Association between Serum Creatinine and Periodontal Disease Severity—A Comparative Clinicobiochemical Study

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Abstract

Objectives: Periodontitis is a chronic inflammatory disease of the periodontium that produces adverse systemic effects including diabetes mellitus, adverse pregnancy outcomes, respiratory illness, etc. Based on new studies, chronic inflammation is speculated as a risk factor for impairment of kidney function. Periodontitis, as long time inflammation is posed as one of the nontraditional risk factors for end-stage renal diseases. Literature search reveals contradicting evidence on the influence of periodontal infection and inflammation on the renal function. In lieu of the above, this study aims in estimating and comparing the serum creatinine (SCR) levels with periodontal disease status in systemically healthy subjects.

Materials and methods: A total of 45 systemically healthy patients were recruited, and based on their periodontal status, they were divided into two groups: Group I ($n = 22$)—subjects with periodontitis and Group II ($n = 23$)—periodontally healthy subjects. Group I was again categorized into mild (CAL 1–2 mm), moderate (CAL 2–4 mm), and severe (CAL $\geq$ 5 mm) based on the severity of the periodontal disease. After assessing the clinical parameters, blood was collected for SCR estimation. The comparison between PPD, CAL, and SCR was done using the paired t-test. The comparison of SCR levels with severity of the periodontitis (CAL) was done using ANOVA. All the statistical analyzes were performed using SPSS 17 software.

Results: The SCR value in Group I was 1.06 ± 0.13 and in Group II, 1.17 ± 0.16. Using the paired t-test to compare the creatinine values revealed that the difference between the two groups was statistically significant ($p = 0.00001$). By comparing the SCR levels with the severity of the periodontal disease, the mean value for mild periodontitis cases was 1.1 ± 0.12; for moderate periodontitis cases, 1.09 ± 0.25; and for severe periodontitis cases, 1.14 ± 0.14. ANOVA test values between the groups showed a statistical significance ($p < 0.01$).

Conclusion: The results from this study showed an inverse relationship between SCR levels and periodontitis. The causal relationship between periodontitis and low SCR could not be established. This inverse relationship might confound the analysis of the link between renal function and periodontal disease. From the results of this study, we conclude that considering other indices such as cystatin C and creatinine clearance is preferable, to explore the association between renal function and periodontal disease.

Keywords: Association, Periodontitis, Renal diseases, Serum creatinine.

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Introduction

Periodontitis by definition is the infectious disease resulting in inflammation within the tissues supporting the teeth, progressive loss of attachment, and bone loss.[1] The link between periodontal disease and other systemic diseases has been extensively explored in the past two decades, leading to the emergence of a new branch of periodontology, the periodontal medicine. Periodontal infections have been found to adversely affect systemic health such as diabetes mellitus, preeclampsia atherosclerotic vascular disease, and metabolic syndrome.[2–6]

The common risk factors for renal dysfunction are diabetic mellitus, hypertension, and atherosclerosis diseases. Recently, systemic chronic inflammation has been speculated as risk factor for impairment of kidney function. Periodontitis, being a long-term inflammatory condition, can pose as one of the nontraditional risk factors. Serum creatinine (SCR) is considered as an indicator for renal function.[7] Serum creatinine levels and glomerular filtration rates (GFRs) are the widely used indicators of renal function.[8]

Studies on the subjects with chronic renal failure revealed increased PPD, CAL as compared to healthy groups.[9] Increased levels of antibodies against *P. gingivalis* were detected in the serum of subjects undergoing dialysis with severe periodontitis.[10] The studies also demonstrate that patients with untreated periodontal

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diseases have increased risk to have lower glomerular filtrate rate and subsequently elevated SCR concentrations.[11] On the contrary, a study in Japanese men showed an inverse association between periodontal disease and normal SCR concentrations.

Aim

The aim of the study was to estimate and compare the SCR levels with periodontal disease status in systemically healthy subjects.

Materials and Methods

The study population was recruited from the patient pool reporting to Dept. of Periodontology of Indira Gandhi Institute of Dental Sciences, Sri Balaji Vidyapeeth, Puducherry. Reported nonsmokers and systemically healthy subjects of 20–60 years of age and with at least 20 natural teeth remaining were included initially. Subjects who were on or require antibiotic treatment during the course of study, women on hormonal contraceptives, pregnant and lactating women, smokers, subjects on steroids or NSAID in the past 3 months, subjects who have undergone any periodontal therapy in the past 6 months were excluded from the study.

For all the subjects initially recruited, body mass index (BMI), systolic and diastolic blood pressure, and serum glucose (PP) were analyzed. Patients with blood pressure variables >130/90, BMI >25.0, and postprandial glucose levels >140 mg/dL were excluded. Thus, a total of 45 subjects were finally selected for the study.

For the study subjects, the following periodontal parameters were recorded: probing pocket depth (PPD) and clinical attachment level (CAL). Based on the periodontal finding, the subjects were divided into two groups: Group I ($n = 22$)—subjects with periodontitis and Group II ($n = 23$)—periodontally healthy subjects.

Chronic periodontitis cases were defined as those having 5 or more teeth with PD $\geq$ 5mm and clinical attachment loss (CAL) >2 mm. Healthy controls were subjected with no probing depth (PD) greater than 4mm and CAL >1 mm. Periodontitis was again categorized as mild (CAL 1–2 mm), moderate (CAL 2–4 mm), and severe (CAL $\geq$5 mm).

Serum sample collection: No special preparation of the patient was required prior to specimen collection. No special additives or preservatives were required. After assessing the clinical parameters, blood was collected for SCR estimation. The blood samples were collected under all aspects of precautions by vein puncture in antecubital vein. The area was cleaned and made aseptic by using a disinfectant solution and dried. 2 cc of venous blood was withdrawn with the help of a 2-mL disposable syringe and a 24-gauge disposable needle. The sample was then distended into a plain test tube.

The collected blood was analyzed for SCR using commercially available kit that uses modified Jaffe's kinetic method for estimation (Creatinine Kit, Tulip Laboratories, Tulip Group, Verna, Goa, India).

Statistics: The comparison between PPD, CAL, and SCR was done using the paired t-test. The comparison of SCR levels with severity of the periodontitis (CAL) was done using ANOVA. All the statistical analyzes were performed using SPSS 17 software.

Results

Comparative analysis of periodontal parameters and SCR levels between the groups shows that the mean PPD in Group I was 5.19 $\pm$ 0.53 and in Group II was 1.81 $\pm$ 0.26. The mean CAL in Group I was 5.51 $\pm$ 0.53 and in Group II was 1.81 $\pm$ 0.26.

The SCR value in Group I was 1.06 $\pm$ 0.13 and in Group II was 1.17 $\pm$ 0.16. The paired t-test to compare the creatinine values revealed that the difference between the two groups were statistically significant ($p = 0.00001$) (Table 1). By comparing the SCR levels with the severity of the periodontal disease, the mean value for mild periodontitis cases was 1.1 $\pm$ 0.12; for moderate periodontitis cases, 1.09 $\pm$ 0.25; and for severe periodontitis cases, 1.14 $\pm$ 0.14. ANOVA test values between the groups showed a statistical significance ($p < 0.01$) (Table 2).

Discussion

The correlation between periodontitis and chronic diseases is well documented. The reason well accepted is that the bacteria and their toxic products can enter the systemic circulation and exert its effects elsewhere in the body. It is also known that they can affect vascular endothelium in the coronary arteries.[12,13] There are possibilities that the same damage can be caused in the kidney endothelium also. Sedý et al. gave evidence that in a dialyzed patient, periodontal pathogens can induce accelerated systemic and local blood-mediated response that can result in premature death.[14]

Sreeram et al. observed an increase in mean CRP, serum urea, and MDA and a decrease in eGFR uric acid and TAC in the patients with periodontitis and concluded that there is an increased risk for the development of CKD in the patients with periodontitis.[15] A systematic review in 2013 showed that there is a positive association between periodontitis and CKD. There was also a beneficial effect periodontal therapy on eGFR.[16]

A study compared the bacterial accumulation in renal patients with periodontitis, and systemically healthy periodontitis cases showed no difference between the groups. In individuals with and without chronic renal failure, no significant differences were observed in most of the clinical periodontal parameters.[17] Wahid et al. in 2014 showed that data from research articles published between 2000 and 2012 indicate a bidirectional relation between CKD and periodontal disease.[18] In Barbudo-Selmi GR et al., there was no difference in serum levels of creatinine in dogs with mild, moderate and severe periodontitis.[19] Also Taylor et al. reported even after extraction of all teeth from periodontitis patients, there was no change in urea levels.[20]

In lieu of the above controversy, this study was undertaken to evaluate the possible association between the periodontal status of the systemically healthy individuals and the SCR level to assess the role of periodontitis on renal function. In this study, we investigated the association between untreated periodontal diseases and renal function in terms of SCR in subjects previously diagnosed with periodontitis (test group) and periodontally healthy subjects (control group).

In most of the studies analyzing the relationship between periodontal status and renal functions/diseases, the study group included the patients with known renal dysfunction. But in this study, systemically healthy individuals with periodontitis were included which might be more appropriate to know if periodontal disease really has a systemic effect as compared to periodontally healthy controls.

Serum creatinine is by far the easiest diagnostic marker renal function and is readily available in laboratory settings.[21] The SCR levels are greatly unaffected by typical diet.[22,23] Since creatinine is derived from skeletal muscle, the levels may directly correlate with the body mass.[24] A study conducted in athletes demonstrated a direct relationship between SCR concentration and BMI.[25] One study demonstrated that only in a younger age group, BMI was associated with periodontal disease, whereas another study showed a direct relationship in adult, nonsmoking females but not in adult males or smoking females.[26,27]

Few studies have shown that low SCR concentrations may suggest low lean body mass, which may be associated with the incidence of type II diabetes. Also, between individuals with and without diabetes, lower levels of SCR were observed in the first group.[28,29] Hence, on the recruitment of cases, BMI, systolic and diastolic blood pressure, and serum glucose (PP) were analyzed.

Table 1: Comparison of serum creatinine values between the two groups

Parameters	Group I		Group II		Test value	p value
	Mean	SD	Mean	SD		
Age	45.14	12.2	44.12	12.0	–	–
BMI	26.20	8.4	25.82	10.2	–	–
Number of teeth	28.09	2.22	23.42	2.32	–	–
PPD	5.19	0.53	1.81	0.26	12.56	0.001
CAL	5.51	0.53	1.81	0.26	12.00	0.001
Serum creatinine	1.06	0.13	1.17	0.16	40.05	0.001

p value < 0.005 shows statistical significance

Table 2: Comparison of serum creatinine values among mild, moderate, and severe periodontitis cases

Disease severity (CAL)	Serum creatinine	
	Mean	SD
1–2 mm (mild)	1.01	0.12
3–4 mm (moderate)	1.09	0.25
≥5 mm (severe)	1.14	0.14
p value	0.01	

p value < 0.005 shows statistical significance

Those with blood pressure variables >130/90, BMI >25.0, and postprandial glucose levels >140 mg/dL were excluded from the study.

The results of this study show that the SCR value in Group I was 1.06 ± 0.13 and in Group II was 1.17 ± 0.16. This was statistically significant. This result suggests an inverse relationship between SCR concentrations and periodontal disease status.

In accordance with the study conducted by Brotto et al.,[30] kidney function markers (urea, creatinine, uric acid, and albumin contents) measured in the serum were measured in periodontally healthy cases and periodontitis controls. Between the test and control groups, no difference was found in the levels of markers. It was also proposed that periodontal diseases did not alter kidney function.

Similarly, Shimazaki Y et al.[31] explored the periodontal status in Japanese middle-aged males with normal SCR levels and found a significant inverse association.

The exact mechanism linking serum concentrations of creatinine and periodontal disease is still unclear. Thus, SCR appears to be a less reliable tool to assess the relationship between kidney function and untreated periodontal disease.[31]

Conclusion

This study shows an inverse relationship between the SCR levels and periodontal status. The causal relationship between periodontitis and low SCR could not be established. This inverse relationship might confound the analysis of the link between renal function and periodontal disease.

Ethical Approval

All the procedures performed in this study involving human participants were in accordance with the ethical standards of the institution and national research committee and with Declaration of Helsinki 1964, and its later amendments.

Informed Consent

Written informed consent was obtained from all the participants in this study.

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