	.57	.31	.15	.23	.28	.06	.78	.20	.45	-.42	.09	.21	.41	.16	.53

C-T2DM: controlled type two diabetes mellitus; IR: insulin resistant; TAC: total antioxidant capacity; TOS: total oxidative status; AGEs: advanced glycation end products; r: person correlation; *: statistical significance (p <0.05).

Multiple Linear Regression of CAL and Salivary Redox Biomarkers

Multiple linear regression analysis demonstrated a negative association between salivary AGEs and CAL (p = 0.013) in the C-T2DM group. However, no significant associations were observed between salivary biomarkers and CAL in the same group, as shown in Table 4.

Table 4: Multiple linear regression of CAL with salivary redox biomarkers in C-T2DM and IR group.

Variables	CAL in IR(R2=69.2%)		CAL in C-T2DM(R2=94.2%)	
	Beta	P value	Beta	P value
TAC	-0.707	0.122	0.183	0.436
TOS	0.400	0.391	0.082	0.668
AGEs	-0.702	0.201	-1.312	0.013*

C-T2DM: controlled type two diabetes; IR: insulin resistant; TAC: total antioxidant capacity; TOS: total oxidative status; AGEs: advanced glycation end products; R2: coefficient of determination; %: percentage; *: statistical significance (p <0.05).

Discussion

The current study demonstrated that periodontal parameters PLI, BOP%, and CAL were significantly worse among IR and C-T2DM subjects compared to the control group. These findings partially align with previous reports [8, 9], which found worsened PLI, BOP%, and CAL in pre-diabetes and T2DM subjects but without significant differences. However, our study uniquely identified significant differences in PLI among the groups, with the highest levels in the IR group, followed by the C-T2DM group, and the lowest in the control group. One potential explanation is that chronic, hyperglycemia in IR and C-T2DM subjects leads to increased production of proinflammatory cytokines compared to normal glucose levels in the control group. Furthermore, experimental studies have confirmed significantly higher interactions between AGEs and their receptors in inflamed periodontal tissues with induced hyperglycemia than

normal glycemic levels [25]. Consequently, it has been suggested that periodontal inflammatory parameters are worse in T2DM subjects and prediabetic individuals, regardless of glycemic control, as reported in previous studies [8, 9]. Nevertheless, our findings indicate that insulin resistance induces initial periodontal inflammation, as evidenced by higher PLI and BOP% values in the IR group.

Notably, PLI was significantly higher in the periodontitis subgroup of the IR subjects, while BOP%, a definitive marker of gingivitis, was highest in the IR group compared to C-T2DM and control groups. Periodontal disease is clinically characterized by gingival erythema, edema, BOP%, periodontal pockets, and destruction of supporting tooth tissues following plaque accumulation and poor oral hygiene [26]. Based on this, insulin resistance may contribute to periodontitis pathogenesis by inducing low-grade inflammation, as indicated by higher PLI and BOP% values. Additionally, our study found a significant positive correlation between PLI and BOP% in the periodontitis subgroup of the IR subjects, consistent with previous research [27, 28].

Regarding PLI, the present study did not find significant differences between periodontal conditions in C- T2DM compared to IR and control groups, which both showed significant differences. This aligns with another study that reported no significant differences in PLI among prediabetes and diabetes control groups [8, 9]. However, our findings contradict a previous study that reported significant differences in PLI between diabetic patients with chronic periodontitis and non-diabetic subjects with chronic periodontitis [29]. These discrepancies may be attributed to differences in the duration of systemic disease and glycemic control cut-offs.

Nevertheless, our results emphasize that diabetic patients tend to have compromised oral environments due to decreased buffering capacity, reduced salivary flow rate, increased salivary viscosity, and alterations in oral microbiota, regardless of glycemic control. Significant differences in BOP% were observed among periodontal conditions (gingivitis, periodontitis, healthy periodontium) in C-T2DM subjects, with the highest mean in the gingivitis subgroup.

However, no significant differences in BOP% were found among the groups. These results partially agree with a previous study that reported a higher bleeding on probing in T2DM subjects compared to the control group, with significant differences between groups. T2DM is often associated with increased gingival inflammation in response to dental plaque biofilm. This response may be related to glycemic control levels, with controlled T2DM subjects exhibiting significantly higher inflammation than IR subjects but lower inflammation than the control group. Regarding PPD, the current study found no significant variance in PPD between the periodontal conditions in each group and between all groups. This outcome was in accordance with previous studies [8, 9].

The non-significant differences in PPD may be attributed to the small sample size. Significant differences in CAL were registered between the periodontal conditions (periodontitis, gingivitis, healthy periodontium) of C-T2DM subjects, with the highest mean in the periodontitis subgroup. Additionally, a significant difference in CAL was found between the groups in the gingivitis and the periodontitis subgroups, with the highest mean of CAL in the C-T2DM group. These outcomes agree with other studies [8, 30] reporting higher CAL with a significant difference in patients with T2DM compared to non-diabetic subjects with chronic periodontitis. However, these findings contradict other results [31].

Compared to non-diabetics, people with T2DM exhibit a higher incidence, prevalence, and severity of periodontitis due to reduced neutrophils functions (adherence, chemotaxis, and phagocytosis), resulting in increased pathogen proliferation and periodontal tissue inflammation. Numerous investigations using salivary redox biomarkers have revealed that diabetic patients have higher blood levels of OS due to increased ROS generation and decreased host antioxidant defense mechanisms [32].

The current study recorded the highest TOS and AGEs levels in the IR group, followed by the C-T2DM, and the lowest in the control group, with significant differences among the periodontitis, gingivitis, and

healthy periodontium subgroups. However, the current study did not reveal a significant difference between groups. The current result agrees with a study demonstrating significantly higher salivary TOS with periodontitis [33]. However, Zhang et al. [34] found no differences in salivary TOS between healthy periodontium and periodontitis. These discrepancies may be attributed to varying participant standards across studies.

On the other hand, salivary TAC was highest in the healthy periodontium subgroup of the control group, followed by the gingivitis subgroup, and lowest in the periodontitis subgroup, with significant differences. This partially agrees with a study [35] study, when compared to a control group, discovered lower salivary TAC in T2DM participants. According to research by Thomas et al. [37], people without periodontitis who are systemically healthy had greater serum TAC levels, whereas people with chronic periodontitis who are systemically healthy had lower levels [36]. When compared to participants with clinically healthy periodontium, a prior investigation showed a substantial drop in TAC [37].

Salivary TAC values in participants with periodontitis were found to be considerably greater than those in the control group. The authors explained that the initial elevation in OS associated with periodontal inflammation was caused by a local reactive or adaptive response, which resulted in an increase in antioxidant response in periodontitis. The persistent generation of ROS may eventually lead to a decline in the adaptive antioxidant defense. Overuse of antioxidants [15]. The aforementioned factors may explain the different results reported in various studies evaluating TAC levels in subjects with periodontitis. The current study recorded a positive significant correlation between salivary TAC and BOP% and an inverse significant correlation between salivary TOS and BOP% in the periodontitis subgroup of the control group, agreeing with Toczewska et al [36], who found significantly higher TOS and lower TAC with periodontal clinical conditions, indicating exacerbated inflammation.

However, TAC and TOS did not differentiate between insulin resistance or C-T2DM. Salivary AGEs levels were associated with CAL in multivariate regression. This finding can be explained by the binding of AGEs to their RAGE receptors when activated, RAGE stimulates cytokine release, osteoblastic bone resorption, monocyte activities, and collagenase. RAGE is upregulated by AGEs concentration. Additionally, AGEs levels were significantly higher in subjects with periodontitis and T2DM compared to the control group [37], explaining the relationship between AGEs levels and the degree of periodontitis, which aligns with the current study's findings. Future studies with larger sample sizes are needed to correlate salivary TAC, TOS, and AGEs with periodontal disease in IR and C-T2DM subjects. The tissue damage caused by periodontitis appears to occur intermittently in sporadic “bursts.” Some people, like those in the control group, may have minimal tissue loss even with inadequate dental hygiene.

However, in vulnerable people, such as those with insulin resistance, it can still be significant and widespread, resulting in tooth loss [29, 40]. These results imply that periodontitis risk is correlated with putative insulin resistance precursors at an earlier age than anticipated. Thus, common causes of chronic non-transmissible diseases that typically manifest later in life, like insulin resistance, T2DM, and periodontitis, should be addressed by preventative programs. However, salivary TAC and TOS were not independently associated with CAL in the multiple regression model, while salivary AGEs levels represented an independent periodontal predictor. This finding suggests that salivary redox biomarkers can be considered causal risk factors leading to increased BOP% and CAL, influencing the extent of gingivitis and periodontitis but not directly predicting them.

Undoubtedly, there is still much to discover about the link between redox biomarkers and periodontal disease. To clarify the function of salivary TAC, TOS, and AGEs in the pathophysiology of periodontitis, insulin resistance, and glycemic management in type 2 diabetes, further prospective investigations should be carried out. Patients with chronic hyperglycemia (such as IR or T2DM) should be made aware of the detrimental impact on their health.

And encouraged to maintain glycemic levels within the normal range (HbA1c levels 4% to 5%). Regular visits to dental healthcare providers and physicians may also be beneficial.

Conclusion

IR and CT2DM individuals had poorer periodontal inflammatory markers than controls. Salivary AGEs were associated with periodontal parameters (CAL). However, salivary TAC and TOS were significant independent predictors of periodontitis and gingivitis.

Conflict of interest

The authors have no conflicts of interest to declare.

Author contributions

HKA, BAY; study conception and design. HKA; data collection. HKA, BAY, SQJ; methodology. HKA, BAY, SQJ and RAD; statistical analysis and interpretation of results. HKA; original draft manuscript preparation. HKA and RAD writing & editing. Supervision; SQJ, BAY and RAD. All authors reviewed the results and approved the final version of manuscript to be published.

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Informed consent

N/A

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المؤشرات الحيوية للاكسدة والاختزال اللعابي المرتبطة بحالات اللثة لدى مقاومة الأنسولين ومرضى السكري من النوع الثاني المنتظم حسب تصنيف 2017

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المستخلص

الخلفية: أمراض اللثة منتشرة بشكل كبير بين الأشخاص الذين يعانون من مقاومة الأنسولين ومرض السكري من النوع الثاني (T2DM) ومع ذلك، فإن التسبب في أمراض اللثة والعوامل المرتبطة بها بين هذه المواضيع ليست معروفة جيدا. في الآونة الأخيرة ، تم الإبلاغ عن أن خلل الأكسدة ومضادات الأكسدة (الأكسدة) قد يلعب دورًا مهمًا في التسبب في أمراض اللثة.

الهدف: تحديد العلاقة بين ثلاثة مؤشرات حيوية للأكسدة والاختزال اللعابي؛ إجمالي قدرة مضادات الأكسدة(TAC) ، وحالة الأكسدة الإجمالية(TOS) ، والمنتجات النهائية للجليكيشن المتقدمة (AGEs)، ومعلمات أمراض اللثة في مقاومة الأنسولين (IR) ومرضى السكر النوع الثاني المنتظم (C-T2DM) T2DM والاصحاء.

الطرق: أجريت دراسة رصدية تحليلية على 180 مشاركاً تتراوح أعمارهم بين 35 و65 عاماً؛ تم تقسيم الذكور والإناث إلى ثلاث مجموعات، تتكون كل منها من 60 فرداً: مجموعة IR، مجموعةC-T2DM، ومجموعة الاصحاءز تم دراسة عمق الجيب (PPD)، ومستوى الارتباط السريري (CAL)، والنزيف عند نسبة الفحصBOP) ٪(، ومؤشر لوحة الأسنان .(PLI) وبناءً على ذلك، تم تشكيل ثلاث مجموعات فرعية (اللثة الصحية، والتهاب اللثة، والتهاب دواعم اللثة). تم الحصول على اللعاب دون تحفيز، وتم قياس المنتجات النهائية للكجليكيشن المتقدمة باستخدام مقايسة الممتز المناعي المرتبط بالإنزيم(ELISA) ، في حين تم قياس TAC و TOSباستخدام مقايسة اللونية. تم تحليل البيانات باستخدام برنامج SPSS الإصدار 21.

النتائج: تم العثور على علاقة ذات دلالة إحصائية بين TOS و PLI وارتباط عكسي بين TAC و PLI في المجموعة الفرعية لالتهاب اللثة في الاشخاص الاصحاء. في تحليل الانحدار المتعدد، ارتبطت AGEs اللعابية و CALعكسيا بين مجموعة C-T2DM.

الاستنتاج: كانت TOS وAGEs اللعابية أعلى في المجموعة الفرعية لالتهاب دواعم اللثة في مجموعتي IR وC-T2DM، مع أدنى TAC اللعابي بالمقارنة مع مجموعة الاصحاء كانت هناك علاقات بين المؤشرات الحيوية للأكسدة والاختزال اللعابي ومعلمات اللثة. أيضًا، تم اعتبار المنتجات النهائية للكجليكيشن المتقدمة مؤشرًا مستقلاً مهمًا لـ CAL.