Clinical Medicine and Health Research Journal (CMHRJ)
Volume 03, Issue 04, July - August, 2023
Page No. 489-494,

Research Article

Effect of Non-Surgical Periodontal Therapy on Renal Function Among Pre-Dialysis Chronic Kidney Disease Patients

Olusoji A. Onabanjo[1], Solomon O. Nwhator[2], Fatiu A. Arogundade[3]

[1]Periodontics Unit, Department of Preventive and Community Dentistry, Obafemi Awolowo University Teaching Hospitals Complex, Ile Ife, Osun State, Nigeria

[2]Periodontology Unit, Department of Preventive and Community Dentistry, Obafemi Awolowo University, Ile Ife, Osun State, Nigeria.

[3]Nephrology Unit, Department of Medicine, Obafemi Awolowo University, Ile Ife, Osun State, Nigeria.

Received: 03 July, 2023 Accepted: 08 August, 2023 Published: 14 August 2023

Abstract:

Background: Association between chronic kidney disease (CKD) and periodontitis has been established. The aim of this study was to determine the effect of non-surgical periodontal therapy (NSPT) on renal function among pre-dialysis CKD patients.

Methods: This is an intervention study involving 120 CKD participants. 60 CKD participants constituted the intervention group while 60 CKD participants constituted the control group. Blood samples were collected from all participants at baseline and after 3 months for the measurement of high sensitivity C-reactive protein (hsCRP), interleukin-6 (IL-6), and serum creatinine for the estimation of glomerular filtration rate (eGFR). Periodontal clinical examination was performed in all participants at six sites per tooth by the researcher for the measurement of Probing Pocket Depth (PPD) and Clinical Attachment Loss (CAL). The intervention group received NSPT (scaling and root planning) and oral hygiene motivation while the control group received only oral hygiene motivation only. Re-evaluation was done after 3 months.

Results: In this study, three months post NSPT, PPD reduced from 5.44mm to 3.17mm ($P < 0.01$) and CAL from 6.29mm to 4.29mm ($P < 0.01$) in the intervention group. There was also a statistically significant reduction in the mean values of hsCRP and IL-6 at 3 months post NSPT in the intervention group ($p<0.01$). However, there was no reduction observed in the control group ($p=0.59$ and 0.66) respectively. Estimated GFR (eGFR) for the intervention group improved from 40.55 mL/min/1.73m^2 to 43.22 mL/min/1.73m^2 three months post NSPT ($P < 0.01$).

Conclusion: This study demonstrates the potential beneficial effects of NSPT on renal function among pre-dialysis CKD participants as estimated by improvement in eGFR.

Keywords: periodontitis; chronic kidney disease; renal function; non-surgical periodontal therapy.

Introduction

Periodontal diseases are a group of conditions that involve certain complex interactions between pathogenic bacteria, the environment and host causing inflammation and destruction to the supporting structures of the teeth [1]. Periodontitis results in pocket formation and progressive loss of alveolar bone around teeth that if left unattended leads to tooth mobility, and eventual tooth loss [2]. Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function, present for ≥ 3 months [3, 4]. Chronic kidney disease has become a public health problem evident by its global prevalence and increasing morbidity and mortality especially in developing countries like Nigeria. The reported prevalence of chronic kidney disease in Nigeria is between 19.9% and 45.5% [5]. The increased prevalence currently among Africans has been attributed to increase in hypertensive heart diseases and diabetes mellitus [6].

Several treatment modalities are in place for the management of CKD including renal transplant but they are very expensive and out of reach of many Nigerians and Africans [7]. The large number of people receiving renal replacement therapy (RRT) and those not having access to it reveal the urgent need to develop low cost treatment modalities and adjunct treatment measures at reducing the impact of CKD worldwide [7]. Some systemic diseases such as Diabetes Mellitus (DM), Chronic Obstructive Pulmonary Disease (COPD), Rheumatoid arthritis, and so on have been associated with periodontitis and the link is systemic hyper-inflammation [8]. Also, periodontal inflammation has been shown to significantly contribute to these systemic hyper-inflammation as revealed by increase in the prevalence and severity of periodontal disease in CKD patients [9, 10] ,[8].

However, non- surgical periodontal therapy (NSPT) has been shown to significantly reduce systemic hyper-inflammation and thus lead to the amelioration of the disease conditions in such patients [8]. CKD, too, has been linked with systemic hyper-

inflammation. Therefore, it is probable that reduction of the hyper-inflammation through NSPT may lead to improvement in renal function in CKD patients. Few studies have evaluated the beneficial effect of non-surgical periodontal therapy on renal function of pre-dialysis CKD patients especially among Africans. Therefore, the aim of this study was to evaluate the effect of non-surgical periodontal on renal function among pre-dialysis CKD patients.

Materials and Methods

The study comprised of consenting, consecutive participants aged 18 years and above recruited from the Nephrology Unit, Department of Medicine, Obafemi Awolowo University Teaching Hospitals Complex, Ile- Ife, Osun State Nigeria for a period of 19 months (June 2019 to December 2020) who had been diagnosed of Chronic Kidney Diseases for at least 3 months and undergoing conservative management (pre-dialysis patients). Those with moderate to severe chronic periodontitis as evidenced by ≥2 interproximal sites with pocket depth ≥5mm (not on same tooth) according to Centers for Disease Control and Prevention in partnership with the American Academy of Periodontology, 2005; modified by Eke and Page, 2012 [11] constituted the intervention group while those without periodontitis with good to fair oral hygiene using the oral hygiene index simplified, 1964 (OHIS) scores constituted the control group. Other inclusion criteria were participants who had never smoked cigarette and those who quitted cigarette smoking more than 5 years, and participants with minimum of 15 teeth. The exclusion criteria include patients who currently smoke or quitted smoking within the last five years, female patients who are pregnant, patients with possible immunosuppression (immunosuppressive drugs, tuberculosis, malnutrition, Acquired Immune Deficiency State, long-term steroid use), patients living with diabetes or with diabetic nephropathy as the cause of CKD, patients who had undergone non-surgical periodontal therapy within the last six months, patients on long term use of anti-inflammatory drugs especially non-steroidal anti-inflammatory drugs, patients with the history of use of antibiotics within the last six months.

The sample size was determined by the formula for sample size estimation for comparing two means which gives the total number of sample size required for the two groups to be 120 participants. The participants were informed about the details of the study before enrolment into the study. The participants were informed that they were free to withdraw from the study without any consequence on their treatment and written informed consent was obtained from each participant. 60 CKD participants with periodontitis constituted the intervention group while 60 CKD participants without periodontitis constituted the control group. Each participant was given an appointment in the Periodontology clinic. On each appointment day, full periodontal examination was carried out in six sites per tooth by the principal investigator who is a periodontologist for the estimation of PPD, CAL, BOP. Oral hygiene index simplified by Greene and Vermillion was used to determine the level of the oral hygiene status of each participant. Blood samples were collected for hsCRP, IL-6, and serum creatinine (for the estimation of GFR) at baseline for both the intervention and control groups and were sent to the Chemical Pathology Laboratory (Point of Care Testing and Metabolic Research Unit) of the institution where sample processing, storage and analysis were done. Blood sample collected in a plain (non-anticoagulated) bottle was allowed to stay for one hour to allow for clot retraction and was centrifuged at 3000 rev/sec for 10 minutes. The resulting supernatant (the serum) was separated into 2mls graduated plain (non-anticoagulated) cryobottle and refrigerated at -80°C for storage.

The participants in the intervention group received non-surgical periodontal therapy consisting of scaling and root planing with local application of doxycycline into the periodontal pocket followed by oral hygiene motivation which was carried out by the principal investigator who is a periodontologist while the control group received only oral hygiene motivation and the two groups were re-evaluated at 3 months. At re-evaluation, blood samples were collected for hsCRP, IL-6, and serum creatinine (for the estimation of GFR) into a plain (non-anticoagulated) bottle and transported within 2 hours of collection to the Chemical Pathology laboratory (Point of Care Testing and Metabolic Research Unit) of the institution where sample processing, storage and analysis were done. The serum hsCRP was analysed according to Accubind ELISA microwells High Sensitivity C-reactive Protein (hsCRP) test kit instruction, the serum IL-6 was analysed according to Elabscience Biotechnology Human IL-6 (Interleukin 6) ELISA test kit instruction while serum creatinine was analysed according to Randox Laboratories Ltd test kit instructions. Participants were also assessed for PPD, CAL, and OHIS for comparison with the baseline values obtained earlier for the two groups (intervention and control groups). The estimation of GFR was done using the Cockcroft-Gault(CG) equation. This was based on the estimating equation that $Ccr = [(140 - age) \times weight/](72 \times Scr) \times 0.85$ (if the subject is female), where Ccr is expressed in milliliters per minute, age in years, weight in kilograms, and serum creatinine (Scr) in milligrams per decilitre. Standardisation of this procedure was achieved by sending all blood specimens to the same diagnostic laboratory as stated above. Data collected was analysed using IBM SPSS Statistics 23.0. Outcome variables such as PPD, CAL, eGFR were analysed using independent *t*-test. Statistical differences of PPD, CAL and eGFR before and after NSPT for intervention and control groups were determined using the paired *t*-test. Regression analysis was also done to adjust for confounders such as age, gender, and socioeconomic status. Statistical significance was set at $P < 0.05$.

Ethics considerations

The Ethics and Research Committee (ERC) of the Obafemi Awolowo University Teaching Hospitals Complex, Ile Ife, Osun State, Nigeria (IRB/IEC/0004553) approved the study.

Results

The age range for the total participants was 19-83 years with their mean age being 45.7 ± 16.63 years. The mean age of the males was 45.97 ± 18.00 years, and 45.44 ± 14.83 years for the

females. A significant variation was noted in the distribution of the participants in the intervention and control group according to their socio-economic classes (Likelihood ratio $\chi 2 = 11.947$, df = 3, P = 0.008) (**Table 1**). Also, a significant variation was noted in the distribution of the study participants in the intervention and control groups according to their educational attainment (Likelihood ratio $\chi 2 = 15.06$, df=6, P = 0.02) (**Table 1**).

Table 1: Socio-demographic characteristics of the participants according to their group

Socio-demographic Characteristic	Intervention n(%)	Control n(%)	Total N(%)	P
Gender				
Male	45(75.0)	23(38.3)	68(56.7)	
Female	15(25.0)	37(61.7)	52(43.3)	
Total	60(100)	60(100)	120(100)	<0.001*
Socio-economic status(SES)				
SES I	0(0.0)	0(0.0)	0(0.0)	
SES II	12(20.0)	3(5.0)	15(12.5)	
SES III	23(38.3)	23(38.3)	46(38.3)	
SES IV	20(33.3)	18(30.0)	38(31.7)	
SES V	5(8.3)	16(26.7)	21(17.5)	
Total	60(100)	60(100)	120(100)	0.008**
Highest Educational Attainment				
Nil	8(13.3)	1(1.7)	9(7.5)	
Primary	8(13.3)	7(11.7)	15(12.5)	
Secondary	13(21.7)	17(28.3)	30(25.0)	
Colleges	3(5.0)	13(21.7)	16(13.3)	
Undergraduate	12(20.0)	10(16.7)	22(18.3)	
HND	1(1.7)	2(3.3)	3(2.5)	
Graduate	15(25.0)	10(16.7)	25(20.8)	
Total	60(100)	60(100)	120(100)	0.02**

**** Likelihood chi square $\chi 2$**

***Pearson chi square $\chi 2$**

The mean scores of the clinical periodontal parameters for the assessment of periodontal status (PPD, CAL) were significantly higher in the intervention group than control (P < 0.01). (**Table 2**). The mean PPD score (mm) was almost three times that of the control. Similarly, the mean CAL score (mm) in the intervention group was three times the mean score in the control group. (**Table 2**). Generally, there was a marked reduction in the mean PPD, CAL scores three months post NSPT in the intervention group. The differences were statistically significant (P < 0.01 respectively) while the reduction in the control group was not (P = 0.26).

Table 2: Comparison of mean Periodontal status at baseline and 3 months in the intervention and control groups

Periodontal Indices	N	Baseline	3 months Post treatment	Mean difference	T	P	95% CI Lower	95% CI Upper
Intervention								
PPD(mm)	60	5.44	3.17	2.27	61.03	<0.01	2.19	2.34
CAL(mm)	60	6.29	4.29	2.00	21.37	<0.01	1.81	2.18
Control								
PPD(mm)	60	2.02	1.99	0.03	1.15	0.26	-0.02	0.08
CAL(mm)	60	2.02	1.99	0.03	1.15	0.26	-0.02	0.08

Paired t-test

There was a statistically significant reduction in the mean values of hsCRP and IL-6 at three months post NSPT in the intervention group (p<0.01). However, there was no reduction observed in the values of the biomarkers in the control group (p=0.59 and 0.66 respectively (**Table 3)**.

Table 3: Comparison of mean Systemic Biomarkers scores at baseline and 3 months in the intervention and control groups.

Biomarkers	N	baseline	3 months Post treatment	Mean diff	t	P	95% CI Lower	Upper
Intervention								
hsCRP(mg/L)	60	3.41	2.03	1.38	8.20	<0.01	1.05	1.72
IL-6(pg/ml)	60	5.51	3.69	1.81	9.71	<0.01	1.44	2.19
Control								
hsCRP(mg/L)	60	2.18	2.13	0.05	0.53	0.59	-0.15	0.25
IL-6(pg/ml)	60	5.69	5.64	0.05	0.44	0.66	-0.16	0.26

Paired t-test

The estimated glomerular filtration rate (eGFR) was used as a marker of renal function and the determinant of the effectiveness of intervention in the participants. Interestingly, participants with good oral hygiene (control group) had significantly higher mean eGFR than those with moderate to severe periodontitis (intervention) at baseline ($P < 0.01$). Also, there was a statistically significant difference in the mean values of eGFR post intervention in both groups ($P < 0.01$) (**Table 4**). However, there was an appreciable improvement in the eGFR for the intervention group three months post NSPT judging by the mean difference observed in both groups (**Table 4**).

Table 4: Comparison of the mean values of renal function at baseline and at three months post intervention

Renal Function	N	Baseline	3 months Post treatment	Mean diff	T	P	95% CI Lower	Upper
Intervention								
Egfr	60	40.55	43.22	-2.67	-8.24	<0.01	-3.31	-2.02
Control								
eGFR	60	62.08	63.15	-1.07	-4.96	<0.01	-1.51	-0.64

Paired *t*-test

To determine the predictors of mean change in the renal function, a generalized linear model regression analysis was performed using the participants' socio demographic characteristics and the study group (intervention or control) as predictors. Only the groups (intervention or control) and the gender were predictors of the mean change in the renal function of the participants. The participants in the intervention group had a significant improvement in their renal function compared to the control group using the mean change in the eGFR as a proxy of renal function ($P < 0.01$) **(Table 5)**. Also, the males showed significant improvement in their renal function compared to the females ($P = 0.02$) **(Table 5)**. The males had worse eGFR at baseline compared to the females. Socio-economic status, smoking status, and alcohol consumption were not predictors of the mean change in the renal function of the participants as shown in the regression model **(Table 5)**.

Table 5: Generalized linear regression of the predictors of the mean change in the renal function 3 months post intervention

Characteristics	B	Std. Error	T	P	95% CI Lower	Upper
Intercept	-4.35	1.025	-4.25	<0.01	-6.38	-2.32
Intervention group	-1.72	0.44	-3.94	<0.01	-2.58	-0.85
Male	0.99	0.43	2.28	0.02	0.13	1.84
social class=2.00]	-0.21	0.75	-0.28	0.78	-1.69	1.27
social class=3.00]	0.37	0.56	0.66	0.51	-0.74	1.47
social class=4.00]	0.77	0.59	1.31	0.19	-0.39	1.93
Never smoked	1.15	0.77	1.49	0.14	-0.38	2.69
Drink alcohol	1.47	0.95	1.55	0.12	-0.41	3.34

*Control group, Social class 5, Quitted smoking after 5 years, never drank alcohol and female gender were used as reference

Discussion

In this study, periodontal status was improved markedly and was statistically significant in the intervention group in comparison with the control group following NSPT. There was a marked reduction in the mean PPD at baseline from 5.44mm to 3.17mm three months post-intervention. Mean CAL also reduced significantly from 6.29mm at baseline to 4.29mm three months post-intervention. Our results showing reduction in periodontal parameters (PPD, CAL) after NSPT are consistent with previous findings [12-16]. In this study, there was a drastic

reduction in the mean PPD and CAL in comparison with the previous studies showing the effectiveness of the NSPT and subsequent significant improvement in the periodontal status in the intervention group.

Subgingival scaling and root planing (SRP) remove embedded calculus, necrotic cementum, and smoothen the root surface. SRP significantly alter the bacterial composition of the pocket reducing the nutritive sources for the proteolytic subgingival bacteria thereby reducing inflammation [14]. This leads to restoration of periodontal health and reduction in pocket depth [15]. NSPT eliminating plaque, calculus, periodontal pathogens or their products and other stimulating factors in the periodontal environment led to reduction in the production and activity of local inflammatory mediators. This control of periodontal infection resulted in improved periodontal status as measured by reduction in the periodontal pocket depth and gain in the clinical attachment loss [17].

This study found a significant reduction in the levels of systemic inflammatory biomarkers (hsCRP and IL-6) following NSPT in the intervention group. This statistically significant reduction in the hsCRP and IL-6 suggests the possible beneficial role of NSPT at reducing the overall inflammatory burden in pre-dialysis CKD patients and subsequent improvement in renal function. The finding in our study was consistent with those of previous studies [13, 15, 16, 18].

The effect of NSPT on renal function was determined in this study using the estimated glomerular filtration rate (eGFR). There was an improvement in the eGFR in both the intervention and control groups with that of the intervention group being significantly higher. This may be explained by the reductions in the clinical parameters of periodontal status in the intervention group; periodontitis being a major contributor to the systemic inflammatory burden in CKD patients. These findings are similar to those of previous studies [18-21]. which reported improvement in the renal function following NSPT. Artese *et al* [19], demonstrated that pre-dialysis CKD patients with periodontitis had a good clinical response from NSPT. There was also an improvement in their renal function as estimated by the GFR. This was also similar to the findings in the present study with improvement in eGFR from 40.55 mL/min/1.73m^2 at baseline to 43.22 mL/min/1.73m^2 at 3 months post NSPT. Almeida *et al* [20], showed that periodontal treatment may be beneficial to the course of CKD as the eGFR of the patients improved 90 days after periodontal treatment. This also corroborated the findings in this present study. Graziani *et al* [22], however, in their own study showed no significant differences in the eGFR between baseline and 90 days after NSPT. A recent systematic review and meta-analyses conducted by Zhao *et al* [13], concluded that there is insufficient evidence on the potential beneficial effect of NSPT on renal function in CKD patients with periodontitis. The review also documented sufficient evidence on the non-directional association between CKD and periodontitis.

The possible beneficial effect of NSPT on renal function as reported in this present study could possibly be explained by the reduction in systemic inflammation; systemic inflammation being the proposed link between CKD and periodontitis [18]. Periodontitis is one of the sources of local and systemic inflammation among CKD patients [23]. Treatment of periodontitis reduces the total inflammatory burden in these patients and subsequently leads to improved renal function [21]. The significant improvement in renal function following NSPT in the participants may also be attributed to the fact that pre-dialysis CKD patients are not yet in severe uraemic state, as observed in dialysis patients [19].

Conclusion

This study showed that there was a statistically significant improvement in the eGFR following NSPT in the intervention group showing the potential beneficial effect of the intervention on renal function.

Conflicts of interests

There is no conflict of interest.

Acknowledgment

Our profound gratitude goes to all the participants of this study.

References

1. Bhansali RS. Non-surgical periodontal therapy: An update on current evidence. World J Stomatol 2014; 3: 38. 2014;51.
2. Opeodu O, Arowojolu M. Effect of social class on the prevalence and severity of periodontal disease. Annals of Ibadan Postgraduate Medicine. 2007;5(1):9-11.
3. Foundation NK. KDIGO 2012 Clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013;3(s1).
4. Levey AS, Coresh J. Chronic kidney disease. The lancet. 2012;379(9811):165-80.
5. Wachukwu CM, Emem-Chioma PC, Wokoma FS et al. Prevalence of risk factors for chronic kidney disease among adults in a university community in southern Nigeria. Pan African Medical Journal. 2015;21(1).
6. Murphy D, McCulloch CE, Lin F et al. Trends in prevalence of chronic kidney disease in the United States. Annals of internal medicine. 2016;165(7):473-81.
7. Liyanage T, Ninomiya T, Jha V et al. Worldwide access to treatment for end-stage kidney disease: a systematic review. The Lancet. 2015;385(9981):1975-82.
8. Hegde R, Awan K. Effects of periodontal disease on systemic health. Disease-a-Month. 2019;65(6):185-92.
9. Tonetti MS, Van Dyke TE, Workshop WGotJEA. Periodontitis and atherosclerotic cardiovascular disease: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. Journal of Clinical Periodontology. 2013;40:S24-S9.
10. Ruospo M, Palmer SC, Craig JC et al. Prevalence and severity of oral disease in adults with chronic kidney disease: a systematic review of observational studies. Nephrology Dialysis Transplantation. 2013;29(2):364-75.

11. Eke PI, Page RC, Wei L et al. Update of the case definitions for population-based surveillance of periodontitis. Journal of periodontology. 2012;83(12):1449-54.
12. Bazyar H, Gholinezhad H, Moradi L et al. The effects of melatonin supplementation in adjunct with non-surgical periodontal therapy on periodontal status, serum melatonin and inflammatory markers in type 2 diabetes mellitus patients with chronic periodontitis: a double-blind, placebo-controlled trial. Inflammopharmacology. 2019;27(1):67-76.
13. Zhao D, Khawaja AT, Jin L et al. Effect of non-surgical periodontal therapy on renal function in chronic kidney disease patients with periodontitis: a systematic review and meta-analysis of interventional studies. Clinical oral investigations. 2020;24(4):1607-18.
14. Javed F, Ahmed HB, Mehmood A et al. Effect of nonsurgical periodontal therapy (with or without oral doxycycline delivery) on glycemic status and clinical periodontal parameters in patients with prediabetes: a short-term longitudinal randomized case–control study. Clinical oral investigations. 2014;18(8):1963-8.
15. Fang F, Wu B, Qu Q et al. The clinical response and systemic effects of non-surgical periodontal therapy in end-stage renal disease patients: a 6-month randomized controlled clinical trial. Journal of clinical periodontology. 2015;42(6):537-46.
16. Tasdemir Z, Tasdemir FÖ, Gürgan C et al. The effect of periodontal disease treatment in patients with continuous ambulatory peritoneal dialysis. International urology and nephrology. 2018;50(8):1519-28.
17. Yue H, Xu X, Liu Q et al. Effects of non-surgical periodontal therapy on systemic inflammation and metabolic markers in patients undergoing haemodialysis and/or peritoneal dialysis: a systematic review and meta-analysis. BMC oral health. 2020;20(1):18.
18. Siribamrungwong M, Yothasamutr K, Puangpanngam K. Periodontal treatment reduces chronic systemic inflammation in peritoneal dialysis patients. Therapeutic apheresis and dialysis. 2014;18(3):305-8.
19. Artese HPC, Sousa COd, Luiz RR et al. Effect of non-surgical periodontal treatment on chronic kidney disease patients. Brazilian oral research. 2010;24(4):449-54.
20. Almeida S, Figueredo C, Lemos C et al. Periodontal treatment in patients with chronic kidney disease: a pilot study. Journal of periodontal research. 2017;52(2):262-7.
21. Siribamrungwong M, Puangpanngam K. Treatment of periodontal diseases reduces chronic systemic inflammation in maintenance hemodialysis patients. Renal failure. 2012;34(2):171-5.
22. Graziani F, Cei S, La Ferla F et al. Effects of non-surgical periodontal therapy on the glomerular filtration rate of the kidney: an exploratory trial. Journal of clinical periodontology. 2010;37(7):638-43.
23. Schöffer C, Oliveira LM, Santi SS et al. C-reactive protein levels are associated with periodontitis and periodontal inflamed surface area in adults with end-stage renal disease. Journal of Periodontology. 2020.