ORIGINAL ARTICLE

Association between Serum and Salivary Uric Acid in Periodontitis Patients with and Without Metabolic Syndrome

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Abstract

Background: Currently, there is limited research on the correlation between Metabolic status and serum and salivary UA in periodontitis patients. **Objectives:** The objective of this study is to evaluate the relationship between serum and salivary uric acid (UA) levels in periodontitis patients with and without metabolic syndrome (MetS). **Materials and Methods:** This cross-sectional study included 156 periodontitis patients (with MetS = 78 and without MetS = 78) receiving routine blood investigations in a private diagnostic center in Bidar, Karnataka. Personal characteristics and MetS components, such as systolic and diastolic blood pressures, were recorded. Blood parameters such as glycated hemoglobin, total cholesterol, high-density lipoprotein, triglycerides, low-density lipoprotein, serum UA, and salivary UA were determined using a biochemical analyzer. Periodontal variables of plaque index, gingival index, probing pocket depth, and clinical attachment loss were recorded. An independent t-test and analysis of variance, followed by Tukey's tests, were applied to compare the serum and salivary UA between MetS-positive and MetS-negative patients and the severity of periodontitis. **Results:** MetS-positive patients showed significantly raised serum UA (6.04 vs. 5.44, $P < 0.001$) and salivary UA (5.51 vs. 3.84, $P < 0.001$) compared to MetS-negative individuals. MetS-positive patients revealed a significant difference in serum UA levels ($F = 88.432$, $P < 0.001$) and salivary UA levels ($F = 22.428$, $P < 0.001$) across different severities of periodontitis. In contrast, MetS-negative patients showed no significant difference in serum UA ($F = 1.216$, $P = 0.302$) and salivary UA ($F = 0.576$, $P = 0.565$) based on the severity of periodontitis. **Conclusion:** Presence of MetS is associated with higher serum and salivary UA levels in individuals with periodontitis. The differences in UA levels by severity of periodontitis suggest that UA may play distinct roles in systemic and local inflammation.

Key words: Metabolic syndrome, periodontitis, saliva, serum, uric acid

INTRODUCTION

Uric acid (UA), a product of purine metabolism, acts as an antioxidant by scavenging oxygen radicals, which aids in stabilizing blood pressure (BP) and reducing oxidative stress. UA is predominantly produced in the liver, with a smaller amount generated in the intestines. The primary mechanism for the elimination of UA is renal excretion.[1] The levels are affected by dietary consumption, especially from animal proteins, and may result in hyperuricemia, which is linked to gout, nephrolithiasis, and various health complications. Researchers are increasingly acknowledging hyperuricemia as a biomarker for various renal, metabolic, and cardiovascular disorders.[1-3] High levels of UA can result from excessive purine and alcohol intake, suggesting hyperuricemia, gout, and cardiovascular issues. Conversely, low UA levels may signal genetic disorders. A healthy individual exhibits a serum UA concentration ranging from 120 to 400 µmol/L, demonstrating a linear correlation between serum and saliva UA levels.[4] Saliva has become an effective non-invasive diagnostic tool due

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to its ease of storage and capacity to reflect systemic health. Practical applications encompass its utilization in mass screenings and public health emergencies, underscoring saliva as a fundamental element for future progress in non-invasive diagnostics.[5] The main salivary antioxidants are UA, albumin, and ascorbic acid.[6] Clinically, salivary UA is utilized as a marker to measure oxidative stress. UA provides 70–85% of the antioxidant capacity in healthy and periodontally compromised resting and stimulated saliva.[7]

Metabolic syndrome (MetS) is a multifaceted condition defined by interrelated risk factors, including obesity, hypertension, and insulin resistance, which increases the likelihood of cardiovascular diseases and type 2 diabetes in adults globally.[8] The global prevalence of MetS in adults is reported to be between 20% and 25%. A significant prevalence of MetS in India has been reported, affecting one quarter of the adult population, with a notable increase among females.[9] Periodontitis is a prolonged inflammation disorder that impacts the supporting structures of the teeth, marked by the gradual deterioration of periodontal attachment and alveolar bone. This represents a significant public health concern due to its prevalence and association with systemic diseases, such as cardiovascular diseases, diabetes mellitus, and MetS.[10,11] Periodontal disease is reported to afflict between 20% and 50% of the worldwide populace, with estimations suggesting that the incidence of this condition exhibits substantial variability across diverse demographic groups.[12] The significant correlation between serum and salivary UA has raised the relevance of salivary UA as an important biomarker for health and disease risk evaluation.[13] UA levels were found to be elevated in individuals with periodontal disease compared to healthy controls, whereas salivary UA considerably decreased in periodontal disease.[14] The concentration of UA in serum, gingival crevicular fluid, and saliva is considerably influenced in cases of periodontitis. Nonetheless, systemic conditions associated with periodontitis revealed a notable correlation with elevated serum UA levels.[15] Research on serum and salivary UA in periodontitis in relation to MetS is important as it can provide valuable insights into the potential link between periodontal disease and systemic health conditions. Understanding the role of UA levels in both serum and saliva could help in identifying biomarkers for the early detection and management of MetS, especially in high-risk populations in India. This study may contribute to the development of targeted interventions for preventing and treating both periodontitis and MetS, ultimately improving overall health outcomes. At present, literature lacks information on the relationship between MetS status and serum and salivary UA among periodontitis patients. Moreover, it was unclear whether the severity of the periodontal disease in MetS patients affects the serum and salivary UA levels. Hence, this study aims to determine the association between serum and salivary UA in periodontitis patients with and without MetS. This study tests the null hypotheses that there would be no significant difference in the serum and salivary UA levels in periodontitis patients with and without MetS. Second, there would be no significant difference in serum and salivary UA based on the severity of the periodontitis in MetS-positive and MetS-negative patients.

MATERIALS AND METHODS

This cross-sectional study was performed at the SMS diagnostic center in Bidar, Karnataka. Data collection lasted from September to December 2023, following to acquiring ethical approval. A convenience sampling strategy was employed to recruit research participants who submitted blood samples for the monitoring of medical problems to the laboratory. The same subjects provided saliva samples. The study received ethical approval from the Saveetha Dental College and Hospitals' scientific review board in Chennai (SRB/SD PhD/0718/17).

In this study, a total sample size of 156 participants was determined using an a priori analysis method. The participants were recruited to provide both blood and saliva samples for monitoring medical conditions in the laboratory. The allocation ratio between the two groups was equal (N2/N1 = 1), with MetS-positive group (n = 78) and MetS-negative group (n = 78) participants. This sample size calculation assumed an effect size (d = 0.523), error probability (α = 0.05), and statistical power ($1-\beta$ = 0.90). The sample selection was based on the following criteria:

This investigation encompassed male and female periodontitis patients, aged 20 years and above, who were undergoing routine hematological analyses for a spectrum of health conditions at a singular private medical laboratory (SMS) and had provided their informed consent. Exclusion criteria encompassed individuals under the age of 20 years, irrespective of sex, presenting with UA-related disorders. Furthermore, patients diagnosed with Sjogren's syndrome and expectant mothers were not included. Individuals afflicted with chronic infections, specifically human immunodeficiency virus, hepatitis B, or pulmonary tuberculosis, were also excluded. In addition, those who had undergone periodontal therapy or utilized an antibacterial mouth rinse within the preceding 6 months were deemed ineligible. Finally, participants receiving phenytoin, cyclosporine, calcium channel blockers, or hormone replacement therapy were systematically excluded from the study. Demographic information, including age and gender, was documented. Anthropometric measurements, including waist circumference, height, and weight, were documented. Waist circumference was measured using a tape at a horizontal plane, equidistant from the inferior margin of the ribs and the superior border of the iliac crest. Weight was measured through a digital weighing scale (Emjoi Power Electronic Scale for Body Fat & Water EF118). The participant's blood pressure (BP) was taken with a completely automatic

BP monitor (Geratherm Desktop, Germany) for the upper arm, while the patient was in a sitting position. Two BP measurements were taken 5 min apart, and their average systolic and diastolic values were recorded. Following an overnight fast, 5 mL of venous blood samples were obtained from the study participants. A blood sample was extracted from the antecubital fossa vein utilizing a sterile disposable syringe, and the blood was transferred into a Vacutainer plain tube for subsequent examination.

The quantitative assessment of blood glucose was conducted utilizing the Erba Mannheim diagnostic reagent. Subsequent to centrifugation for a duration of 10 min, serum designated for biochemical analysis was cryopreserved at a temperature of −20°C. The comprehensive biochemical analyses involved the quantification of total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and UA, for which reagents manufactured by ERBA Diagnostic Mannheim, GmbH, Mallaustr-68219, Mannheim, Germany, were employed. According to the International Diabetes Federation Global Consensus Declaration, study participants exhibiting three or more of the following five characteristics were classified as having MetS (MetS-positive), while others were categorized as lacking MetS (MetS-negative).

1. Increased waist circumference: ≥90 cm in men and ≥80 cm in women.
2. High TG: ≥150 mg/dL (1.7 mmol/L) or history of specific treatment for this lipid abnormality.
3. Reduced HDL cholesterol: < 40 mg/dL (1.03 mmol/l) in males and < 50 mg/dL (1.29 mmol/l) in females or history of specific treatment for this lipid abnormality.
4. Increased BP: Systolic BP ≥ 130 mm Hg or diastolic BP ≥ 85 mm Hg or on treatment for previously diagnosed hypertension.
5. High fasting plasma glucose: ≥100 mg/dL or previously diagnosed type 2 diabetes mellitus expressed as glycated hemoglobin value ≥5.6.

Unstimulated saliva was collected from subjects between 8 and 10 am to minimize circadian variations. Participants were asked to remain seated, swallow saliva, and remain quiet while allowing saliva to passively flow over the lower lip into a sterile plastic container for 10 min. The modified Navazesh method was utilized in the experiment to gather saliva. Then, the saliva samples were collected and processed to remove all cellular debris. The leftover supernatants were immediately frozen at −80°C for further analysis. An enzymatic method utilizing the Erba kit quantified salivary UA levels. The concentration of quinone imine was associated with the UA content in the sample when measured at 505 nm. All biochemical analyses were conducted at the Private Diagnostic Center in Bidar. Serum and salivary parameters obtained from patients with and without MetS were collected and subjected to statistical analysis.

After the dental examination, periodontal indices – namely, plaque index, gingival index (GI), Probing pocket depth (PD), and clinical attachment loss (CAL) – were documented. The plaque and gingival indices were analyzed at four locations per tooth, whereas probing depth, clinical attachment level, and bleeding on probing were assessed at six sites per tooth. Gingival inflammation was assessed utilizing the GI as modified by Loe and Silness in 1963, eliminating third molars. The GI scoring system categorizes gingival health as normal (score 0), mildly inflamed (score 1), moderately inflamed (score 2), or severely inflamed (score 3). After probing each quadrant, blood on probing was assessed and documented, with scores designated as 0 for absence of blood and 1 for presence of bleeding. Gingival recession and probing depth (PD) were assessed utilizing the University of North Carolina-15 probe, a manual periodontal tool manufactured by Hu-Friedy, Chicago, Illinois. The categorization of periodontitis severity adhered to the standards established by the American Academy of Periodontology. Based on these parameters, mild chronic periodontitis is characterized by CAL of 1–2 mm, moderate instances exhibit 3–4 mm CAL, and severe periodontitis is defined by a CAL of 5 mm or more.

The Kolmogorov–Smirnov test and a visual inspection of the histograms were used to determine data normality. The results suggested that the data followed a near-normal distribution. Categorical variables were analyzed using descriptive statistics, which included percentages and frequency distributions. Continuous variables such as PI, GI, PPD, CAL, and blood and salivary UA levels were analyzed using the mean, standard deviation, median, and range. An independent *t*-test was employed to compare serum and salivary UA levels in patients with and without MetS. An analysis of variance (ANOVA) test was used, followed by Tukey's multiple comparisons, to assess serum and salivary UA based on periodontitis severity. $P < 0.05$ was considered statistically significant in all analyses. All the statistical investigations used IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Table 1 outlines the characteristics of the study participants. A total of 156 patients consented to take part in this study. The predominant age group of participants was 60 and older, with a greater proportion of males than females. The majority of participants indicated that they employed a horizontal oral hygiene technique once during the morning hours. About 20% of the participants indicated that they were smokers. Fifty percentages of the participants were identified as having MetS, whereas the other 50% were categorized as not having MetS. The distribution of periodontal diagnosis was consistent across mild, moderate, and severe categories.

Table 2 shows the descriptive statistics for the study variables. The results of the study show that the mean WC

Table 1: Characteristics of the study participants (*n*=156)

Variables	*N*	%
Age		
20–39	29	18.6
40–59	59	37.8
≥60	68	43.6
Gender		
Male	107	68.6
Female	49	31.4
Oral hygiene method		
Horizontal	126	80.8
Vertical	17	10.9
Circular	13	8.3
Oral hygiene frequency		
Once-morning	141	90.4
Twice-morning and night	15	9.6
Smoker		
Yes	35	22.4
No	121	77.6
Met status		
MetS-positive	78	50.0
MetS-negative	78	50.0
Periodontal diagnosis		
Mild	52	33.4
Moderate	52	33.3
Severe	52	33.3

Table 2: Descriptive statistics for MetS components, uric acid, and periodontal parameters

Variables	Mean	SD	Median	Min	Max
MetS components					
WC (cms)	84.41	18.68	88.00	34.00	124.00
SBP (mmHg)	137.09	17.77	131.00	108.00	185.00
DBP (mmHg)	83.88	8.52	83.00	60.00	104.00
HB1AC (%)	7.30	1.51	7.00	5.00	11.20
TC (mg/dL)	178.70	50.38	165.00	113.00	305.00
HDLc (mg/dL)	43.82	5.67	43.00	36.00	56.00
TG (mg/dL)	212.46	89.66	191.00	117.00	431.00
LDLC (mg/dL)	97.56	40.45	99.80	39.00	211.40
Uric acid					
Serum UA	5.74	0.74	5.75	3.70	7.40
Salivary UA	4.67	1.34	4.80	1.70	7.50
Periodontal parameters					
PI	0.92	0.28	1.00	0.22	1.54
GI	1.09	0.47	1.02	0.13	2.65
PPD	2.80	1.12	2.69	0.40	4.60
CAL	3.04	1.32	3.00	1.00	5.00

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

was 84.41 cm with a standard deviation of 18.68 cm and a median of 88.00 cm. The minimum WC measured was 34.00 cm, while the maximum was 124.00 cm. Similarly, the mean SBP was 137.09 mmHg with a standard deviation of 17.77 mmHg and a median of 131.00 mmHg. The minimum SBP recorded was 108.00 mmHg, while the maximum was 185.00 mmHg. Other variables such as DBP, Glycated Hemoglobin (HB1AC), TC, High Density Lipoprotein Cholesterol (HDLc), TG, Low Density Lipoprotein Cholesterol (LDLC), serum UA, salivary UA, PI, GI, PPD, and CAL also showed varying means, standard deviations, minimums, and maximums in the study participants.

Table 3 shows MetS components between MetS-positive and MetS-negative patients. When comparing the variables between MetS-positive and MetS-negative individuals, it is clear that those with MetS-positive have significantly higher levels of HbA1c (8.00 vs. 6.59, $P < 0.001$), TC (212.09 vs. 145.31, $P < 0.001$), HDLc (47.27 vs. 40.37, $P < 0.001$), TG (256.45 vs. 168.47, $P < 0.001$), and LDLC (119.64 vs. 75.47, $P < 0.001$) compared to those with MetS-negative status. Similarly, WC (90.32 vs. 78.51, $P < 0.001$), SBP (141.76 vs. 132.42, $P = 0.001$), and DBP (86.03 vs. 81.74, $P = 0.002$) were found to be significantly higher in MetS-positive than MetS-negative participants.

Table 4 shows the comparison of periodontal variables between MetS-positive and Mets-negative individuals. When examining the variables between MetS-positive and MetS-negative individuals, it is evident that those with MetS-positive showed significantly elevated PI (0.99 vs. 0.84, $P = 0.001$), GI (1.26 vs. 0.92, $P < 0.001$), PPD (3.34 vs. 2.49, $P < 0.001$), and CAL (3.27 vs. 2.81, $P = 0.028$) than MetS-negative individuals.

Table 5 shows the comparison of uric UA in various groups. When examining the UA between MetS-positive and MetS-negative individuals, it is evident that those with MetS-positive showed significantly elevated serum UA (6.04 vs. 5.44, $P < 0.001$) and salivary UA (5.51 vs. 3.84, $P < 0.001$) [Figure 1]. Comparison of serum and salivary UA within MetS-positive and MetS-negative periodontitis patient is shown in Figure 2. The MetS-positive patients with periodontitis revealed a statistically significant increase in serum UA compared to salivary UA (6.04 vs. 5.51, $P < 0.001$). Similarly, MetS-negative periodontitis patients showed a significantly higher serum uric acid than salivary uric acid (5.44 vs. 3.84, $P < 0.001$).

Table 3: Comparison of components between MetS-positive and MetS-negative patients

Components	Met status	Mean	SD	t	df	*P*	MD	95% CI of the difference	
								Lower bound	Upper bound
WC (Cms)	MetS-positive	90.32	19.23	4.15	154	<0.001	11.81	6.19	17.44
	MetS-negative	78.51	16.19						
SBP (mmHg)	MetS-positive	141.76	18.55	3.38	149.99	0.001	9.33	3.89	14.78
	MetS-negative	132.42	15.73						
DBP (mmHg)	MetS-positive	86.03	6.05	3.23	126.55	0.002	4.28	1.66	6.90
	MetS-negative	81.74	10.02						
HB1AC (%)	MetS-positive	8.00	1.61	6.53	129.26	<0.001	1.41	0.98	1.83
	MetS-negative	6.59	1.01						
TC (mmHg)	MetS-positive	212.09	45.75	11.05	126.24	<0.001	66.78	54.82	78.74
	MetS-negative	145.31	27.51						
HDLc (mmHg)	MetS-positive	47.27	4.90	9.56	154	<0.001	6.90	5.47	8.32
	MetS-negative	40.37	4.07						
TG (mmHg)	MetS-positive	256.45	84.35	7.01	150.12	<0.001	87.97	63.20	112.75
	MetS-negative	168.47	71.74						
LDL (mmHg)	MetS-positive	119.64	41.66	8.12	122.71	<0.001	44.17	33.40	54.93
	MetS-negative	75.47	23.89						

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, SD: Standard deviation, df: Degrees of freedom, MD: Mean difference, CI: Confidence interval, MetS: Metabolic syndrome

Table 4: Comparison of periodontal variables between MetS-positive and Mets-negative patients

Variables	Mean	SD	t	df	*P*	MD	95% CI of the difference	
							Lower bound	Upper Bound
PI								
MetS-positive	0.99	0.25	3.44	150.63	0.001	0.14	0.06	0.23
MetS-negative	0.84	0.29						
GI								
MetS-positive	1.26	0.58	4.70	103.33	<0.001	0.33	0.19	0.47
MetS-negative	0.92	0.24						
PPD								
MetS-positive	3.34	1.25	4.70	154.00	<0.001	0.86	0.18	0.50
MetS-negative	2.49	1.02						
CAL								
MetS-positive	3.27	1.42	2.21	148.72	0.028	0.46	0.05	0.87
MetS-negative	2.81	1.17						

PI: Plaque index, GI: Gingival index, PPD: Probing pocket depth, CAL: Clinical attachment loss, SD: Standard deviation, df: Degrees of freedom, UA: Uric acid, MD: Mean difference, CI: Confidence interval, MetS: Metabolic syndrome

Table 6 displays the mean serum and salivary UA levels corresponding to varying severities of periodontitis in MetS-positive patients. One-way ANOVA was conducted to compare serum and salivary UA levels in individuals with mild, moderate, and severe periodontitis. The results indicated a significant difference in serum UA levels ($F = 88.432$, $P < 0.001$) and salivary UA levels ($F = 22.428$, $P < 0.001$) across the periodontitis severity. Specifically, serum UA levels were highest in individuals with mild periodontitis (M = 6.60, standard deviation [SD] = 0.40), followed by moderate periodontitis (M = 6.15, SD = 0.41), and lowest in severe periodontitis (M = 5.38, SD = 0.08). On the other hand, salivary UA levels were highest in individuals with moderate periodontitis (M = 6.12, SD = 0.99) and severe periodontitis (M = 5.86, SD = 1.00), whereas individuals with mild periodontitis had the lowest salivary UA levels (M = 4.54, SD = 0.72).

Table 5: Uric acid levels in different groups

Variables	Mean	SD	t	df	*P*	MD	95% CI of the difference	
							Lower bound	Upper bound
Serum UA								
MetS-positive	6.04	0.60	5.54	154	<0.001	0.60	0.38	0.81
MetS-negative	5.44	0.75						
Salivary UA								
MetS-positive	5.51	1.14	9.99	148.61	<0.001	1.67	1.34	2.00
MetS-negative	3.84	0.94						
MetS-positive								
Serum UA	6.04	0.60	3.672	117.03	<0.001	0.54	0.25	0.83
Salivary UA	5.51	1.14						
MetS-negative								
Serum UA	5.44	0.75	11.790	146.66	<0.001	1.60	11.79	146.65
Salivary UA	3.84	0.94						

PI: Plaque index, GI: Gingival index, PPD: Probing pocket depth, CAL: Clinical attachment loss, SD: Standard deviation, df: Degrees of freedom, UA: Uric acid, MD: Mean difference, CI: Confidence interval, MetS: Metabolic syndrome

Table 6: Severity of the periodontitis and UA levels in MetS-positive patients

Variables	n	Mean	SD	Std. error	95% CI for mean		F	*P*
					Lower bound	Upper bound		
Serum UA								
Mild	26	6.60	0.40^{A}	0.08	6.43	6.76	88.432	<0.001
Moderate	26	6.15	0.41^{B}	0.08	5.99	6.31		
Severe	26	5.38	0.08^{C}	0.02	5.35	5.41		
Total	78	6.04	0.60	0.07	5.91	6.18		
Salivary UA								
Mild	26	4.54	0.72^{A}	0.14	4.25	4.83	22.428	<0.001
Moderate	26	6.12	0.99^{B}	0.20	5.72	6.52		
Severe	26	5.86	1.00^{B}	0.20	5.46	6.26		
Total	78	5.51	1.14	0.13	5.25	5.76		

n: Sample size, SD: Standard deviation, Std. Erro: Standard error, CI: Confidence interval, MetS: Metabolic syndrome, UA: Uric acid, ^{ABC}superscript with different alphabetical letter across column indicates significant difference at $P<0.05$

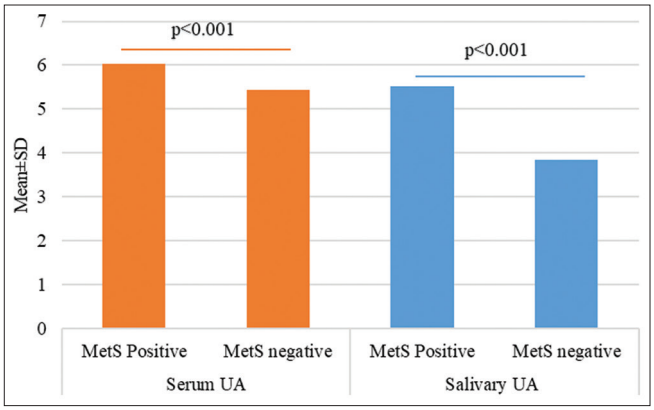

Figure 1: Serum and salivary uric acid (UA) between metabolic syndrome (MetS)-positive and MetS-negative patients with periodontitis

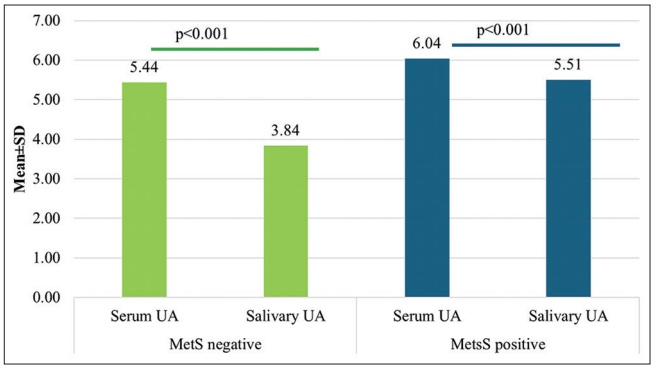

Figure 2: Serum and salivary uric acid (UA) levels within metabolic syndrome (MetS)-positive and MetS-negative periodontitis patients

Table 7 presents the UA levels associated with varying severity of periodontitis in MetS-negative patients. The ANOVA results indicate that there is a difference in serum UA levels among individuals with different severities of periodontitis (mild, moderate, and severe), but the difference

Table 7: Severity of periodontitis and UA levels in MetS-negative patients

Variables	N	Mean	SD	Std. Error	95% CI for mean		F	*P*
					Lower bound	Upper bound		
Serum uric acid								
Mild	26	5.52	0.42	0.08	5.35	5.69	1.216	0.302
Moderate	26	5.54	0.50	0.10	5.34	5.74		
Severe	26	5.25	1.11	0.22	4.80	5.70		
Total	78	5.44	0.75	0.08	5.27	5.61		
Salivary uric acid								
Mild	26	3.70	0.99	0.19	3.30	4.10	0.576	0.565
Moderate	26	3.98	1.11	0.22	3.53	4.43		
Severe	26	3.83	0.68	0.13	3.56	4.11		
Total	78	3.84	0.94	0.11	3.63	4.05		

n: Sample size, SD: Standard deviation, Std. Erro: Standard error, CI: Confidence interval

was not statistically significant (F = 1.216, P = 0.302). Similarly, for salivary UA levels, there is no significant difference among individuals with different severities of periodontitis (F = 0.576, P = 0.565). It was also observed that individuals with severe periodontitis showed slightly lower serum and salivary UA levels compared to those with mild or moderate periodontitis.

DISCUSSION

At present, the literature reveals a significant lack of evidence regarding the connection between MetS status and serum and salivary UA levels in patients suffering from periodontitis. Hence, this study was conducted to investigate the relationship between serum and salivary UA in periodontitis patients with and without MetS. The study results revealed that the serum and salivary UA levels were significantly elevated among MetS-positive patients compared to MetS-negative patients with periodontitis. Consequently, the null hypothesis stating that there is no significant difference in serum and salivary UA levels among periodontitis patients with and without MetS has been rejected. The present study findings can be explained by the fact that UA, a recognized antioxidant, has been associated with a variety of inflammatory conditions, such as periodontitis and MetS. Research suggests that the two conditions are connected by shared inflammatory pathways and risk factors.[16]

MetS is a cluster of conditions, including obesity, hypertension, and dyslipidemia, which collectively increase the risk of cardiovascular diseases and diabetes. These conditions are also associated with elevated serum UA levels, which may contribute to the inflammatory milieu observed in periodontitis. Both MetS and periodontitis are influenced by persistent inflammation, with pro-inflammatory cytokines significantly contributing to their development.[17] In addition, previous investigations have shown that serum UA levels are generally higher in individuals with periodontitis compared to healthy controls. This increase is more pronounced in those with MetS, suggesting a potential link between systemic inflammation and elevated UA levels in these patients.[14] The present study observed that the serum UA was significantly greater than salivary UA in both MetS-positive and MetS-negative periodontitis patients. This finding is consistent with that of Ye *et al*., who found higher blood UA levels and lower salivary UA levels in periodontitis patients.[18]

In this study, MetS-positive patients with mild-to-moderate periodontitis demonstrated a significantly higher level of UA compared to severe periodontitis. However, salivary UA levels were found to be significantly lower in mild periodontitis than moderate-to-severe periodontitis. Consequently, the second null hypothesis, which posited no significant change in serum and salivary UA levels based on the severity of periodontitis in individuals with and without MetS, has been rejected. This could be due to the bidirectional relationship between MetS and periodontitis where each condition exacerbates the other. Chronic systemic inflammation is a common pathophysiological mechanism linking the two, with pro-inflammatory mediators playing a crucial role.[17] Elevated serum UA levels, often seen in MetS, may contribute to the progression of periodontitis by enhancing systemic inflammation. Conversely, periodontitis may worsen MetS components, such as insulin resistance and dyslipidemia, through inflammatory pathways.[10] Current findings are supported by the study reported by Chen *et al*., 2024, in which the presence of hyperuricemia has been associated with an increased risk of developing moderate-to-severe periodontitis. This risk is further amplified in individuals with MetS, where systemic inflammation may exacerbate periodontal disease.[19] Contrarily, MetS-negative cases did not show any significant difference in serum and salivary UAs based on the severity of the periodontitis. This finding aligns with the study reported by Nkeck among Cameroonian adults, who found that in individuals without elements of MetS, hyperuricemia affects one in five people

with periodontal disease. There appears to be no link between serum UA and overall periodontal status.[20]

Unlike other studies, this study also has some limitations. The study was conducted in a single private diagnostic center to reduce variability in biochemical measurements, thereby preventing inconsistencies that may result from the use of various analyzers across multiple facilities. The investigation's cross-sectional design restricts the ability to establish causal relationships between the occurrence of periodontitis and serum and salivary UA levels among MetS-positive and MetS-negative patients. The UA levels in the serum and saliva of the study participants may have been influenced by the absence of comprehensive information regarding their affective state, nutritional intake, and alcohol consumption. Anatomical considerations may have resulted in inaccurate probing, which could have influenced CAL measurement discrepancies. Due to the single-center study, caution should be exercised while generalizing study results to other wider population.

The future studies should include additional serum and salivary biomarkers along with UA to improve research by examining changes associated with periodontitis and MetS. The varying UA levels in serum and saliva suggest that UA serves different roles in systemic and localized inflammation. Consequently, further investigation is necessary to elucidate these pathways and their clinical ramifications. Understanding these connections may lead to the formulation of more effective management methods for people with both periodontitis and MetS.

CONCLUSION

The findings of the current investigation clearly reveal the relationship between serum and salivary UA levels in periodontitis patients with MetS. The presence of MetS notably elevates serum and salivary UA levels in individuals with periodontitis. The differing UA levels in serum and saliva based on severity of the periodontitis indicate that UA serves distinct functions in systemic and local inflammation suggesting underlying mechanisms remain complex. Therefore, additional research is required to clarify these mechanisms and their clinical implications. The comprehension of these interactions could result in the development of more effective management strategies for patients who have both periodontitis and MetS. Moreover, salivary UA can serve as a valuable non-invasive biomarker for diagnosing and monitoring patients' metabolic condition.

CONFLICTS OF INTEREST

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

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