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Periodontitis associated with Chronic Kidney Disease among Mexican Americans

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Abstract

Objective—In comparison to non-Hispanic whites, a number of healthcare disparities, including poor oral health, have been identified among Hispanics in general and Mexican-Americans in particular. We hypothesized that Mexican-Americans with Chronic Kidney disease (CKD) would have higher prevalence of chronic periodontitis compared to Mexican Americans with normal kidney function, and that the level of kidney function would be inversely related to the prevalence of periodontal disease.

Method—We examined this hypothesis using the National Health and Nutrition Examination Survey 1988–1994 (NHANES III) dataset. We followed the American Academy of Periodontology (AAP)/Center for Disease Control and Prevention (CDC) case definition for periodontitis. Glomerular filtration rate was estimated using the CKD-Epidemiology (EPI) equation for Hispanic populations. The classification to CKD stages was based on the National Kidney Foundation Kidney Disease Outcomes Quality Initiative.

Results—Periodontitis prevalence increased across the kidney function groups showing a statistically significant dose-response association ($p<0.001$). Mexican Americans with reduced kidney function were 2-fold more likely to have periodontitis compared to Mexican Americans with normal kidney function after adjusting for potential confounders such as smoking, diabetes and socioeconomic status. Multivariate adjusted Odds Ratio for periodontitis significantly increased with 1, 5 and 10 mL/minute eGFR reduction from the mean.

Conclusion—This is the first report, to the best our knowledge, that showed an increase of periodontitis prevalence with decreased kidney function in this population.

Keywords

NHANES; periodontitis; chronic kidney disease; disparities; CKD-EPI; Mexican Americans

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Introduction

Chronic periodontitis is a predominantly Gram-negative infection of the oral cavity that is initiated in the gingiva and, if untreated, leads to alveolar bone destruction and eventual tooth loss (1). Poor oral health outcomes have been observed in racial and ethnic sub-groups (2). Additionally, people with low socioeconomic status (SES) are more likely to have periodontitis compared to people with high SES (3). Mexican-Americans have been shown to have significantly higher rates of periodontitis compared to non-Hispanic Whites (4) but this sub-group has been under-studied and the specific reasons for the higher frequency of periodontitis are not well understood (5).

Recent studies have shown that Hispanics, the fastest growing population in the US (6) have higher prevalence of microalbuminuria compared to non-Hispanic Whites (7). Additional evidence supports higher rates of progression of Chronic Kidney Disease (CKD) to End Stage Renal Disease (ESRD) in Hispanics compared with non-Hispanic whites (8, 9). It is well recognized that diabetes is highly prevalent in Hispanic populations (8, 10). However, genome-wide studies have identified linkage peaks for CKD phenotypes in Mexican-Americans that sustained significance after adjustment for diabetes duration and hypertension (11).

Previously, our group confirmed a black-white disparity in periodontitis prevalence among CKD individuals using the Modification of Diet in Renal Disease (MDRD) Study equation for glomerular filtration rate (eGFR) estimation (12). However, the MDRD equation utilized only two coefficients for race/ethnicity (13) and was not validated for Hispanic populations (14) (15). The recent development and evaluation of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation for GFR estimation in Hispanic populations (16) has offered a more precise tool for CKD diagnosis and classification in this population.

Thus, we hypothesized that Mexican-American patients with reduced kidney function would have higher prevalence of chronic periodontitis compared to Mexican-American individuals with normal kidney function. Hence, we examined this question in a large (n=3686), representative sample of the US population using the National Health and Nutrition Examination Survey 1988 to 1994 (NHANES III).

Material and Methods

Study population

The National Health and Nutrition Examination Survey 1988–1994 (NHANES III), a periodic survey conducted by the National Center of Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC), provides national estimates of the health and nutritional status of the civilian, noninstitutionalized population of the United States aged 2 months or older (17). The NHANES protocols were approved by the NCHS institutional review board and informed consent was obtained from all participants. Individuals participated in interviews conducted at home and in extensive physical examination performed at an examination center that included blood and urine collection. Given that Mexican-Americans represent 92% of the total Hispanic population in NHANES III, we decided to limit our analysis to Mexican-American for population homogeneity. We further limited the study population to: 1) aged 21 years of age and older, 2) dentate, and 3) for whom there were no missing data from the examination and interview data, including serum creatinine values. The study sample included 3686 dentate adults based on these inclusion criteria.

Information on age, sex, race and smoking history was based on self-report during the survey interview. Smoking status was determined using the answers to the questions: “Have you smoked at least 100 cigarettes in your life?” and “Do you smoke cigarettes?” Additionally, diabetes was defined based on the answer to the question: “Have you been told by your doctor that you have diabetes?” Glycated hemoglobin was used as an indicator of diabetes control with a cutoff of 7% (18). Hypertension was determined based on the answer to the question: “Have you ever been told by your doctor or other health professional that you have hypertension or else called high blood pressure?” Dental visit frequency was determined based on the response to the question: “How often do you go to the dentist or dental hygienist?”

Variables for education, health perception and income were constructed based on previously reported cutoff points (19). Body mass index (BMI) was calculated as body weight (km) divided by height squared (m^2).

Periodontitis Case Definition

Each mouth is divided in four quadrants. Full mouth periodontal examination (FMPE) is considered the “gold standard” of periodontal examination and includes periodontal assessment of 6 sites per tooth in all four quadrants. The NHANES III periodontal examination protocol was conducted as a partial mouth periodontal examination (PMPE) assessing 2 sites per tooth in 2 randomly chosen quadrants (half jaws). All third molars (wisdom teeth) were excluded.

For this study, we followed the American Academy of Periodontology (AAP)/CDC case definition for moderate periodontitis and used at least two interproximal sites with clinical attachment loss (CAL)≥4mm or at least two sites with probing depth (PD)≥5mm not on the same tooth (20). This definition was used as the final outcome definition in all analyses.

However, the use of PMPE in NHANES III has been shown to underestimate periodontitis prevalence (21). Therefore, only for the descriptive analysis, an inflation factor was calculated as the inverse function of sensitivity:

$$\text{Inflation factor} = \text{True prevalence (using FMPE)} / \text{Prevalence (using PMPE)}$$

For the adjusted prevalence calculation, we applied the inflation factor of 2.4 (ratio of True Prevalence to Observed Prevalence), which was previously reported for the use of the AAP/CDC definition in NHANES III dataset (22). The adjusted prevalence would more accurately estimate periodontitis prevalence, had participants been subjected to the FMPE.

CKD Definition and Measures of Kidney Function

Based on the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (K/DOQI), the criteria for CKD definition are: 1) kidney damage for 3 months or longer or 2) eGFR less than 60 ml/min/1.73m^2 for 3 months or longer with or without kidney damage (23). The classification to CKD stages was based on K/DOQI guidelines (24). More specifically, CKD stage 1 (kidney damage with normal eGFR), when eGFR≥90ml/min/1.73m^2, CKD stage 2 (kidney damage with mildly decreased eGFR), when eGFR=60–89 ml/min/1.73m^2, CKD stage 3 (moderately decreased eGFR), when eGFR is 30–59 ml/min/1.73m^2, CKD stage 4 (severely decreased eGFR), when eGFR is 15–29 ml/min/1.73m^2 and CKD stage 5 (kidney failure, dialysis), when eGFR<15 ml/min/1.73m^2 (24).

Estimated glomerular filtration rate (eGFR) was calculated based on serum creatinine levels. Serum creatinine (Scr) in NHANES III was calibrated to standardized creatinine with the

equation: 0.184+0.960 × NHANES III uncalibrated serum creatinine (25, 26). EGFR was estimated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation developed for Mexican Americans (16, 27).

The eGFR equation validated for Mexican-Americans is as follows:

$$\mathrm{eGFR} = 141 \times \min(\mathrm{Scr}/k, 1)^{a} \times \max(\mathrm{Scr}/k, 1)^{-1.210} \times 0.993^{\mathrm{age}} \times 1.018\,(\text{if female}) \times 1.01,$$

where k is 0.7 for females and 0.9 for males, a is −0.328 for females and −0.412 for males, min indicates the minimum of Scr/k or 1 and max indicates the maximum of Scr/k.

Estimated GFR is reported in ml/min/1.73m^2. All eGFR values above 200 ml/min/1.73m^2 were truncated at that level (15). The two subjects with eGFR<15 ml/min/1.73m^2 were excluded due to high chances of being on dialysis or being seriously ill with low response rate. We constructed a CKD variable that adhered to the cutoff points of CKD stages previously described (15). However, due to the small sample of the severely reduced GFR population (n=8), we combined moderately and severely reduced eGFR populations in one category.

Statistical Analyses

Analyses were performed using PAWS Version 18 with Complex Sample Module incorporating sampling weights following the NHANES recommended procedures for weights (17, 28). Descriptive statistics for the population characteristics and the prevalence of periodontitis as well as the adjusted prevalence of periodontitis were calculated. The adjusted prevalence of periodontitis was used only in the descriptive analysis and not in the regression models. Categorical variables were tested with the Pearson Chi-Square Test and continuous variables were tested with the t-Test for Independent Samples. In order to assess a possible dose-response association, we performed the Rao-Scott adjusted chi-square statistics with CKD status divided into 3 categories (normal eGFR, mildly reduced eGFR, moderately/severely reduced eGFR) using established criteria (24).

Binary Logistic Regression was performed to calculate crude Odds Ratios (OR) and 95% Confidence Intervals (CI) as an estimate of prevalence ratio for periodontitis among CKD cases. Participants with GFR≥90 ml/min/1.73m^2 constituted the referent group. We performed multivariable logistic regression to examine full and reduced models adjusting for the effects of potential confounders on the association of CKD and periodontitis: Model 1 – age and sex; Model 2 was based on two prior studies (15, 29) - age, sex, diabetes, diabetic control and duration, BMI, smoking, frequency of dental visits and hypertension; and, Model 3 included variables in Model 2 and factors related to socioeconomic status. Covariates were added to the models if they were associated ($p<0.1$) with periodontitis and CKD in this population.

In order to further assess the effect of eGFR decrease on periodontitis prevalence and confirm a possible dose-response association, we designed three fully adjusted regression models (Model A, B and C in Table 3) including all independent variables described above and using eGFR as a continuous/predictor variable. In these models, we calculated the ORs between periodontitis and the decreased mean eGFR by 1 unit in Model A, 5 units in Model B and 10 units in Model C. P-value of < 0.05 was accepted as statistically significant in all analyses.

Results

Descriptive characteristics of the study sample are presented in Table 1. Out of the 3686 subjects, 3163 (91.2%) had normal kidney function, 464 (8.0%) had mildly reduced kidney function and 59 (0.8%) had moderately to severely reduced kidney function. Based on this information, the estimated Mexican American population with normal, mildly reduced and moderately to severely reduced kidney function was 6.5 million, 612,225 and 57,175, respectively. Periodontitis was significantly more prevalent among moderately/severely reduced GFR cases compared to mildly reduced or normal GFR (40.4% vs. 22.6% and 7.9% respectively, $P < 0.0001$). Approximately, 23,117 Mexican Americans with moderately to severely reduced kidney function were estimated to have periodontitis compared to 138,564 with mildly reduced kidney function and 546,234 with normal kidney function. Prevalence of periodontitis increased across the kidney function groups showing a dose-response association between kidney function and periodontitis prevalence that was statistically significant ($p<0.0001$).

Inflation-adjusted periodontitis prevalence among normal, mildly and moderately/severely reduced kidney function cases was 15.8%, 54.2% and 96.9%, respectively.

The univariate logistic regression analysis (Table 2) showed that periodontitis was nearly eight times more prevalent among those with moderately/severely reduced renal function compared to those with normal kidney function (OR=7.94, 95% CI 4.03 to 15.65, $p<0.001$). In multivariate models accounting for age and sex (Model 1), age, sex and covariates used in other studies of the prevalence of periodontal disease (Model 2), and models adding in socioeconomic status (Model 3), the association remained statistically significant but somewhat attenuated. After adjusting for all covariates, individuals with moderately reduced kidney function were 2.6-fold more likely to have periodontitis (Table 2).

Likewise, when compared to their counterparts with normal kidney function (Table 2), the mildly reduced renal function individuals were over 3-fold more likely to have periodontitis (OR=3.42, 95% CI 2.52–4.63) in the univariate analysis. When using the multivariate models 1, 2 and 3, the ORs followed the movement of the moderately/severely reduced kidney function models. In the final model and after adjusting for all confounders, individuals with mildly reduced renal function were almost 1.8-fold more likely to have periodontitis.

When we used eGFR as a continuous/predictor variable in the full regression model, eGFR emerged as a significant predictor for periodontitis in this population. More specifically, for 1 mL/minute reduction of eGFR from the mean, the OR for periodontitis is 1.07, 95% CI 1.03–1.12. For 5 mL/minute reduction from the mean, the OR for periodontitis was 1.16, 95% CI 1.07–1.25 and for 10 reduction, the OR was 1.25 95% CI 1.11–1.41 (Table 3).

Discussion

In a nationally representative sample of Mexican American adults, we found that the prevalence of periodontitis increased with decreasing levels of kidney function. Compared to individuals with normal kidney function, individuals with reduced kidney function had higher prevalence of periodontitis. Furthermore, our analysis demonstrated a statistically significant dose-response effect between stage of kidney dysfunction and periodontitis prevalence. A multivariate logistic regression model showed that Mexican Americans with reduced kidney function were 2-fold more likely to have periodontitis compared to Mexican Americans with normal kidney function after adjusting for potential confounders, particularly diabetes. The latter results were confirmed by a full regression model, which included eGFR as the predictor variable and verified a significant association between

periodontitis and eGFR unit reductions from the mean. This model suggested that the more the eGFR decreased, the higher the odds for periodontitis.

Mexican-Americans are characterized by higher prevalence of CKD as compared with non-Hispanic whites, which has been attributed to higher prevalence of type 2 diabetes, diabetic nephropathy, lower SES and lower acculturation (9). Additionally, periodontitis prevalence studies have confirmed a higher prevalence of periodontitis in this racial group (3). Our current findings further verify the importance of this public health problem by noting a significant dose-response association of decreased kidney function and periodontitis in Mexican-American populations. More specifically, in this study, the moderately to severely reduced kidney function group was characterized by high periodontitis prevalence as well as other confounders such as low SES, high prevalence of poorly controlled longstanding diabetes, hypertension and CVD, which could verify the dose-response and the initial hypothesis.

Several biological mechanisms have been implicated to the increased rates of infections in CKD. There has been a wealth of evidence that disorders of both the innate and adaptive immune systems including functional abnormalities of monocytes, neutrophils and dendritic cells (30, 31) and impaired maturation of T helper (Th) lymphocytes (32) have been linked to uremia. Furthermore, diabetes, one of the main CKD risk factors, has been associated with chronic activation of the innate immune system and has been characterized by increased macrophage activation in the pancreatic islets resulting in elevated levels of circulating cytokines (33). It has been hypothesized that one of the major sequelae stemming from uremia-induced dysregulation of the immune system would be an increase in opportunistic infections, such as chronic infection by *Chlamydia pneumoniae* (34) or chronic periodontitis, a common, polymicrobial and predominantly Gram-negative infection.

Currently, evidence has supported the contribution of periodontal infections to systemic inflammation in the general population (35) as well as in the CKD population (36). Persistent periodontal inflammation usually evidenced by elevated serum cytokine levels is considered to be a non-traditional risk factor for the development of (or incident) cardiovascular disease in patients with CKD (37). In combination with chronic inflammation, inadequate nutritional intake and increased markers of oxidative stress have been strongly linked to malnutrition(38) (39). Poor oral health leading to tooth loss as well as limited masticatory function could directly affect nutritional intake (40) and worsen malnutrition among CKD patients with periodontitis.

Epidemiological evidence based on population studies has shown that periodontitis prevalence has ranged between 5.5–14.7% among CKD subjects (41) (42, 43) without assessing any racial stratification. When examining the prevalence of periodontitis in the ESRD populations, other groups have reported high prevalence ranging between 29–64% (44). Although these were small sample size studies with varied periodontitis case definitions, and unclear confounding factors, they still verified the link between reduced kidney function and oral health (44). Our group has previously shown that the prevalence of periodontitis was significantly higher in subjects with reduced kidney function as compared to individuals with normal kidney function regardless of any racial stratification (41).

Given that reduced kidney function has been the diagnostic marker for CKD, many epidemiological studies have examined the prevalence of periodontitis in individuals with reduced kidney function using a eGFR cutoff of 60ml/min/1.73m^2, which represents the group of moderately to severely reduced kidney function in our analyses. Data from the Dental Atherosclerosis Risk in Communities study has shown that among individual with reduced kidney function, the total periopathogenic bacteria counts were significantly higher

as compared to subjects with normal renal function (45). Additionally, the same group has shown a statistically significant correlation between initial or severe periodontitis and reduced kidney function in the general population (46). Although, there are few methodological differences between the above studies and our study as far as periodontitis definition and cutoff points as well as GFR estimated equation, there was an overall agreement in the final results.

Although our study was the first one to focus on the Mexican-American population with reduced kidney function, we offer several important methodological advancements. First, compared to previous periodontitis prevalence studies (5, 12, 46), we used the CKD-EPI equation for GFR estimation that has been shown to be more accurate than the previous equations in the Mexican American populations (16). In addition, we calibrated creatinine levels as recommended (25) for NHANES III.

Compared to previous studies, (5, 46), we used a more recent periodontitis case definition (20), which has been adopted in official US public health publications on national prevalence of periodontitis (47). Our group has shown previously that the choice of periodontitis case definition could affect associations with kidney function (48). Furthermore, unlike prior studies (5), we limited our analysis to dentate adults since, due to the NHANES data limitations, we were unable to determine the edentulism frequency attributed to periodontitis. Our study also used multivariate regression models that incorporated socioeconomic status variables.

The main limitation of our study was the cross-sectional design that prevented assessing temporality. Another limitation was the use of partial mouth periodontal examination that tends to underestimate disease prevalence, which we attempted to address using an inflation factor-adjusted analysis to better estimate true periodontitis prevalence. Although in our analyses we employed regression models accounting for potential confounding, residual confounding could still be a limitation. For example, incorporating age at diagnosis of diabetes might provide more information about duration of this key exposure. Given that NHANES III survey was conducted in 1988–1994, our findings should be cautiously interpreted with respect to the survey period.

On the basis of this analysis, Mexican-Americans with reduced kidney function are 2-fold more likely to have periodontitis even after adjusting for comorbid factors. This is the first report, to the best our knowledge, that showed an increase of periodontitis prevalence with decreased kidney function in this population. Our findings warrant additional studies to elucidate the underlying mechanisms linking periodontitis with CKD among diverse populations.

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References

1. Offenbacher S, Barros SP, Singer RE, Moss K, Williams RC, Beck JD. Periodontal disease at the biofilm-gingival interface. J Periodontol. 2007 Oct; 78(10):1911–25. [PubMed: 18062113]
2. Sabbah W, Tsakos G, Sheiham A, Watt RG. The effects of income and education on ethnic differences in oral health: a study in US adults. J Epidemiol Community Health. 2009 Jul; 63(7): 516–20. [PubMed: 19254911]

3. Borrell LN, Crawford ND. Social disparities in periodontitis among United States adults 1999–2004. Community Dent Oral Epidemiol. 2008 Oct; 36(5):383–91. [PubMed: 18924254]
4. Borrell LN. Racial identity among Hispanics: implications for health and well-being. Am J Public Health. 2005 Mar; 95(3):379–81. [PubMed: 15727961]
5. Fisher MA, Taylor GW, Shelton BJ, Jamerson KA, Rahman M, Ojo AO, et al. Periodontal disease and other nontraditional risk factors for CKD. Am J Kidney Dis. 2008 Jan; 51(1):45–52. [PubMed: 18155532]
6. Day, J. Population Projections of the United States by Age, Sex, Race and Hispanic Origin: 1995 to 2050. US Bureau of the Census, Current Population Reports; Washington, DC: 1996. p. 25-1130.
7. Lora CM, Daviglus ML, Kusek JW, Porter A, Ricardo AC, Go AS, et al. Chronic kidney disease in United States Hispanics: a growing public health problem. Ethn Dis. 2009 Autumn;19(4):466–72. [PubMed: 20073150]
8. United States Renal Data System: USRDS. 2009 Annual Data Report: Atlas of End-Stage Renal Disease in the United States. National Institute of Health, National Institute of Diabetes and Digestive and Kidney Disease; 2009.
9. Peralta CA, Shlipak MG, Fan D, Ordonez J, Lash JP, Chertow GM, et al. Risks for end-stage renal disease, cardiovascular events, and death in Hispanic versus non-Hispanic white adults with chronic kidney disease. J Am Soc Nephrol. 2006 Oct; 17(10):2892–9. [PubMed: 16959827]
10. Romero LJ, Lindeman RD, Liang HC, Koehler KM, Baumgartner RN, Garry PJ. Prevalence of self-reported illnesses in elderly Hispanic and non-Hispanic Whites in New Mexico. Ethn Dis. 2001 Spring-Summer;11(2):263–72. [PubMed: 11456001]
11. Arar NH, Voruganti VS, Nath SD, Thameem F, Bauer R, Cole SA, et al. A genome-wide search for linkage to chronic kidney disease in a community-based sample: the SAFHS. Nephrol Dial Transplant. 2008 Oct; 23(10):3184–91. [PubMed: 18443212]
12. Ioannidou E, Swede H. Disparities in Periodontitis Prevalence Among Chronic Kidney Disease Patients. J Dent Res. 2011 Mar 21.
13. Levey AS, Coresh J, Greene T, Marsh J, Stevens LA, Kusek JW, et al. Expressing the Modification of Diet in Renal Disease Study equation for estimating glomerular filtration rate with standardized serum creatinine values. Clin Chem. 2007 Apr; 53(4):766–72. [PubMed: 17332152]
14. Stevens LA, Schmid CH, Greene T, Zhang YL, Beck GJ, Froissart M, et al. Comparative performance of the CKD Epidemiology Collaboration (CKD-EPI) and the Modification of Diet in Renal Disease (MDRD) Study equations for estimating GFR levels above 60 mL/min/1.73 m2. Am J Kidney Dis. 2010 Sep; 56(3):486–95. [PubMed: 20557989]
15. Coresh J, Selvin E, Stevens LA, Manzi J, Kusek JW, Eggers P, et al. Prevalence of chronic kidney disease in the United States. Jama. 2007 Nov 7; 298(17):2038–47. [PubMed: 17986697]
16. Stevens LA, Claybon MA, Schmid CH, Chen J, Horio M, Imai E, et al. Evaluation of the Chronic Kidney Disease Epidemiology Collaboration equation for estimating the glomerular filtration rate in multiple ethnicities. Kidney Int. 2011 Mar; 79(5):555–62. [PubMed: 21107446]
17. National Health and Nutrition Examination Survey (NHANES III). (NCHS). CoDCaPCNCfHS. Analytic and reporting guidelines. Hyattsville, MD: p. 1988-94.
18. ADA. Executive summary: standards of medical care in diabetes--2011. Diabetes Care. 2011 Jan; 34(Suppl 1):S4–10. [PubMed: 21193627]
19. Borrell LN, Burt BA, Gillespie BW, Lynch J, Neighbors H. Periodontitis in the United States: beyond black and white. J Public Health Dent. 2002 Spring;62(2):92–101. [PubMed: 11989212]
20. Page RC, Eke PI. Case definitions for use in population-based surveillance of periodontitis. J Periodontol. 2007 Jul; 78(7 Suppl):1387–99. [PubMed: 17608611]
21. Susin C, Kingman A, Albandar JM. Effect of partial recording protocols on estimates of prevalence of periodontal disease. J Periodontol. 2005 Feb; 76(2):262–7. [PubMed: 15974851]
22. Eke PI, Thornton-Evans GO, Wei L, Borgnakke WS, Dye BA. Accuracy of NHANES Periodontal Examination Protocols. J Dent Res. 2010 Sep 21.
23. Levey AS, de Jong PE, Coresh J, El Nahas M, Astor BC, Matsushita K, et al. The definition, classification, and prognosis of chronic kidney disease: a KDIGO Controversies Conference report. Kidney international. 2011 Jul; 80(1):17–28. [PubMed: 21150873]

24. Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Coresh J, Rossert J, et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int. 2005 Jun; 67(6):2089–100. [PubMed: 15882252]
25. Coresh J, Astor BC, McQuillan G, Kusek J, Greene T, Van Lente F, et al. Calibration and random variation of the serum creatinine assay as critical elements of using equations to estimate glomerular filtration rate. Am J Kidney Dis. 2002 May; 39(5):920–9. [PubMed: 11979335]
26. Selvin E, Manzi J, Stevens LA, Van Lente F, Lacher DA, Levey AS, et al. Calibration of serum creatinine in the National Health and Nutrition Examination Surveys (NHANES) 1988–1994, 1999–2004. Am J Kidney Dis. 2007 Dec; 50(6):918–26. [PubMed: 18037092]
27. Levey AS, Stevens LA. Estimating GFR using the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation: more accurate GFR estimates, lower CKD prevalence estimates, and better risk predictions. Am J Kidney Dis. Apr; 55(4):622–7. [PubMed: 20338463]
28. Mohadjer, L.; Montaquila, JM.; Waksberg, J.; Bell, B.; James, P.; Flores-, Cervantes I.; Montes, M. Statistics NCfH. National Health and Nutrition Examination Survey III: Weighting and Estimation methodology. Hyattsville, MD: 1996.
29. Fisher MA, Taylor GW, West BT, McCarthy ET. Bidirectional relationship between chronic kidney and periodontal disease: a study using structural equation modeling. Kidney Int. Oct 6.
30. Anding K, Gross P, Rost JM, Allgaier D, Jacobs E. The influence of uraemia and haemodialysis on neutrophil phagocytosis and antimicrobial killing. Nephrol Dial Transplant. 2003 Oct; 18(10): 2067–73. [PubMed: 13679482]
31. Carracedo J, Merino A, Nogueras S, Carretero D, Berdud I, Ramirez R, et al. Online hemodiafiltration reduces the proinflammatory CD14+CD16+ monocyte-derived dendritic cells: A prospective, crossover study. J Am Soc Nephrol. 2006 Aug; 17(8):2315–21. [PubMed: 16825330]
32. Ando M, Shibuya A, Yasuda M, Azuma N, Tsuchiya K, Akiba T, et al. Impairment of innate cellular response to in vitro stimuli in patients on continuous ambulatory peritoneal dialysis. Nephrol Dial Transplant. 2005 Nov; 20(11):2497–503. [PubMed: 16077138]
33. Donath MY, Boni-Schnetzler M, Ellingsgaard H, Halban PA, Ehses JA. Cytokine production by islets in health and diabetes: cellular origin, regulation and function. Trends Endocrinol Metab. 2010 May; 21(5):261–7. [PubMed: 20096598]
34. Stenvinkel P, Heimburger O, Jogestrand T, Karnell A, Samuelsson A. Does persistent infection with Chlamydia pneumoniae increase the risk of atherosclerosis in chronic renal failure? Kidney Int. 1999 Jun; 55(6):2531–2. [PubMed: 10400517]
35. Ebersole JL, Cappelli D. Acute-phase reactants in infections and inflammatory diseases. Periodontol. 2000 Jun.23:19–49.
36. Ioannidou E, Swede H, Dongari-Bagtzoglou A. Periodontitis Predicts Elevated C-reactive Protein Levels in Chronic Kidney Disease. Journal of dental research. 2011 Dec; 90(12):1411–5. [PubMed: 21940520]
37. Sarnak MJ. Cardiovascular complications in chronic kidney disease. Am J Kidney Dis. 2003 Jun; 41(5 Suppl):11–7. [PubMed: 12776309]
38. Himmelfarb J. Linking oxidative stress and inflammation in kidney disease: which is the chicken and which is the egg? Semin Dial. 2004 Nov-Dec;17(6):449–54. [PubMed: 15660575]
39. Stenvinkel P. Malnutrition and chronic inflammation as risk factors for cardiovascular disease in chronic renal failure. Blood Purif. 2001; 19(2):143–51. [PubMed: 11150801]
40. Budtz-Jorgensen E, Chung JP, Rapin CH. Nutrition and oral health. Best Pract Res Clin Gastroenterol. 2001 Dec; 15(6):885–96. [PubMed: 11866483]
41. Ioannidou E, Swede H. Disparities in Periodontitis Prevalence among Chronic Kidney Disease Patients. Journal of Dental Research. 2011 Jun; 90(6):730–4. [PubMed: 21422478]
42. Fisher MA, Taylor GW, West BT, McCarthy ET. Bidirectional relationship between chronic kidney and periodontal disease: a study using structural equation modeling. Kidney international. 2011 Feb; 79(3):347–55. [PubMed: 20927035]
43. Fisher MA, Taylor GW, Papapanou PN, Rahman M, Debanne SM. Clinical and serologic markers of periodontal infection and chronic kidney disease. J Periodontol. 2008 Sep; 79(9):1670–8. [PubMed: 18771368]

44. Akar H, Akar GC, Carrero JJ, Stenvinkel P, Lindholm B. Systemic consequences of poor oral health in chronic kidney disease patients. Clin J Am Soc Nephrol. 2011 Jan; 6(1):218–26. [PubMed: 21115624]

45. Kshirsagar AV, Offenbacher S, Moss KL, Barros SP, Beck JD. Antibodies to periodontal organisms are associated with decreased kidney function. The Dental Atherosclerosis Risk In Communities study. Blood purification. 2007; 25(1):125–32. [PubMed: 17170550]

46. Kshirsagar AV, Moss KL, Elter JR, Beck JD, Offenbacher S, Falk RJ. Periodontal disease is associated with renal insufficiency in the Atherosclerosis Risk In Communities (ARIC) study. Am J Kidney Dis. 2005 Apr; 45(4):650–7. [PubMed: 15806467]

47. Dye BA, Tan S, Smith V, Lewis BG, Barker LK, Thornton-Evans G, et al. Trends in oral health status: United States, 1988–1994 and 1999–2004. Vital Health Stat. 2007 Apr; 11(248):1–92.

48. Ioannidou E, Shaqman M, Burleson J, Dongari-Bagtzoglou A. Periodontitis case definition affects the association with renal function in kidney transplant recipients. Oral Dis Oct. 16(7):636–42.

Table 1

Clinicopathological characteristics of Mexican-American subjects (n=3686).

	Normal Kidney Function (eGFR≥90) (n=3163) % (SE)	Mildly Reduced Kidney Function (eGFR=60–89) (n=464) % (SE)	Moderately/Severely Reduced Kidney Function (eGFR<60) (n=59) % (SE)	P-Value
Age				
≥ 60 years	4.1 (0.3)	41.8 (2.9)	78.7 (8.2)	0.0001
Sex				
Female	47.4 (1.0)	41.8 (3.0)	41.4 (7.9)	0.125
Periodontitis	7.9 (0.5)	22.6 (2.4)	40.4 (8.1)	0.0001
Inflation-Adjusted Periodontitis Prevalence	18.9	54.2	96.9	0.0001
Dental Visits				
Sporadic or never	67.0 (1.0)	57.3 (3.1)	74.4 (6.9)	0.002
Education				
<12 years	56.0 (1.0)	4.7 (0.3)	0.4 (0.1)	0.001
Perception of Health				
Fair-Poor	29.9 (0.9)	36.6 (2.9)	53.4 (8.3)	0.001
Income				
Low	51.8 (1.1)	50.7 (3.3)	75.9 (7.3)	
Medium	38.4 (1.1)	34.8 (3.2)	21.2 (7.0)	0.027
High	9.8 (0.7)	14.5 (2.7)	2.9 (2.9)	
Diabetes	5.5 (0.4)	12.1 (1.8)	27.4 (0.4)	0.001
Diabetic Duration				
≥10 years	23.2 (3.6)	43.7 (7.9)	83.2 (9.8)	0.001
Diabetic Control				
HbA1c≥7%	4.5 (0.4)	7.6 (1.4)	23.1 (6.0)	0.001
Hypertension	14.1 (0.7)	32.1 (2.8)	58.9 (8.4)	0.001
CVD (%)	0.9 (0.2)	4.8 (1.0)	13.8 (5.3)	0.001
Smoking Status				
Current	23.2 (0.9)	17.5 (2.4)	7.5 (3.8)	
Past	19.0 (0.8)	36.3 (2.9)	43.6 (8.1)	0.001
Never	57.8 (1.0)	46.2 (3.1)	48.9 (8.3)	
BMI				
Low < 18.5	1.1 (0.2)	0.6 (0.3)	0.0 (0.0)	0.005
Normal (18.5–24.9)	34.0 (1.0)	23.2 (2.5)	31.2 (8.3)	

	Normal Kidney Function (eGFR≥90) (n=3163) % (SE)	Mildly Reduced Kidney Function (eGFR=60–89) (n=464) % (SE)	Moderately/Severely Reduced Kidney Function (eGFR<60) (n=59) % (SE)	P-Value
Overweight (25.0–29.9)	38.1 (1.0)	43.9 (3.1)	53.1 (8.3)	
Obese (24.9–30.0)	18.1 (0.8)	23.2 (2.6)	11.4 (5.5)	
Morbidly Obese (≥35)	8.7 (0.6)	9.2 (1.8)	4.3 (2.4)	

Table 2

Logistic regression analysis for the association of periodontitis prevalence (dependent variable) and kidney function in relation to individuals with normal kidney function (GFR≥90) (referent group).

	Crude	Model 1	Model 2	Model 3
Kidney Function Variables	**OR (95% CI)**			
Mildly Reduced Kidney Function (GFR=59–89)	3.42 (2.52–4.63)*	1.67 (1.12–2.48)*	1.92 (1.29–2.86)*	1.75 (1.13–2.71)*
Moderately/Severely Reduced Kidney Function (GFR<60)	7.94 (4.03–15.65)*	2.42 (1.19–5.02)*	2.49 (1.08–5.76)*	2.56 (1.01–6.48)*

Model 1 adjusted for: age and sex. Model 2 adjusted for: age, sex, smoking, diabetic control and duration, BMI, dental visit frequency and hypertension. Model 3 adjusted for: all variables in Model 2 as well as SES variables.

* Indicates statistical significance

Table 3

Logistic regression models (Models A, B, and C) assessing the association of eGFR (mean: 119.23 ml/min/ 1.73m^2) after adjusting for age, gender, smoking, BMI, diabetes duration and control, hypertension, dental visits in the entire population as well as using eGFR changes as predictor variable. Note that the OR for periodontitis increased with decreasing the mean eGFR by 1unit in Model A, 5units in Model B and 10 units in Model C.

Dependent Variable	OR, 95% CI		
	Model A	Model B	Model C
	Mean eGFR-1 mL/min	Mean eGFR-5 mL/min	Mean eGFR-10 mL/min
Periodontitis	1.07 (1.03–1.12)*	1.16 (1.07–1.25)*	1.25 (1.11–1.41)*

*Indicates statistical significance