Association of Periodontal Disease and Impaired Renal Function: Evaluation of the National Health and Nutrition Examination Survey (NHANES) 2011-2016

Alireza Hatamifar[1], Apexa Patel[1], Rania Melhem[1] and Thomas Wiedemann[1*]

[1]Oral and Maxillofacial Surgery, New York University College of Dentistry, New York, United States

*Corresponding Author: Thomas G. Wiedemann MD, PhD, DDS, Clinical Associate Professor, Department of Oral and Maxillofacial Surgery, New York University College of Dentistry, New York, United States.

Abstract

Background: There are numerous risk factors associated with the development and progression of periodontal disease such as smoking, poor oral hygiene, and diabetes. Systemic inflammation has been proposed as a possible link between periodontitis and chronic kidney disease (CKD). Although an association of periodontal disease and other systemic conditions has been established in literature, a correlation between periodontal disease and CKD is currently not well-established.

Objective: The aim of this study is to assess whether there is a correlation between periodontal disease and impaired renal function.

Methods: NHANES survey data from years 2011-2016 was used and all analyses were conducted using SAS9.4. Descriptive statistics were conducted for characteristics including age, gender, race/ethnicity, periodontal disease, advanced periodontal disease, and impaired renal function. Logistic regression analysis was conducted to explore the association between periodontal disease and impaired renal function.

Results: The results of this study show that there is an association between increasing age and impaired renal function. Specifically, participants aged 65 years and older had increased odds for impaired renal function with an OR of 3.89. The results of this study also showed increased odds for impaired renal function for participants that were Non-Hispanic Black and Hispanic compared to non-Hispanic white with an odds ratio of 1.62 and 1.45 respectively. Participants who had advanced periodontal disease had increased odds for impaired renal function compared to participants who did not have advanced periodontal disease.

Conclusion: Participants with advanced periodontal disease had increased odds for impaired renal function compared to participants who did not have advanced periodontal disease. Further research is

needed to determine a direct correlation and whether there are positive clinical effects of non-surgical periodontal therapy in improving outcomes in patients with CKD.

Introduction

Periodontitis is an inflammatory condition characterized by specific bacteria that are associated with influencing a host-mediated inflammatory response, resulting in loss of periodontal attachment [1,2]. Chronic Kidney Disease is defined as abnormal kidney structure or function lasting more than three months with various health implications [3]. According to the National Kidney Foundation (NFK), chronic kidney disease (CKD) can be classified into 5 stages [4]. This classification is primarily determined by evidence of renal function as measured by glomerular filtration rate (GFR). However, stages 1 and 2 may include additional clinical parameters such as proteinuria, albuminuria, hematuria, or structural kidney damage [5].

According to the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions, three forms of periodontitis can be identified: Necrotizing Periodontitis, Periodontitis as a manifestation of systemic disease, and Periodontitis (formerly chronic & aggressive) [6,7]. Among other risk factors [2], systemic inflammation has been proposed as a possible link between periodontitis and CKD.

The association of periodontal disease and other systemic conditions mediated by acute or chronic inflammation has also been established in literature [8-11]. In fact, severe periodontitis is associated with increased CRP levels and carotid intima media wall thickness (IMT) in otherwise healthy middle-aged adults [9,10].

Similar findings can also be found with respect to diabetes, where it has been shown that TNF-alpha plays an important role in both obesity and increasing severity of chronic periodontitis [11,12].

A correlation between periodontal disease and CKD is currently not well-established, necessitating a thorough review of the literature to determine if one exists. Given this background, the objective of this study is to assess whether there is an association between periodontal disease and impaired renal function.

Materials and methods

Statistical analysis

For this research study, NHANES survey data from years 2011-2016 was used and all analyses were conducted using SAS 9.4. This study had a sample size of 17,048 US adults, 20 years and older, excluding participants who were younger than 20 years and participants who had missing data on the variables of interest. For all 17,048 survey participants, descriptive statistics were conducted for characteristics including age, gender, race/ethnicity, periodontal disease, advanced periodontal disease, and impaired renal function. Logistic regression analysis was conducted to explore the association between periodontal disease and impaired renal function. Results from the logistic regression analysis were reported as odds ratios and 95% confidence intervals. For this study, a two-sided P value <0.05 was considered statistically significant for the analysis of the regression models.

Results

Characteristics of the Sample Population (Table 1)

Of the total study population, 45.23% participants were age 20-44 years, 35.84% participants were age 45-64 years, and 18.93% participants were 65 years and older. 48.03% survey respondents were male, and 51.97% survey respondents were female. 65.36% participants were Non-Hispanic Whites, 14.76% participants were Hispanics, 11.43% participants were Non-Hispanic Blacks, and 8.45% participants were from another race. Survey respondents who had periodontal disease were 18.63% and who did not have periodontal disease were 62.29%. Survey participants who had advanced periodontal disease were 11.42% and who did not have advanced periodontal disease were 69.42%. Survey participants who had impaired renal function were approximately 3% and Survey participants who did not have impaired renal function were 96.96%.

Survey Characteristics	Frequency-n (%)
Age (years)	
20-44	7349(45.23%)
45-64	5765(35.84%)
≥65	3934(18.93%)
Gender	
Male	8245(48.03%)
Female	8803(51.97%)
Race/ Hispanic Origin	
Hispanic	4156(14.76%)
Non- Hispanic Black	3830(11.43%)
Other (including multiracial)	2686(8.45%)
Non- Hispanic White	6376(65.36%)
Impaired Renal Function	
Yes	626(2.92%)
No	16400(96.96%)
Did not find	22(0.11%)
Periodontal Disease	
Yes	3375(18.63%)
No	10666(62.29%)
Did not find	3007(19.08%)
Advanced Periodontal Disease	
Yes	1987(11.42%)
No	12019(69.42%)
Did not find	3042(19.16%)

Table 1: A General description of the Sample of US Adults 20 years and older, from NHANES 2011-2016 Data.

Regression Analysis from Unadjusted Model (Table 2)

- Age/ Gender: Participants aged 45-64 years old had increased odds for the impaired renal function (oR=1.59, 95% CI=1.07-2.36) compared to participants who were 20-44 years old. Participants aged 65

years and older had increased odds for impaired renal function (oR=3.89, 95% CI=2.81-5.40) compared to participants who were 20-44 years old. Female survey respondents had increased odds (oR=1.31, 95% CI=1.03-1.67) for impaired renal function compared to the male survey respondents.

- Race: Survey participants who were Hispanics had increased odds (oR=1.45, 95% CI=1.15-1.84) for impaired renal function compared to Non-Hispanic Whites. Survey participants who were Non-Hispanic Black had increased odds (oR=1.62, 95% CI=1.21-2.16) for

impaired renal function compared to Non-Hispanic Whites.

- Periodontal Disease: Survey participants with periodontal disease had decreased odds (OR=0.89, 95% CI=0.59-1.32) of impaired renal function versus participants with no periodontal disease. These findings are not statistically significant as the p>0.05 in the tested sample. Participants with advanced periodontal disease had an increased odds (oR=1.43, 95% CI=1.03-1.98) for impaired renal function compared to survey participants who did not have advanced periodontal disease.

Survey Characteristics	Impaired Renal Function Odds Ratio (95% CI)	p-Value
Age (years)		
20-44	Ref	
45-64	1.59 (1.07-2.36)	p<0.001
≥65	3.89 (2.81-5.40)	p<0.001
Gender		
Female	1.31 (1.03-1.67)	p<0.05
Male	Ref	
Race/ Hispanic Origin		
Hispanic	1.45(1.15-1.84)	p<.01
Non- Hispanic Black	1.62(1.21-2.16)	p<.01
Other (including multiracial)	0.94(0.63-1.40)	p>0.05
Non- Hispanic White	Ref	
Periodontal Disease		
Yes	0.89(0.59-1.32)	p>0.05
No	Ref	
Advanced Periodontal Disease		
Yes	1.43(1.03-1.98)	p<.05
No	Ref	

Table 2: Summary of Regression Analysis results from unadjusted model.

Regression Analysis of Adjusted model (Table 3)

When adjusted for age, gender and race, results of the adjusted regression model found that survey participants with

periodontal disease had a slight increased odds for impaired renal function (OR=1.03 95% CI=0.71-1.51). These findings were not statistically significant as p>0.05. Considering participants with advanced periodontal disease, the results showed an

increased odds (oR=1.59, 95% CI=1.17-2.16) for impaired renal function compared to survey participants who did not have advanced periodontal disease. These findings were statistically significant as the p<0.01.

Survey Characteristics	Impaired Renal Function Odds Ratio (95% CI)	p-Value
Periodontal Disease		
Yes	1.03(0.71-1.51)	p>0.05
No	Ref	
Advanced Periodontal Disease		
Yes	1.59(1.17-2.16)	p<.01
No	Ref	

Table 3: Summary of Regression Analysis from the Adjusted Model.

Discussion

This study investigated the association between periodontal disease and impaired renal function in a large nationally representative sample of US adults using SAS9.4. The results of this study show that there is an association between increasing age and impaired renal function. Specifically, participants aged 65 years and older had increased odds for impaired renal function with an OR of 3.89. The results of this study also showed increased odds for impaired renal function for participants that were Non-Hispanic Black and Hispanic compared to non-Hispanic white with an odds ratio of 1.62 and 1.45 respectively. Lastly, this study found that participants who had advanced periodontal disease had increased odds for impaired renal function compared to participants who did not have advanced periodontal disease.

An evaluation of these findings reveal that the results of this study are consistent with existing literature. In a study published in 2016, the association between increasing age and overall renal function has been examined. The results of this study found that normal aging of the kidney is marked by progressive nephrosclerosis, loss of functioning glomeruli, and decreasing overall kidney function as measured by GFR [13]. Furthermore, in a study published by Gupta et al. [14], a higher incidence of impaired renal function was found in Hispanics and Blacks. The contrast was attributed to barriers in access which includes early nephrology consultation and longer wait times associated with dialysis and determining eligibility for a transplant. With advances in genetic testing, other research articles have identified an association between the polymorphisms of the apolipoprotein L1 (APOL1) gene, found on chromosome 22, and the increased incidence of end-stage renal disease in African Americans (AA) [15].

Other clinical studies have found that AAs with the high-risk variants of the APOL1 gene (G1 or G2) had an increased incidence of biopsy- proven focal segmental glomerulosclerosis (FSGS) associated ESKD, hypertensive ESKD, and HIV associated nephropathy when compared to AAs with no copies of the APOL1 allele [16,17].

As for the association between periodontal disease and impaired renal function, the findings of this research support the notion that these disease states are not mutually

exclusive, and that the presence or severity of one often directly impacts the other. More specifically, periodontal disease and CKD are characterized by a chronic inflammatory state, with elevated levels of inflammatory biomarkers such as TNF-alpha, IL-1β, IL-6, and C-reactive protein (CRP) [18,19]. It has been proposed that non-surgical periodontal therapy can be used to effectively reduce the systemic inflammatory response and improve outcomes in patients with both periodontitis and CKD [20,21]. In a recent article by Vachhani et al., researchers found that non-surgical periodontal therapy (NSPT) not only improved periodontal health, but also decreased levels of CRP, improved urine albumin-to-creatinine ratio (UACR) and increased the estimated GFR (eGRR) in CKD patients with periodontal disease [19].

While these results are promising, it should be noted that the findings of are limited to an 80-patient sample, and as a result, cannot be generalized to the entire population. At the present time, there is insignificant evidence to prove a direct association between the positive effects of non-surgical periodontal therapy and patients with CKD [22,19] Further interventional investigations in terms of well-designed clinical trials are needed to determine the clinical effects of non-surgical periodontal therapy on renal function in patients with CKD.

Study limitations

- The use of a logistic regression model, as opposed to a quantile regression, could have led to information loss as it operated under the assumption that each outcome was categorical rather than continuous.
- Participants were excluded due to missing information which may have led to statistical bias.
- The data for this study was analyzed from a cross-sectional survey which limits how these findings can be generalized to the total population.

Conclusions

The objective of this study was to assess whether there is an association between periodontal disease and impaired renal function. The findings of this study suggest that patients with advanced periodontal disease have increased odds for impaired renal function compared to patients who did not have advanced periodontal disease. These findings support the current consensus that both disease states are linked and characterized by a chronic inflammation. That notwithstanding, further research is needed to determine a direct association, and more importantly, the clinical importance of non- surgical periodontal therapy in improving outcomes in patients with CKD.

References

1. Groeger SE, Meyle J. Epithelial Barrier and Oral Bacterial Infection. Periodontology 2000. 2015;69(1):46-67. PubMed | CrossRef
2. Neville B. W., St. Louis. Oral Maxillofac Pathol. 2009.
3. Stevens PE, Levin A, Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group Members. Evaluation and Management of Chronic Kidney Disease: Synopsis of the Kidney Disease: Improving Global Outcomes 2012 Clinical Practice Guideline. Ann Intern Med. 2013;158(11):825-30. PubMed | CrossRef
4. Chronic Kidney Disease: Evaluation, Classification, and Stratification. 2002.

5. Chronic Kidney Disease: National Clinical Guideline for Early Identification and Management in Adults in Primary and Secondary Care. NCCCC. Royal College of Physicians. PubMed | CrossRef

6. Tonetti MS, Greenwell H, Kornman KS. Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. J Periodontol. 2018;89:159-72. PubMed | CrossRef

7. Lertpimonchai A, Rattanasiri S, Vallibhakara SA, Attia J, Thakkinstian A. The Association between Oral Hygiene and Periodontitis: A Systematic Review and Meta-Analysis. Int Dent J. 2017;67(6):332-43. PubMed | CrossRef

8. Hegde R, Awan KH. Effects of periodontal disease on systemic health. Dis Mon. 2019;65(6):185-92. PubMed | CrossRef

9. Ebersole JL, Kryscio RJ, Campbell C, Kinane DF, McDevitt J, Christodoulides N, et.al. Salivary and Serum Adiponectin and C-Reactive Protein Levels in Acute Myocardial Infarction Related to Body Mass Index and Oral Health. J Periodontal Res. 2017;52(3):419-27. PubMed | CrossRef

10. Beck JD, Elter JR, Heiss G, Couper D, Mauriello SM, Offenbacher S. Relationship of Periodontal Disease to Carotid Artery Intima-Media Wall Thickness: The Atherosclerosis Risk in Communities (ARIC) Study. Arterioscler Thromb Vasc Biol. 2001;21(11):1816-22. PubMed | CrossRef

11. Emrich LJ, Shlossman M, Genco RJ. Periodontal Disease in Non-Insulin-Dependent Diabetes Mellitus. J Periodontology. 1991;62(2):123-31. PubMed | CrossRef

12. Hotamisligil GS, Budavari A, Murray D, Spiegelman BM. Reduced Tyrosine Kinase Activity of the Insulin Receptor in Obesity-Diabetes. Central Role of Tumor Necrosis Factor-Alpha. J Clin Invest. 1994;94(4):1543-9. PubMed | CrossRef

13. Denic A, Glassock RJ, Rule AD. Structural and Functional Changes with the Aging Kidney. Adv Chronic Kidney Dis. 2016;23(1):19-28. PubMed | CrossRef

14. Gupta R, Woo K, Jeniann AY. Epidemiology of End-Stage Kidney Disease. Semin Vasc Surg. 2021;34(1):71-78. PubMed | CrossRef

15. Umeukeje EM, Young BA. Genetics and ESKD Disparities in African Americans. Am J Kidney Dis. 2019;74(6):811-21. PubMed | CrossRef

16. Genovese G, Friedman DJ, Ross MD, Lecordier L, Uzureau P, Freedman BI et.al. Association of Trypanolytic Apol1 Variants with Kidney Disease in African Americans. Science. 2010;329(5993):841-5. PubMed | CrossRef

17. Kopp JB, Nelson GW, Sampath K, Johnson RC, Genovese G, An P, et.al. APOL1 Genetic Variants in Focal Segmental Glomerulosclerosis and HIV-Associated Nephropathy. J Am Soc Nephrol. 2011;22(11):2129-37. PubMed | CrossRef

18. Vachhani KS, Bhavsar NV. Effects of Non-Surgical Periodontal Therapy on Serum Inflammatory Factor High-Sensitive C-Reactive Protein, Periodontal Parameters and Renal Biomarkers in Patients with Chronic Periodontitis and Chronic Kidney Disease. Dent Med Probl. 2021;58(4):489-498. PubMed | CrossRef

19. Hao D, Khawaja AT, Jin L, Chan KW, Tonetti M, Tang SCW, 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. Clin Oral Investig. 2020;24(4):1607-1618. PubMed | CrossRef

20. Tavares LT, Saavedra-Silva M, López-Marcos JF, Veiga NJ, Castilho RD, Fernandes GV. Blood and Salivary Inflammatory Biomarkers Profile in Patients with Chronic Kidney Disease and Periodontal Disease: A Systematic Review. Diseases. 2022;10(1):12. PubMed | CrossRef

21. Yue H, Xu X, Liu Q, Li X, Xiao Y, Hu B. 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. PubMed | CrossRef

22. Kapellas K, Singh A, Bertotti M, Nascimento GG, Jamieson LM, Perio-CKD collaboration. Periodontal and Chronic Kidney Disease Association: A Systematic Review and Meta-Analysis. Nephrology. 2019;24(2):202-12. PubMed | CrossRef