ORIGINAL ARTICLE

A Descriptive Study to Determine the Serum and Salivary Uric Acid among Individuals With and Without Periodontitis

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Abstract

Aim: To compare serum and salivary uric acid levels among adults suffering from and without periodontitis and to see their correlation with periodontal parameters. **Materials and Methods:** A cross-sectional study was conducted at a diagnostic center in Bidar, Karnataka, enrolling 316 adults (158 periodontitis cases and 158 controls) who underwent routine blood examination. Serum uric acid was assessed using a biochemical analyser, and sampling of unstimulated saliva followed for uric acid estimation. Various parameters such as personal characteristics (age, gender, smoking) and blood pressure, biochemical parameters (HbA1C, cholesterol, HDL, LDL, triglycerides), and periodontal parameters (plaque index, gingival index, probing pocket depth, clinical attachment loss) were recorded. Mann-Whitney test was used for comparison of uric acid levels between the two groups, and Spearman's test assessed correlations. **Results:** Patients suffering from periodontitis exhibited significantly high serum uric acid (median = 6.30) as compared to the controls (median = 5.60; $P < 0.001$). On the same note, salivary uric acid in patients with periodontitis was also higher (median = 6.10) when compared to the control group (median = 4.80; $P < 0.001$). Serum uric acid positively correlated with probing pocket depth (r = 0.226, $P < 0.001$); however, salivary uric acid correlated even better (r = 0.402, $P < 0.001$). Elevation of triglycerides, diastolic blood pressure, and LDL contributed significantly to variation in uric acid ($P < 0.05$). **Conclusion:** Serum and salivary uric acid levels were elevated in patients suffering from periodontitis and correlated with its severity. Salivary urid acid may thus act as a good and reliable noninvasive biomarker for periodontitis.

Key words: Blood pressure, low-density lipoprotein, periodontitis, salivary uric acid, serum uric acid, triglycerides

INTRODUCTION

Periodontitis is considered a prolonged inflammatory condition that impacts tooth-supporting structures and is marked by increasing deterioration of periodontal attachment and alveolar bone. This is a main public health concern because of its high occurrence and relationship with systemic diseases, including heart diseases, blood sugar regulation, and metabolic syndrome.[1] The prevalence of periodontal disease varies significantly across different populations, with estimates suggesting that 20–50% of the global population is afflicted by the condition.[2] Periodontal diseases poses a substantial concern due to its links with multiple health disorders and its intricate associations with a wide range of medical illnesses.[1] The interconnectedness of this condition with other health issues not only complicates diagnosis and treatment but also amplifies the overall burden on healthcare systems.[3] As it often coexists with chronic illnesses such as diabetes, cardiovascular diseases, and autoimmune disorders, addressing this condition requires a comprehensive approach that considers its broader implications on individual and community health.[4] Uric acid, the final outcome of purine metabolism, is recognized for its double function, as an antioxidant and a pro-inflammatory mediator. While it can protect against oxidative stress, high uric acid concentrations have been implicated in several inflammatory conditions.[5] The connection between uric acid and periodontal disorder is of particular interest, as increased levels may exacerbate inflammatory responses

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within the periodontal ligament resulting in tissue damage and loss of teeth.[6] The presence of uric acid in saliva serves as a non-invasive biomarker continuously gaining attention recently for its potential role in monitoring oral health and disease.

The content of uric acid in saliva may correlate with serum levels and provide insights into the inflammatory condition of the periodontal apparatus.[7] The investigation of uric acid concentrations in saliva as a means of diagnosis presents novel opportunities for comprehending the pathogenesis of periodontal disease. Current developments indicate that salivary uric acid levels may serve as an useful marker of systemic inflammation, potentially reflecting the severity of periodontal disease.[6] This correlation emphasizes the quest for further research into the underlying mechanisms through which uric acid affects periodontal inflammation, particularly as it relates to the activation of immune responses and the role of cytokines in tissue degradation.[8] The integration of salivary diagnostics with traditional blood tests could enhance patient management strategies, allowing for more personalized treatment approaches that address both local and systemic health concerns.[7] Recently published systematic review and meta-analyses reveal a significant elevation in blood uric acid among periodontal disease patients relative to healthy adults without periodontal disease, but salivary uric acid concentrations seem diminished in these patients.[9] A recent investigation found that the periodontitis and uric acid concentration in serum are related significantly suggesting increased uric acid may play an essential role in the inflammatory mechanisms associated with periodontal disease.[6] Examining the disparities of uric acid in blood and saliva of patients with and without periodontitis may enhance the understanding of the pathophysiology and apprise treatment approaches. This research elucidates the correlation between blood and salivary uric acid levels to enhance comprehension of their functions in periodontal disease and general health. Therefore, the current descriptive investigation seeks to determine serum and salivary uric acid levels in adults with and without periodontitis. The secondary objective was to ascertain the correlation of serum and salivary uric acid levels in individuals with and without periodontitis. The null hypothesis of this study asserts that the uric acid level in serum and saliva do not differ significantly between individuals with periodontitis and those without it.

MATERIALS AND METHODS

This study was conducted in accordance with Good Clinical Practice guidelines and the principles of the Declaration of Helsinki. The scientific review board of Saveetha Dental College Chennai provided ethical approval for this study (SRB/SDPhD/0718/17)_B). Descriptive cross-sectional research was undertaken at the private x diagnostic center in Bidar, Karnataka. Data collection was performed from September 1st 2023, to December 30th, 2023, following the acquisition of ethical clearance. The study's objective was clearly explained to the subjects, and formally informed consent was obtained. The identifiers of research participants were anonymized, and data were gathered ensuring data privacy and confidentiality. The participants were notified that their data will be utilized solely for research and publication purposes. Everyone who took part in the study gave their written permission after being fully informed. A convenience sampling method was employed to recruit research participants who provided blood samples for monitoring their medical conditions. The same participants also provided saliva samples for uric acid analysis.

Participants

Eligibility criteria

Inclusion criteria

Male and female patients aged ≥20 years and undergoing routine blood investigation for their various medical conditions in SMS medical laboratory were considered in this study.

Exclusion criteria

Male and female patients <20 years and suffering from uric acid related diseases were excluded from the study. Individuals who had Sjogren's syndrome, an autoimmune disease, or pregnancy were not allowed to take part because those conditions are known to affect salivation. Individuals with prolonged infections such as human immunodeficiency virus, hepatitis B and pulmonary Tuberculosis those were not recommended for periodontal probing due to medical concerns. Participants who received periodontal treatment or on antimicrobial mouth rinses, such as chlorhexidine, those who took systemic antibiotics or anti-inflammatory medications within the past 6 months, and individuals reporting the use of phenytoin, cyclosporine, calcium channel blockers, or hormone replacement therapy were omitted from the investigation.

Sample size calculation

A sample size of 316 (Group 1 without-periodontitis [$n = 158$] and Group 2 with periodontitis [$n = 158$]) was calculated based on the equation:

$n=Z_{1-\alpha/2}^{2}\, p(1-p)/d^2$ with the power of the study >0.80.

$Z_{1-\alpha/2}$ = Standard normal variate (1.96).
p = Expected proportion in population having periodontitis with hyperuricemia based on previous study 0.29.
d= Precision (0.05)

Variables

Demographic details of age, sex, and smoking habit were recorded for each participant. Body measurements–such as waist circumference, height, and weight–were documented

for all the participants. Waist circumference was assessed using a flexible tape positioned horizontally halfway between the lower end of the ribs and the upper edge of the iliac crest. Weight was assessed using a digital scale (Emjoi Power Electronic Scale for Body Fat & Water, EF118). Blood pressure measurement was taken while subject was seated on a comfortable chair. A fully automated upper-arm monitor (Geratherm Desktop, Germany) was used to record BP. Two readings were taken 5 min apart, and the average systolic and diastolic values were recorded.

The patient's forearm was extended to examine the antecubital fossa for a prominent, suitably large, straight, and unobstructed vein. The tourniquet was placed roughly 4–5 fingerbreadths above the venipuncture location. Hand hygiene was performed, and the venipuncture site was disinfected by gently swabbing with 70% alcohol for 30 s, and then allowed to dry totally for an additional 30 s. The vein was stabilized by immobilizing the patient's arm and keeping thumb beneath the venipuncture site. The patient was instructed to clench the first to improve visibility of the vein; the needle was then promptly inserted into the vein at an angle of 30 degrees or less, while slowly advancing it along the vein. After obtaining a sufficient volume of blood, the tourniquet was removed before extracting the needle. Following an overnight fast, five milliliters of venous blood were drawn from the research subjects. A blood sample was taken from vein located in antecubital fossa utilizing a sterile, disposable syringe, subsequently transferred into a conventional vacutainer tube for comprehensive analytical assessment. The Erba Mannheim diagnostic reagent was utilized for the quantitative measurement of blood glucose. Serum for biochemical analysis was preserved at −20°C following centrifugation for 10 min. The biochemical analyses encompassed the quantification of total cholesterol (TC), triglycerides (TG), high-density lipoprotein, low-density lipoprotein (LDL), and uric acid with reagents produced by ERBA Diagnostic Mannheim, GmbH, Mallaustr-68219, and Mannheim, Germany. Following the dental examination, basic periodontal indices such as plaque index (PI), gingival index (GI), probing pocket depth (PPD), and clinical attachment loss (CAL) were documented. The PI and GI were analyzed at four locations per tooth, whereas PPD, CAL, and bleeding on probing (BOP) were measured at six sites per tooth. Gingival inflammation was measured using the GI as revised by Loe and Silness in 1963, excluding third molars. According to the GI scoring system, gingival condition was classified as: normal (score 0), mild (score 1), moderate (score 2), or severe (score 3) inflammation.

The dental plaque was assessed using a scale ranging from 0 to 3. The plaque accumulation on the buccal surfaces of teeth was recorded. A score of '0' indicated no visible plaque on the clinical crown, while a score of '3' represented soft deposits covering more than two-thirds of the crown surface. Following the probing of each quadrant, BOP was evaluated and recorded, with scores defined as 0 for no bleeding and 1 for the presence of bleeding. Gingival recession and probing depth were measured using the University of North Carolina-15 (UNC-15) probe, a manual periodontal instrument produced by Hu-Friedy, Chicago, Illinois. A set of criteria established by the American Academy of Periodontology served as the basis for the grading of the severity of periodontitis. These criteria state that mild chronic periodontitis is characterized by CAL of 1–2 mm, moderate instances have CAL of 3–4 mm, and severe periodontitis is characterized by CAL of 5 mm or more. Unstimulated salivary samples were obtained from the study subjects between 8:00 and 10:00 a.m. to mitigate the effects of circadian rhythms. Before collection, each participant was instructed to thoroughly rinse their mouth and remove any remaining saliva. Participants were instructed to sit conveniently with their eyes open and their heads slightly inclined forward, remaining still for 5 min while minimizing or facial movements. During this period, saliva was allowed to passively accumulate and drip from the lower lip into a sterile, graduated plastic container. At the end of the collection period, participants expectorated any remaining saliva into the same container. The Navazesh technique was employed for standardized collection. Saliva samples were obtained and centrifuged to eliminate cellular debris. The resulting supernatants were promptly stored at –80°C for later analysis. Salivary uric acid concentrations were measured by enzymatic assay method using the Erba diagnostic kit. The Trivedi and Kabasakalian method, which is a modified version of the Trinder peroxidise approach and involves 2,4,6-tribromo-3-hydroxybenzoic acid, was utilized in order to ascertain the quantities of uric acid present in the blood. The intensity of the quinone imine that ended up being produced, which was detected at 505 nm, was directly related to the amount of uric acid that was present in the sample. The amounts of uric acid in both the serum and the saliva from individuals with and without periodontitis were analyzed using statistical methods.

Statistical analysis

The data normality was ascertained using Kolmogorov–Smirnov test and a visual examination of the histograms. The results indicated a non-normal and skewed distribution ($P < 0.05$) of the data. Descriptive statistics, encompassing percentages and frequency distributions, were obtained for categorical data. The mean, standard deviation, median, and interquartile range were computed for continuous data, including PI, GI, PPD, CAL, serum and salivary uric acid. Non-parametric Mann–Whitney U test compared the serum and salivary uric acid values between individuals with and without periodontitis. Spearman's test was utilized to evaluate the relation of serum and salivary uric acid values across the entire study sample. The same correlation analysis was conducted separately within the periodontitis and non-periodontitis groups to evaluate group-specific associations. A value of $P < 0.05$ was considered statistically significant for all analyses. All the analyses were carried out utilizing IBM-SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Table 1 displays the frequency distribution (n = 316) as well as the percentages associated with the demographics of the participants. Majority of the study participants were male in the aged 51–65, and non-smokers. A substantial number of the study participants had systolic and diastolic blood pressures (DBPs) of >130 mmHg and <84 mmHg. Nearly 142 (44.9%) of the study participants had their HbA1c 5.6–6.9. Most of the participants showed normal levels of TC and LDL. Contrarily, most of the participants showed high triglyceride levels.

Descriptive statistics related to uric acid in serum and saliva, and periodontal parameters are shown in Table 2. A relatively higher mean ± SD score of serum uric acid (5.93 ± 1.14) compared to salivary uric acid (5.47 ± 4.35) was observed. The mean ± SD values of PI, GI, PPD, and CAL were found to be 1.18 ± 0.48, 1.21 ± 0.53, 3.44 ± 1.53, and 2.01 ± 1.78, respectively.

Comparison of serum and salivary uric acids between without periodontitis and with periodontitis patients is shown in Table 3. Patients with periodontitis showed significantly higher serum uric level than patients without periodontitis ($P < 0.001$). Similarly, patients with periodontitis exhibited significantly higher salivary uric acid than those without periodontitis ($P < 0.001$).

The variables influencing serum and salivary uric acid levels are summarized in Table 4. Uric acid in serum showed a significant relationship with age group, TC, TG, LDL, and DBP (all $P < 0.05$). Pairwise comparisons revealed that individuals aged over 66 years showed significantly lesser serum uric acid compared to those aged 36–50 years. Similarly, patients with normal TC exhibited significantly lower serum uric acid levels compared to those with borderline-high and high TC. An elevation in serum uric acid was particularly notable among those with high TC levels. Patients with normal TG levels were found to have significantly reduced serum uric acid than borderline or high TG cases. Likewise, individuals with high LDL demonstrated significantly higher serum uric acid than those with borderline-high or normal LDL. Elevated DBP (>85 mmHg) was also associated with increased serum uric acid levels.

In contrast, salivary uric acid measure was significantly influenced by gender ($P = 0.006$), smoking status ($P = 0.013$), HbA1c ($P < 0.001$), TG ($P < 0.001$), LDL ($P < 0.001$), and DBP ($P < 0.001$). Male participants revealed significantly elevated salivary uric acid compared to their female counterparts. Smokers compared to non-smokers demonstrated an elevated salivary uric acid. Participants with HbA1c values between 5.6–6.9% and >7% had significantly raised salivary uric acid than those within the 3.9–5.5% range. Participants with high TG levels exhibited significantly greater salivary uric acid

Table 1: Characteristics of the study participants (n=316)

Characteristics	*n*	%
Age		
20–35	37	11.7
36–50	62	19.6
51–65	160	50.6
>66	57	18.0
Gender		
Male	192	60.8
Female	124	39.2
Smoker		
Yes	69	21.8
No	247	78.2
WC (cms)		
<Males 80, <Female 70	22	7.0
Males 80–90, Females 70–80	20	6.3
>Males 90, >Females 80	274	86.7
HbA1C		
3.9–5.5	42	13.3
5.6–6.9	142	44.9
7 or above	132	41.8
SBP (mm Hg)		
<119	38	12.0
120–129	80	25.3
>130	198	62.7
DBP (mm Hg)		
<84	161	50.9
>85	155	49.1
TC (mmHg)		
Normal	141	44.6
Borderline high	90	28.5
High	85	26.9
HDL (mm Hg)		
<40 mg/dL in males<50 mg/dL in females	302	95.6
>40 mg/dL in males>50 mg/dL in females	14	4.4
TG (mmHg)		
Normal	96	30.4
Borderline	98	31.0
High	122	38.6
LDL (mmHg)		
Normal	191	60.4
Borderline high	109	34.5
High	16	5.1

WC: Waist circumference, HbA1C: Glycated hemoglobin, TC: Total cholesterol, HDL: High-density lipoprotein, TG: Triglycerides, LDL: Low-density lipoprotein, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, mmHg: Millimeter of mercury, mg/dL: Milligram per deciliter, cms: centimeters

than those with borderline TG levels. Notably, those with borderline LDL levels had lower salivary uric acid compared to subjects with normal and high LDL levels, though no statistical difference was found between the normal and high LDL groups. In addition, patients with DBP >85 mmHg had significantly higher salivary uric acid than those with lower DBP. Among all variables, TG, LDL, and DBP emerged as common factors significantly associated with both serum and salivary uric acids.

Table 5 presents Spearman's correlation analysis of serum and salivary uric acid concentration and the severity grades of periodontitis. The correlation coefficient showed a significant weak and moderate positive relationship between serum uric acid and PPD ($r = 0.226$, $P < 0.001$) and salivary uric acid and PPD ($r = 0.402$, $P < 0.001$), suggesting a stronger association between salivary uric acid levels and periodontal disease severity. Spearman's tests of serum and salivary uric acid, along with and without periodontitis patients, is shown in Table 6. A significantly negative correlation was found between uric acid in serum and saliva of patients without periodontitis ($r = -0.318$, $P < 0.001$). However, periodontitis patients showed an insignificant positive correlation between serum and salivary uric acid ($r = 0.055$, $P = 0.491$).

DISCUSSION

Periodontitis presents a persistent inflammatory condition that impacts the tissues surrounding the teeth, and, if neglected, can result in tooth loss. This study sought to assess blood and salivary uric acid concentrations, as well as the prevalent factors affecting them, in individuals with and without periodontitis. The secondary purpose was to examine the correlation between serum and salivary uric acid of individuals depending on their periodontal health status.

The findings of this study reveal that the patients with periodontitis exhibited markedly raised serum uric acid levels compared to those without the condition. The average serum uric acid concentration was 5.52 mg/dL in subjects without periodontitis and 6.33 mg/dL in those with periodontitis. Thus, the initial null hypothesis, which asserted no difference in serum uric acid levels between the two groups, was rejected. This result corresponds with prior studies that have consistently indicated increased blood uric acid levels in persons with periodontitis relative to healthy controls. This increase is believed to be linked to the body's reaction to inflammation and oxidative stress, which are characteristic hallmarks of periodontitis.[7,9,10] However, Xu *et al.* noted that a marginal escalation in the incidence of periodontitis was observed in conjunction with a statistically non-significant elevation in serum uric acid concentrations; however, deleterious effects manifested exclusively subsequent to the attainment of a specific threshold of serum uric acid. Consequently, it has been suggested that augmented serum uric acid levels confer a protective effect against the development of periodontitis, exhibiting a range in which the risk diminishes, subsequently followed by a non-significant tendency to rise.[11] In a related study, Chen *et al.* explored the association of hyperuricemia and periodontitis using data from a nationwide representative sample of adults obtained through the National Health and Nutrition Examination Survey. The data analysis revealed that the patients with hyperuricemia showed 0.281 times increased odds of getting Stage III/IV periodontitis than those without hyperuricemia. Furthermore, for every 1 mg/dL rise in serum uric acid above the threshold of 5.9 mg/dL, the risk of developing advanced periodontitis (Stages III/IV) increased by 0.156. Thus, providing the first initial direct evidence of hyperuricemia relates to Stages III/IV periodontitis.[12] Contrarily, Nkeck *et al.* observed that the individuals not having metabolic syndrome elements, increased serum uric acid affects one in five people with periodontitis. Furthermore, an absence of correlation between blood uric acid levels and overall periodontal health was seen in the Cameroonian population.[13] However, Narendra *et al.* found no variation in serum uric acid concentration between periodontitis and healthy groups.[10]

Table 2: Serum and salivary uric acid and periodontal parameters

Variables	Mean	SD	Median	Min	Max
Serum uric acid	5.93	1.14	5.80	3.70	8.60
Salivary uric acid	5.47	4.35	5.70	1.70	7.00
PI score	1.18	0.48	1.17	0.13	2.30
GI score	1.21	0.53	1.17	0.13	2.46
PPD	3.44	1.53	3.10	0.57	6.50
CAL	2.01	1.78	1.00	0.50	7.17

PI: Plaque index, GI: Gingival index, PPD: Probing pocket depth, CAL: Clinical attachment loss, SD=Standard deviation, Min: Minimum, Max: Maximum

Table 3: Levels of serum and salivary uric acids between patients without periodontitis and those with periodontitis

Status	Serum uric acid					Salivary uric acid				
	Mean	SD	Median	IQR	*P*	Mean	SD	Median	IQR	*P*
Without periodontitis	5.52	0.79	5.60	1.00	<0.001	4.45	1.78	4.80	3.00	<0.001
With periodontitis	6.33	1.28	6.30	1.90		6.05	0.93	6.10	1.32	

SD: Standard deviation, IQR: Inter-quartile range

Table 4: Factors affecting serum and salivary uric acid

Variables	Serum uric acid			Salivary uric acid		
	Median	IQR	*P*	Median	IQR	*P*
Gender						
Male	5.65	5.00–6.55	0.118	5.90	4.80–6.30	0.006
Female	6.00	5.60–6.50		5.40	2.30–6.25	
Age (years)						
20–35	5.70	5.60–6.00[ab]	0.021	6.00	5.10–6.20	0.535
36–50	6.20	5.80–6.80[a]		5.90	3.30–6.30	
51–65	5.90	5.20–6.50[ab]		5.75	4.80–6.30	
>66	5.40	4.80–6.00[b]		5.00	4.50–6.00	
Smoker						
Yes	5.90	5.30–6.50	0.601	6.10	5.10–6.50	0.013
No	5.80	5.10–6.50		5.40	4.10–6.30	
WC (cms)						
<M 80; < F 70	5.80	5.80–5.80	0.675	2.30	2.30–6.50	0.082
M 80–90; F 70–80	5.70	5.60–5.80		6.10	6.00–6.20	
>M 90; >F 80	5.90	5.10–6.50		5.50	4.50–6.30	
HbA1C (%)						
3.9–5.5	5.60	5.10–6.00	0.059	4.50	3.30–5.50[a]	<0.001
5.6–6.9	6.00	5.20–6.80		5.50	3.90–6.30[b]	
7 or above	5.70	5.20–6.50		5.90	5.10–6.40[b]	
TC (mg/dL)						
Normal	5.50	4.60–6.20[a]	<0.001	5.90	4.70–6.30	0.169
Borderline high	5.95	5.50–6.20[b]		5.80	1.70–6.10	
High	6.50	5.80–6.80[c]		5.60	4.20–6.50	
HDL (mg/dL)						
<40 in men; <50 in women	5.80	5.10–6.50	0.213	5.70	4.50–6.30	0.249
>40 in men; >50 in women	6.15	5.60–6.90		6.40	4.10–6.50	
TG (mg/dL)						
Normal	5.50	4.70–6.15[a]	<0.001	5.00	3.60–6.20[ab]	<0.001
Borderline	6.00	5.30–6.50[b]		4.85	2.30–6.10[a]	
High	6.10	5.60–6.80[b]		6.10	5.30–6.80[b]	
LDL (mg/dL)						
Normal	5.60	4.90–6.50[a]	<0.001	5.90	5.00–6.30[b]	<0.001
Borderline high	5.90	5.30–6.30[a]		4.80	2.30–6.50[a]	
High	7.45	6.50–8.40[b]		6.40	5.30–6.50[b]	
SBP (mmHg)						
<119	5.85	5.60–6.80	0.327	5.10	3.60–6.10	0.176
120–129	5.80	4.70–6.80		5.90	4.10–6.30	
>130	5.90	5.20–6.50		5.85	4.70–6.40	
DBP (mmHg)						
<84	5.80	5.10–6.00	<0.001	5.10	3.10–6.30	<0.001
>85	6.00	5.30–6.80		5.90	5.10–6.40	

WC: Waist circumference, HbA1C: Glycated hemoglobin, TC: Total cholesterol, HDL: High-density lipoprotein, TG: Triglycerides, LDL: Low-density lipoprotein, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, mmHg: Millimeter of mercury, mg/dL: Milligram per deciliter, Cms=Centimeters. [abc]Superscript with different alphabetical letter across columns indicates a significant difference at $P<0.05$

Table 5: Correlation between serum and salivary uric acid in periodontitis patients

Variables	Serum uric acid	Salivary uric acid	PPD
Serum uric acid			
CC	1.000	0.073	0.226**
P		0.193	<0.001
N	316	316	316
Salivary uric acid			
CC	0.073	1.000	0.402**
P	0.193	.	<0.001
N	316	316	316
PPD			
CC	0.226**	0.402**	1.000
P	<0.001	<0.001	.
N	316	316	316

CC: Correlation coefficient, PPD: Probing pocket depth. **Correlation is significant at the 0.01 level (2-tailed)

Table 6: Spearman correlation test between serum and salivary uric acid

Variables	Serum uric acid	Salivary uric acid
Without periodontitis		
Serum uric acid		
CC	1.000	−0.318**
P	.	<0.001
Salivary uric acid		
CC	−0.318**	1.000
P	<0.001	.
With periodontitis		
Serum uric acid		
CC	1.000	0.055
P	.	0.491
Salivary uric acid		
CC	0.055	1.000
P	0.491	.

CC: Correlation coefficient. **Correlation is significant at the 0.01 level (2-tailed)

This study found a substantial rise in salivary uric acid levels in participants with periodontitis. This finding aligns with the study conducted by Rizal and Vega, which identified a markedly elevated level of salivary uric acid in periodontitis compared to gingivitis.[14,15] Prior studies demonstrate that salivary uric acid concentrations elevate in periodontitis patients subsequent to non-surgical treatment.[16,17] The non-surgical method aids in reducing oxidative stress levels resulting from the buildup of bacterial byproducts. The elimination of bacterial byproducts has been observed to facilitate an elevation in uric acid concentrations within healthy individuals.[18] Conversely, only few investigations demonstrated that the patients afflicted with periodontitis presented with attenuated salivary uric acid levels when contrasted with individuals devoid of the condition.[9,19,20] A contemporary investigation, employing a systematic review and meta-analysis methodology, indicated a correlation between periodontitis and diminished salivary uric acid concentrations. This suggests that inflammatory mediators may exert an influence upon uric acid metabolism and excretion, thereby culminating in reduced salivary concentrations. The presence of oxidative stress within periodontal tissues may impinge on uric acid levels, considering its established function as an antioxidant. However, the exact mechanism remains unknown.[8] In this study, increased salivary uric acid among periodontitis patients may indicate the presence of several medical conditions that may have affected the salivary uric acid production and excretion.

Research indicates that periodontitis is associated with aberrant urine metabolism, leading to heightened uric acid concentrations and increased expression of xanthine oxidoreductase (XOR) in periodontal tissues. XOR and uric acid function as pro-oxidative and pro-inflammatory agents, exacerbating inflammation and oxidative stress.[21] Zhang *et al*. noted that oxidative stress is the primary driver of periodontitis, and important OS-genes are turned on. These genes participate in inflammatory pathways, including leukocyte transendothelial migration and osteoclast development. Given that oxidative stress and inflammation are fundamental to the pathogenesis of periodontitis, they may affect biochemical indicators such as uric acid in saliva.[22] A linear association of serum and salivary uric acid concentrations and the severity of periodontitis was revealed through Spearman correlation analysis. This indicates that augmented uric acid levels are correlated with more advanced manifestations of periodontal disease. A modest correlation was discerned with serum uric acid, whereas a moderate association was identified with salivary uric acid concentrations. These results are congruent with the investigation carried out by Bai *et al.*, which established a linear correlation between increased serum uric acid concentration and the prevalence of moderate-to-severe periodontitis.[7]

Previous investigation by Bai *et al.*[7] found that, in contradistinction to male subjects, the serum uric acid concentrations and periodontitis prevalence in female subjects evinced a U-shaped curvilinear relationship, exhibiting inflection points at 4.3 mg/dL and 7.7 mg/dL, as evidenced through a regression model. A discernible inverse relationship was noted between the prevalence of periodontitis and an increase in serum uric acid levels, thereby suggesting a gender-specific association. Notwithstanding this, the current investigation did not ascertain any statistically significant differences in serum uric acid between male and female cohorts. Conversely, salivary uric acid concentrations demonstrated a statistically significant divergence between the

sexes. This observed variance may potentially be attributed to the influence of sex steroids on the prevalence of periodontitis, particularly through their role in bone metabolism.[23] As estrogen suppresses the cytokine expression involved in resorption of the bone, and its dearth may contribute to the initiation or advancement of periodontal disease.[24] In addition, men with diminished testosterone influenced by sex hormone-binding globulin have been demonstrated to be at higher risk for developing periodontitis.[25] The increased incidence of chronic periodontitis among males indicates suboptimal lifestyle or environmental influences, including inadequate dental hygiene practices, elevated tobacco consumption, and reduced or irregular oral health care utilization.[26] This investigation meticulously analyzed the common determinants influencing both serum and salivary uric acid concentrations in individuals, encompassing those afflicted with periodontitis and those without. It was observed that TG, LDL, and DBP constituted the predominant elements exhibiting an increase commensurate with elevated uric acid levels. This phenomenon is elucidated by the concomitant rise in blood uric acid and triglyceride concentrations, a condition potentially augmenting the susceptibility to cardiovascular disease and metabolic syndrome. Elevated uric acid levels are posited to precipitate metabolic syndrome, a condition typified by hypertriglyceridemia, visceral adiposity, insulin resistance, and hypertension.[27] Given the strong correlation between serum and salivary uric acid levels, it is highly probable that salivary uric acid concentrations experienced a parallel increase. Consequently, uric acid in saliva may constitute an important non-invasive biomarker for predicting systemic disease risk.[28]

Velioğlu *et al.*[29] examined longitudinal studies that employed consistent methodologies and standardized diagnostic criteria, offering clearer insights into the association between periodontal disease and metabolic syndrome. Their findings revealed a bidirectional relationship, indicating that each condition may influence the development or progression of the other. Metabolic syndrome was positively linked to the periodontal disease, with underlying mechanisms involving elevated pro-inflammatory agents–such as cytokines, reactive oxygen species, and C-reactive protein, as well as the continuous translocation of periodontal pathogens into the bloodstream.[30] However, age and TC were the two additional factors that affected the serum uric acid. This observation is corroborated by the tendency for blood uric acid levels to increase with age, particularly in males over 20 and women post-menopause.[31] This study identified notable disparities in blood uric acid levels between the age groups of 36–50 and over 66 years. No similar change was observed in salivary uric acid levels.

The current investigation revealed a considerable difference in blood TC levels, with elevated levels positively associated with increased serum uric acid concentrations.[32] Prior research indicated a correlation between high TC levels and the occurrence of periodontitis, although the precise nature of this association is still being explored. Few researches indicate that increased uric acid levels may affect the onset of hypercholesterolemia. In younger males, elevated serum uric acid positively correlates with elevated TC and other lipid measures. Both dyslipidemia–particularly elevated cholesterol–and hyperuricemia have been independently linked to a heightened risk of periodontitis and may act synergistically in its progression.[33,34] Asoka *et al.*[35] showed the utility of saliva as a diagnostic fluid for uric acid assessment, establishing a reference range of 0.29–6.11 mg/dL in accordance with Clinical and Laboratory Standards Institute guidelines (EP-28A3C). Their findings revealed a moderate correlation between salivary and serum uric acid. The present investigation found that salivary uric acid levels varied between 1.70 mg/dL and 7 mg/dL, with a mean of 5.47 ± 4.35 mg/dL. However, a weak insignificant correlation between serum and salivary uric acid was noted.

This study's findings indicate that salivary uric acid is impacted by gender, smoking status, and HbA1c levels. Male individuals demonstrated markedly elevated salivary uric acid levels relative to females. This result corresponds with the findings of Martinez *et al.* who indicated increased serum uric acid levels in adult males compared to females. Gender-based differences in salivary uric acid are apparent across diverse age demographics and between healthy people and those with particular medical problems. Research has emphasized the intricate relationship among salivary uric acid, gender, and variables including body fat percentage and metabolic syndrome.[36,37] In contrast, increased salivary uric acid concentrations were found to be linked with the premature development of diseases such as preeclampsia, gestational hypertension, and pre-term birth. Consequently, salivary uric acid may function as a prospective early biomarker for hypertensive problems in pregnancy and spontaneous preterm delivery.[38]

Prior studies have consistently indicated that smokers exhibit reduced salivary uric acid levels in comparison to non-smokers, presumably attributable to the antioxidant characteristics of uric acid and the free radical-scavenging capabilities of cigarette smoke.[39,40] Nonetheless, in contrast to these findings, the current investigation noted significantly increased salivary uric acid levels in smokers in comparison to the non-smokers. This conclusion may be ascribed to the comparatively smaller sample of smokers than nonsmokers seen in this study. This conclusion aligns with the study of Lesan *et al.*, which demonstrated a negligible increase in salivary uric acid levels among smokers compared to nonsmokers.[41] Furthermore, the existence of periodontal disease influenced salivary uric acid levels.[39] Glycated hemoglobin (HbA1c) and salivary uric acid are both indicators of metabolic status—HbA1c reflects long-term glycemic control, while salivary uric acid may be linked to insulin resistance and development of type 2 diabetes risk among the subjects. Studies have reported a complex connection between these markers, with some reporting a

positive correlation, particularly in individuals with diabetes, while others suggest an inverse or non-linear association.[42]

The current investigation found that participants with elevated HbA1c levels demonstrated significantly increased salivary uric acid compared to those with lower values. A notable negative relationship was seen between serum and salivary uric acid in subjects without periodontitis. A slight correlation of serum and salivary uric acids was identified in patients with periodontitis. This may signify varying levels of oxidative stress attributable to periodontitis and other health issues. The relationship between serum uric acid levels and the occurrence of periodontitis in non-Hispanic blacks demonstrates an inverted U-shaped curve, with a breaking point at 6.6 mg/dL.[7] The main feature of this investigation is the analysis of serum and salivary uric acid levels in individuals with and without periodontitis within an Indian context. The study also examined prevalent factors that substantially influence serum and salivary uric acid levels. It also assessed the relationship between these two biomarkers in persons both with and without periodontitis. The determined sample size is adequate to yield significant data concerning the serum and salivary uric acid correlations.

This study utilized enzymatic colorimetric assay kits for the quantification of uric acid, a method widely favored in clinical research for salivary analysis due to its simplicity, rapid processing, minimal equipment requirements, and broad commercial availability. Despite these advantages, certain limitations persist. Some assays may exhibit cross-reactivity, and most kits are designed to measure only one analyte. Moreover, sensitivity may be insufficient when utilized in intricate biological matrices like dental calculus. The relatively high cost of these assays also poses a challenge for large-scale studies.[43] This descriptive cross-sectional study presents certain limitations. Due to its time-constrained design, the volume of data collected and analysed, particularly regarding serum and salivary uric acid levels among patients undergoing routine blood investigations was limited. To minimize variability in biochemical measurements, the study was executed in a single private diagnostic center, thereby avoiding inconsistencies that may arise from using different analysers across multiple facilities. In addition, the cross-sectional nature of the investigation limits the capacity to ascertain causal correlations between serum and salivary uric acid levels and the incidence of periodontitis. Bias resulting from additional possible variables that were not controlled in this study cannot be ruled out. The lack of comprehensive information concerning emotional state, nutritional intake, and alcohol consumption might have affected the uric acid level in serum and saliva of the study participants. Anatomical considerations, including the positioning of the site relative to the tooth, particularly variations in crown curvature and root angulations, might have led to inaccurate probing, thereby affecting CAL measurement discrepancies. The future studies should include additional serum and salivary biomarkers along with uric acid to improve research by examining changes associated with periodontitis. Advanced biosensors are the latest domain in equipment that is expected to be more extensively utilized for uric acid assessment in clinical research. The current generation of biosensor devices demonstrates stability, reliability, and biocompatibility. Therefore, these devices must be employed for the measurement of uric acid.

CONCLUSION

The current study concludes that patients with periodontitis demonstrated elevated uric acid in both serum and saliva. Triglyceride levels, LDL, and DBP were identified as the prevalent biochemical variables influencing serum and salivary uric acid levels. Age and fluctuations in TC were identified as the principal factors affecting serum uric acid levels. Conversely, salivary uric acid levels were markedly influenced by gender, smoking status, and HbA1c concentrations. A substantial correlation was found between serum and salivary uric acid and PPD, indicating that elevated uric acid levels are linked to greater severity of periodontitis. Thus, an increased concentration of uric acid in serum and saliva may act as a biomarker for periodontitis. Consequently, increased serum and salivary uric acid concentrations in periodontitis patients should be associated with underlying metabolic disease factors.

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Authors declare that they have no conflicts of interest to disclose.

Author's contribution

All authors contributed equally to this manuscript. All authors participated significantly to the study design and execution, and have read, revised, and approved the final manuscript.

REFERENCES

1. Petersen PE, Ogawa H. The global burden of periodontal disease: Towards integration with chronic disease prevention and control. Periodontol 2000 2012;60:15-39.
2. Nazir MA. Prevalence of periodontal disease, its association with systemic diseases and prevention. Int J Health Sci 2017;11:72-80.
3. Genco RJ, Sanz M. Clinical and public health

implications of periodontal and systemic diseases: An overview. Periodontol 2000 2020;83:7-13.
4. Chandan S, Das AC, Panda S, Nayak R, Mohanty R, Kumar M. Global burden of periodontal diseases: A literature review. Indian J Forensic Med Toxicol 2020;14:8597-602.
5. Choi HK, Mount DB, Reginato AM, American College of Physicians, American Physiological Society. Pathogenesis of gout. Ann Intern Med 2005;143:499-516.
6. Wu Z, Zhao L, Guo Y, Lin C, Lu P, He Q, *et al*. Hyperuricemia exacerbates experimental periodontitis via uric acid-induced periodontal inflammation and oxidative stress. J Clin Periodontol 2025;52:773-86.
7. Bai J, Zhou C, Liu Y, Ding M, Zhang Z, Chen Z, *et al*. Relationship between serum uric acid levels and periodontitis-A cross-sectional study. PLoS One 2024;19:e0310243.
8. Ye LW, Zhao L, Mei ZS, Zhou YH, Yu T. Association between periodontitis and uric acid levels in blood and oral fluids: A systematic review and meta-analysis. BMC Oral Health 2023;23:178.
9. Uppin RB, Varghese SS. Estimation of serum, salivary, and gingival crevicular uric acid of individuals with and without periodontal disease: A systematic review and meta-analysis. J Int Soc Prev Community Dent 2022;12:393-403.
10. Narendra S, Das UK, Tripathy SK, Sahani NC. Superoxide dismutase, uric acid, total antioxidant status, and lipid peroxidation assay in chronic and aggressive periodontitis patients. J Contemp Dent Pract 2018;19:874-80.
11. Xu J, Jia Y, Mao Z, Wei X, Qiu T, Hu M. Association between serum uric acid, hyperuricemia and periodontitis: A cross-sectional study using NHANES data. BMC Oral Health 2023;23:610.
12. Chen Y, Lu P, Lin C, Li S, Zhu Y, Tan J, *et al*. Hyperuricemia and elevated uric acid/creatinine ratio are associated with stages III/IV periodontitis: A population-based cross-sectional study (NHANES 2009-2014). BMC Oral Health 2024;24:1389.
13. Nkeck JR, Ndjoh JJ, Meyo Mvondo GF, Ondoa ME, Takam O, Mbouna SF, *et al*. Periodontal disease and serum uric acid levels in the absence of metabolic syndrome: Is there a link? A study on a sample of Cameroonian adults. BMC Oral Health 2024;24:1519.
14. El Baz MK, Abd El Gwad A, Awadallah HI, Mahallawy OS. The use of antioxidants in treatment of patients with gingivitis and chronic periodontits-intervention study. J Environ Sci 2021;50:217-37.
15. Rizal MI, Vega S. Level of salivary uric acid in gingivitis and periodontitis . Sci Dent J 2017;1:7-10.
16. Priya KL, Mahendra J, Mahendra L, Kanakamedala A, Alsharif KF, Mugri MH, *et al*. Salivary biomarkers in periodontitis post scaling and root planing. J Clin Med 2022;11:7142.
17. Sayar F, Shariatmadar Ahmadi R, Montazeri M. Effect of nonsurgical periodontal therapy on the level of salivary antioxidants in patients with generalized moderate-to-severe chronic periodontitis. J Adv Periodontol Implant Dent 2019;11:21-7.
18. Ghezzi P, Jaquet V, Marcucci F, Schmidt HH. The oxidative stress theory of disease: Levels of evidence and epistemological aspects. Br J Pharmacol 2017;174:1784-96.
19. Lorente L, Marrero EH, Abreu-Gonzalez P, Martín AD, González-Rivero AF, González MJ, *et al.* Low salivary uric acid levels are independently associated with periodontitis. World J Clin Cases 2025;13:105911.
20. Shetty M, Talaviya D. Determination of salivary uric acid levels in periodontitis and health: A case control study. J Health Allied Sci NU 2020;2:54-6.
21. Li Y, Wu Z, Wang Z, Yu X, Liu X, Yu T. Research advances in the therapeutic potential of xanthine oxidoreductase inhibitors for periodontitis. J Prev Treat Stomatol Dis 2023;31:901-6.
22. Zhang Z, Zheng Y, Bian X, Wang M, Chou J, Liu H, *et al*. Identification of key genes and pathways associated with oxidative stress in periodontitis. Oxid Med Cell Longev 2022;2022:9728172.
23. Steffens JP, Wang X, Starr JR, Spolidorio LC, Van Dyke TE, Kantarci A. Associations between sex hormone levels and periodontitis in men: Results from NHANES III. J Periodontol 2015;86:1116-25.
24. Orwoll ES, Chan BK, Lambert LC, Marshall LM, Lewis C, Phipps KR. Sex steroids, periodontal health, and tooth loss in older men. J Dent Res 2009;88:704-8.
25. Su X, Jin K, Zhou X, Zhang Z, Zhang C, Li Y, *et al*. The association between sex hormones and periodontitis among American adults: A cross-sectional study. Front Endocrinol 2023;14:1125819.
26. Haytac MC, Ozcelik O, Mariotti A. Periodontal disease in men. Periodontol 2000 2013;61:252-65.
27. Si SA, Chen MQ, Zhang GJ. Association of serum uric acid with hypertriglyceridemia in children and adolescents: A cross-sectional study. Lipids Health Dis 2024;23:195.
28. Jaiswal A, Madaan S, Acharya N, Kumar S, Talwar D, Dewani D. Salivary uric acid: A noninvasive wonder for clinicians? Cureus 2021;13:e19649.
29. Velioğlu EM, Aydındoğan S, Hakkı SS. Metabolic syndrome and periodontal disease. Curr Oral Health Rep 2023;10:43-51.
30. Aizenbud I, Wilensky A, Almoznino G. Periodontal disease and its association with metabolic syndrome-a comprehensive review. Int J Mol Sci 2023;24:13011.
31. Kuzuya M, Ando F, Iguchi A, Shimokata H. Effect of aging on serum uric acid levels: Longitudinal changes in a large Japanese population group. J Gerontol Ser A 2002;57:M660-4.
32. Peng TC, Wang CC, Kao TW, Yi-Hsin Chan J, Yang JH, Chang YW, *et al*. Relationship between hyperuricemia and lipid profiles in US adults. Biomed Res Int 2015;2015:127596.
33. Ding C, Du F, Li L, Chen Y. Synergistic effect of blood

lipids and uric acid on periodontitis in patients with type 2 diabetes. Am J Transl Res 2023;15:1430-7.
34. Jayashankar CA, Andrews HP, Vijayasarathi, Pinnelli VB, Shashidharan S, Nithin Kumar HN, *et al*. Serum uric acid and low-density lipoprotein cholesterol levels are independent predictors of coronary artery disease in Asian Indian patients with type 2 diabetes mellitus. J Nat Sci Biol Med 2016;7:161-5.
35. Asok A, Ramlingareddy MD, Avinash SS. Establishment of reference range of uric acid in saliva. Int J Acad Med Pharm 2023;5:1238-43.
36. Martínez AD, Ruelas L, Granger DA. Association between body mass index and salivary uric acid among Mexican-origin infants, youth and adults: Gender and developmental differences. Dev Psychobiol 2017;59:225-34.
37. Soukup M, Biesiada I, Henderson A, Idowu B, Rodeback D, Ridpath L, *et al*. Salivary uric acid as a noninvasive biomarker of metabolic syndrome. Diabetol Metab Syndr 2012;4:14.
38. Püschl IC, Bonde L, Reading IC, Maguire P, Macklon NS, Van Rijn BB. Salivary uric acid as a predictive test of preeclampsia, pregnancy-induced hypertension and preterm delivery: A pilot study. Acta Obstet Gynecol Scand 2020;99:1339-45.
39. Fatima G, Uppin RB, Kasagani S, Tapshetty R, Rao A. Comparison of salivary uric acid level among healthy individuals without periodontitis with that of smokers and non-smokers with periodontitis. J Adv Oral Res 2016;7:24-8.
40. Siddique HM, Shaukat Z, Shah SM, Waqas MA, Kanju A, Mansoor E, *et al*. Comparison of salivary antioxidant level in smokers and non-smokers. Pak J Physiol 2025;21:100-2.
41. Lesan S, Khatibi M, Firoozan S. Salivary levels of uric acid, lactate dehydrogenase, and amylase in smokers versus non-smokers. J Res Dent Maxillofac Sci 2021;6:18-22.
42. Donkeng M, Kuaté D, Koudjou PN, Noubiap JJ, Kuiate JR. Association between hyperuricemia and glycated hemoglobin in type 2 diabetes at the District Hospital of Dschang. Pan Afr Med J 2021;40:177.
43. Vernerová A, Krčmová LK, Melichar B, Švec F. Non-invasive determination of uric acid in human saliva in the diagnosis of serious disorders. Clin Chem Lab Med 2020;59:797-812.

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