

Effect of periodontal treatment on some serum biochemistry of patients with end-stage-kidney disease (A pilot study)

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Abstract

Background: Periodontal diseases are inflammatory diseases that affect the supporting structures of the teeth which could lead to tooth loss and contribute to systemic inflammation. End stage kidney disease (ESKD) is an established kidney failure which requires dialysis or a kidney transplant. Several studies have investigated the relationship between kidney diseases and periodontal disease. **Objectives:** This study aimed to investigate the effect of nonsurgical periodontal treatment on the serum chemistry of patients with ESKD. **Methods:** A randomized control trial was designed. Patients with periodontitis and ESKD were divided into two groups: the test group received nonsurgical periodontal treatment just prior to the hemodialysis appointment. The control group did not receive any periodontal treatment except oral hygiene instructions. Clinical periodontal parameters for all participants were recorded at baseline and one month follow-up. Serum albumin, creatinine, urea, total protein, alkaline phosphatase, phosphorus, and calcium levels were measured at baseline and one month follow-up too. Descriptive analysis in addition to t-test and univariate analysis were conducted. **Results:** This study showed no statistically significant change in any serum biochemistry measured between the two groups. **Conclusion:** Nonsurgical periodontal treatment does not have any effect on the studied serum biochemistry of patients with ESKD. However, ESKD patients suffer from moderate to severe periodontitis.

Clinical implication: we suggest a collaboration between periodontists and medical doctors to manage patients with chronic diseases. This will increase the patients' quality of life and may improve the prognosis of the systemic disease.

Keywords: Periodontitis, periodontal treatment, end stage kidney disease.

Introduction

Periodontal disease is an inflammatory process that affects the periodontium [1]. It is one of the most widespread chronic inflammatory diseases affecting about half of the adult population worldwide, with 23% of them suffering from severe form of periodontitis [2]. Inflammation in periodontal tissue occurs in response to bacteria and their products in dental plaque, that represent the primary causative factor [3–5]. Various cytokines and inflammatory mediators are involved in the pathogenesis of periodontitis [6]. These inflammatory mediators and cytokines increase vascular permeability, which can increase bacteremia and trigger a systematic inflammatory response and cytokine production [7,8]. The presence of periodontal pathogens and their metabolic byproducts in the oral cavity may modulate the immune response beyond the oral cavity, thus promoting the development of systemic diseases [9]. Periodontitis is thought to

amplify the systemic inflammatory response and therefore considered a risk factor for many non-communicable diseases such as cardiovascular disease, diabetes mellitus, and chronic kidney disease (CKD) [10–12]. Chronic kidney disease is a progressive, life-threatening disease that leads to gradual and progressive deterioration of kidney functions due to destruction of the nephrons [13,14]. The most common causes of CKD are diabetes and hypertension [15]. Diabetes is also a risk factor for periodontal disease [10]. Controlling diabetes has been shown to improve renal function [16] and stabilize periodontal condition [10]. Levey et al. [17]. stated that the control of periodontal disease improves glycemic control, which in turn improves renal function by reducing the systemic inflammatory burden. Chronic kidney disease is classified into 5 stages based on glomerular filtration rate, which is an indicator for evaluating kidney function. The 5th stage is

referred to as end-stage kidney disease (ESKD) when the glomerular filtration rate is <15 ml/min/1.73m². The progression to ESKD is considered a critical condition. Patients with ESKD require kidney transplantation or frequent hemodialysis to compensate kidney function. Periodontal disease may be a risk factor for CKD. Many studies have investigated the relationship between CKD and periodontal disease [18,19], and some of these studies reported that periodontal disease is common in CKD patients [20,21]. There was also a positive correlation between the severity of periodontal disease and the impairment of kidney function [22]. Elevated levels of immunoglobulin G (IgG) against the periodontal pathogen, *P. gingivalis* have been shown to positively correlate with the onset and progression of CKD [23]. Both periodontitis and CKD have an inflammatory background and similar risk factors [20].

The previous randomized-controlled clinical trials on the effect of nonsurgical periodontal therapy in ESKD patients mentioned different results [24–26], and there is still uncertainty about the effect of periodontal treatment on the prognosis of ESKD. Therefore, in this study, we aimed to investigate the effect of professional mechanical plaque removal (PMPR) on some serum biochemistry of patients with ESKD.

Materials and Methodologies

This study was conducted on hemodialysis patients suffering from periodontitis who are attending the hemodialysis department at Tikrit Teaching Hospital (Salahiddin), from September 2022 to February 2023. Informed consent was obtained from each participant and a case sheet was used to record the background information, dental and medical history of the participants and periodontal parameters. The ethical principles of Declaration of Helsinki 2008 were followed. This study was approved by the scientific committee in meeting no.1 for the academic year 2022-2023, which was held on 1st September 2022, and registered in the annual research plan of the department of

periodontology, College of Dentistry, Tikrit University.

Periodontitis patients were diagnosed according to the criteria of the 2017 Classification of Periodontal and Peri-implant Diseases and Conditions [27]. Patients suffering from stage 2 periodontitis (clinical attachment loss =3-4mm at site of greatest loss) and stage 3 periodontitis (clinical attachment loss ≥ 5 mm at site of greatest loss) were included in this study.

Periodontal parameters including plaque index (PLI) [28], clinical attachment loss (CAL) [29], and bleeding on probing (BoP) [30] were recorded on six sites around all the teeth in the patients using the periodontal probe UNC-15.

Inclusion and exclusion criteria:

patients who were treated in the Artificial Kidney Unit and diagnosed with periodontitis stage 2& 3 were recruited. We excluded patients with infectious diseases (such as hepatitis).

The recruited patients were randomly divided into two groups. The test group received nonsurgical periodontal treatment in the form of supragingival PMPR. For this procedure, we used an ultrasonic scaler and a portable suction device. The treatment was administered to the patient on the day of their hemodialysis appointment, just before they received heparin in the dialysis chair. The control group received no periodontal intervention. Only periodontal parameters were recorded prior to hemodialysis. Blood samples were collected from all the patients in both groups in a plain test tube by a nurse. The samples were analyzed in the hospital laboratory unit. Blood samples were left to clot then centrifuged 1500-2000 round per minute for 10 minutes to separate the serum from the blood. Laboratory tests included serum urea, creatinine, albumin, alkaline phosphatase, total protein, phosphorus and calcium levels were measured in both groups at baseline. A spectrophotometer was used to analyze the serum biochemistry. A 1-month follow-up was performed to record periodontal measures and serum biochemistry for both groups.

The IBM Statistics Package for Social Science (SPSS) version 25 was used for statistical analysis. Both descriptive and analytical

statistics were used. Statistical significance of differences between means was calculated using the t-test. Differences were considered significant when the probability value $p < 0.05$. Univariate analysis was performed to compare the mean values of serum markers between the two groups after adjusting for baseline values, mean PLI, mean BoP, and stage of periodontitis.

Results and Discussion

A total of 30 patients with ESKD participated in this study, with a male-to-female ratio of 2:1. All patients were on hemodialysis. There was no dropout. The mean age and standard deviation (SD) of the participants was (48.6 ± 13.3) years.

Fourteen subjects were assigned to the test group. The mean age and SD were 51.14 ± 11.98 years. Seven of the 14 subjects were female. About 35% of the test group residents in Tikrit city and the rest were from different parts of Salaheddin governorate. Stage II periodontitis was predominant among test group (71.4%), while the rest of the patients were diagnosed with stage III periodontitis.

In the control group, 16 subjects were recruited. The mean age and SD = 46.43 ± 14.63 . 75% of them were male and only 25% were female. Half of them were diagnosed with stage II periodontitis and the other half with stage III periodontitis. (Table 1).

Table 1: General characteristics of study subjects.

Characteristics		Test group	Control group
Age	Mean \pm SD	51.14 \pm 11.99	46.43 \pm 14.63
Gender	male: female ratio	1:1	3:1
Residency	Tikrit city	5	7
	Others	9	9
Stage of periodontitis	II	10	8
	III	4	8

Periodontal health of the recruited subjects

Both the test group and the control group showed high values in the plaque accumulation

and bleeding on probing at baseline. However, BoP was not as high as PLI. After 1- month follow-up, a decrease in mean PLI and BoP was observed only in the test group. Generally, CAL was above 4 mm in both groups. Unfortunately, data for CAL were not collected at follow-up due to the limited time available before starting the hemodialysis, and the difficulty of recording CAL during the hemodialysis. Please refer to Table 2 for further details.

Table 2 Plaque index, Bleeding on probing and clinical attachment loss mean (\pm standard deviation) for the test group and the control group

		Test group mean \pm SD	Control group mean \pm SD	t-test p-value
PLI	Baseline	1.99 \pm 0.32	1.65 \pm 0.42	0.02*
	One month follow up	1.54 \pm 0.39	1.70 \pm 0.40	0.2
	t-test p-value	0.005*	0.47	
BoP	Baseline	12.01 \pm 4.20	12.97 \pm 8.45	0.7
	One month follow up	10.20 \pm 3.40	13.60 \pm 8.64	0.17
	t-test p-value	0.014*	0.53	
CAL	Baseline	5.12 \pm 1.00	4.15 \pm 1.31	0.03*
	One month follow up	n/a	n/a	

* $p < .05$; ** $p < .01$

Comparison of serum markers before and after professional mechanical plaque removal (PMPR) in test group.

Generally, there was no statistically significant difference between baseline and follow-up measurements for almost all the biomarkers in both groups. However, it is worth noting that the baseline urea values in the test group was already higher than in the control group. After one month, the urea level in the test group showed no change, but it increased in the control group. For alkaline phosphatase, the baseline values in the test group were within normal range, while they were higher than

normal compared to the control group. After one month follow-up, the test group showed a stable serum level of alkaline phosphatase compared to the control group, which showed a decrease to normal levels. Please refer to Table 3 for more details.

Analysis of variance was performed to assess the difference between the two groups after adjusting the baseline values for all serum markers. PLI, BoP and stage of periodontitis were taking into account as confounders during analysis. However, no statistically significant difference was found between the two groups.

Table 3 Comparison of serum markers before and after one month of PMPR in test and control groups

		Test mean s ±SD	Contro ls means ±SD	Univa riate analy sis P- value ¹	Univa riate analys is P- value ²
Albumin	Baseline	3.89 ±0.68	3.41 ±0.94	0.94	0.463
	One month after	3.89 ±0.52	3.90 ±0.51		
	Paired t-test P-value	0.971	0.129		
Creatini ne	Baseline	9.55 ±3.16	8.86 ±3.83	0.819	0.133
	One month follow up	9.90 ±2.88	9.47 ±3.30		
	Paired t-test P-value	0.676	0.658		
Alkaline phospha tase	Baseline	120.0 ±50.7 2	162.28 ±89.91	0.50	0.256
	One month follow up	118.2 ±52.3 7	123.63 ±72.64		
	Paired t-test P-value	0.684	0.288		
Total protein	Baseline	6.23 ±1.45	6.56 ±2.15	0.88	0.559

¹ Univariate analysis was conducted to compare the results between the test and the control groups adjusted for baseline readings

² Univariate analysis was conducted to compare the results between the test and control groups adjusted for baseline readings, mean bleeding on probing, mean plaque index, and stage of periodontitis

		Test mean s ±SD	Contro ls means ±SD	Univa riate analy sis P- value ¹	Univa riate analys is P- value ²
Phospho rus	One month follow up	6.72(1.07)	6.60 ±0.87	0.21	0.328
	Paired t-test P-value	0.522	0.940		
	Baseline	7.09 ±2.38	5.90 ±1.67		
Calcium	One month follow up	6.90 ±2.22	5.60 ±1.48	0.45	0.137
	Paired t-test P-value	0.803	0.632		
	Baseline	8.76 ±1.03	8.19 ±1.04		
Urea	One month follow up	8.99 ±1.45	8.42 ±1.45	0.89	0.801
	Paired t-test P-value	0.625	0.685		
	Baseline	175.3 7 ±65.1 3	144.23 ±46.48		
Total protein	One month follow up	179.3 6 ±48.2 0	169.98 ±45.28	0.830	0.091
	Paired t-test P-value	0.830	0.091		

Discussion:

Several studies have described the association between periodontal disease and CKD, especially in hemodialysis patients. In recent years, there has been a general agreement on the high prevalence of periodontal disease in hemodialysis patients compared to their healthy counterparts [31]. This may be due to the uremic osteodystrophy associated with ESKD. Patients with ESKD may suffer from a number of osteopathies, including osteoporosis, osteopenia, and bone resorption. This could be due to abnormal bone deposition and remodeling [32].

This study showed that all recruited patients suffered from periodontitis at different stages. Most of them were at the stage II periodontitis. This is supported by previous studies that

showed an increase in periodontal parameters in patients with CKD [18, 20,21,22, 31].

There was no difference in serum biomarkers between the test group and the control group. These results are consistent with other studies [26,33]. However, some studies are in contrast to these results and showed a positive effect of nonsurgical periodontal treatment on CKD patients and an improvement in prognosis [34]. This study showed no statistically significant increase in albumin levels in the test group after one month of periodontal treatment. Some previous studies reported a decrease in serum albumin levels in CKD patients with chronic periodontitis [35]. Others indicated a significant increase in this biomarker after surgical periodontal treatment [36].

Serum albumin has many important roles in the body, including maintenance of colloidal osmotic pressure, binding and transport of various molecules such as nutrients and drugs, and antithrombotic activity [37,38]. Its normal range is between 3.5 and 5.2 g/dl. It represents one of the prognostic tools in ESKD. Patients with ESKD who have a low serum albumin level may indicate a poor prognosis, because it is associated with poor clinical outcomes, an increase cardiac diseases and mortality [39,40]. Serum creatinine is a commonly used marker to estimate Glomerular filtration rate and renal function. The normal range for serum creatinine is 0.700-1.300 mg/dl. In patients with CKD, serum creatinine is elevated due to decreased renal clearance [41]. In our study, the test group receiving PMPR showed a stable level of creatinine. This may be due to the small sample size of the study and the lack of a long follow-up period. Others showed a significant increase in creatinine level with the severity of periodontitis [42].

Notably, in this study, the clinical signs of gingivitis were not clear, and the gingiva was pale, although plaque deposits were present. Our finding is consistent with a previous study that found that uremia in hemodialysis patients can suppress inflammatory responses in tissues, resulting in signs of gingival inflammation being hidden [43].

Due to the debilitation, poor immune response, and persistent inflammation, hemodialysis patients are more susceptible to infections. Oral infections and inflammations may also be exacerbated [44].

Hemodialysis patients may neglect oral hygiene or overall dental care because they spend long periods of time in the dialysis center. Chronic severe systemic illness as well as low social levels in most cases may lead to non-compliance with dental treatments and neglect of oral care. Therefore, it can be concluded that a high plaque score in this study was due to poor oral hygiene rather than the effects of uremia in hemodialysis patients. The medical staff in the hospital need to be aware of the importance of oral and dental health care and its impact and relationship to the patient's overall health.

One of the major limitations in this study was the short follow-up time. There are other obstacles, including the lack of a systemic computerized archive of patient information and laboratory test results.

Stage II periodontitis was predominant in the test group. In contrast, both stages II and III were evenly distributed in the control group. As a result, augmentation for the results might be seen. It is good to note that the laboratory measurements were standardized for all participants, because they were all performed at a single facility.

Longitudinal studies are needed to determine the extent to which periodontal disease is related to CKD and whether it is a true risk factor for CKD and the extent to which treatment of periodontal disease affects the progression of kidney function over time.

Conclusions

this study showed no effect of the nonsurgical periodontal treatment on the serum biochemistry of patients with renal failure. The small sample size and short period of follow-up have affected the results. Therefore, a large randomized control trial with long period of follow-up is recommended to confirm the results. It is recommended to follow patients at the early

stages of kidney diseases to increase the accuracy of the results and increase the time of monitoring and follow-up of patient's condition.

Conflict of interest

The authors declare that there is no conflict of interest. No fund was received to conduct this study.

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