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The role of physiological markers of health in the association between demographic factors and periodontal disease

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Background and Objective: Age is highly related to oral health status. The higher prevalence of oral disease within subgroups of the population may reflect a tendency towards "early aging" and dysregulation of multiple physiological systems. This study examines whether the association between periodontal disease and demographic factors is mediated by physiological measures of health.

Material and Methods: Logistic regression was used to examine whether biomarkers and demographic factors, such as socio-economic status (SES) and race/ethnicity, were associated with periodontal disease, and then whether the strength of these relationships could be attributed to associations between demographic variables and physiological measures of systemic health.

Results: Periodontal disease was associated with measures of SES and race/ethnicity. Furthermore, 1-unit increases in cytomegalovirus (CMV), optical density, C-reactive protein (CRP) and glycated hemoglobin (HbA1c) were associated with a 25% [odds ratio (OR) = 1.25; 95% confidence interval (CI): 1.14–1.36], 13% (OR = 1.13; 95% CI = 1.03–1.24) and 19% (OR = 1.19; 95% CI = 1.12–1.27) increased likelihood of periodontal disease, respectively. However, when biomarkers and socio-demographic variables were both included in the model, their associations with periodontal disease were significantly reduced or eliminated.

Conclusions: The risk of periodontal disease is higher among black and/or low-income individuals; however, these associations appear to be partly due to the greater probability of elevated levels of CRP, CMV or HbA1c among these groups.

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With the demographic shift toward an aging society, further understanding of the relationships between age-associated changes and oral disease has become an important research topic in public health. The pervasiveness of oral disease has implications for other health conditions, given its association with subsequent stroke, cardiovascular disease, diabetes, osteoporosis and mortality (1–5). In addition, oral disease has been shown to have negative economic, social and psychological impacts, which may ultimately lead to decreases in quality of life and well-being (6, 7).

Age is an important factor in oral health status. Approximately one-third

of noninstitutionalized adults, ≥ 65 years of age, reported edentulism in 1993 and one-third of those with natural teeth had untreated dental cavities (8). The severity and prevalence of periodontal disease has also been shown to increase with age (9). While the prevalence of periodontal disease is only 6% for individuals 25–34 years of age, it is over 40% for individuals ≥ 65 years of age (10). However, age differences are changing as younger cohorts demonstrate a transformation in our ability to prevent or combat a number of oral health problems (11). Nevertheless, while the prevalence of early-life oral health problems has been declining over time, stark differences exist between racial and ethnic subgroups of the population as well as in groups with different socioeconomic status (SES) (12,13).

The association between aging and oral health is complex and multifaceted. Declining oral health status over the life span may be partly attributed to physiological changes resulting from the breakdown of various biological systems and the onset of diseases. For instance, cytomegalovirus (CMV), an indicator of immune-system health and functioning at older ages, is thought to increase the risk for periodontal disease through the release of tissue-destructive cytokines, the initiation of cytotoxic events and an overgrowth of pathogenic periodontal bacteria (14–16). Elevated C-reactive protein (CRP), a marker of systemic inflammation and related to cardiovascular conditions and mortality, has also been shown to increase the risk for development of periodontal disease and oral health (17–23). Blood glucose levels may also be related to periodontal disease. For instance, individuals with diabetes are at increased risk of periodontal disease (24) and the occurrence of severe periodontal disease has been shown to increase blood sugar, thus further exacerbating the negative complications associated with diabetes.

This study aims to examine how the association between demographic predictors of periodontal disease is mediated by also examining biological measures of inflammation, immune function and glucose clearance. We hypothesize that the increased risk of periodontal disease among various racial/ethnic and SES populations may be caused by physiological dysregulation and compromised function of multiple biological systems.

Material and methods

Study population

The study population included adults ≥ 20 years of age from the third National Health and Nutrition Examination Survey (NHANES III), a nationally representative, cross-sectional study conducted by the National Center for Health Statistics (25) between 1988 and 1994. NHANES III was based on a complex, multistage, stratified, clustered sample design of the civilian, noninstitutionalized population. Individuals > 60 years of age, African Americans, Mexican Americans and low-income white Americans were oversampled to ensure appropriate sample sizes for analysis. Data for NHANES III were collected during at-home interviews, and dentist and physician examinations were performed in a mobile examination center. Further details on recruitment, procedures and study design are available from the Centers for Disease Control and Prevention (25). The total sample size for the adult population in NHANES III who were examined in the mobile examination center was 16,573, of whom 11,295 had surplus sera available and were included in our analysis.

Periodontal disease

Periodontal disease was operationalized using the definition developed by the Centers for Disease Control and Prevention Periodontal Disease Surveillance Workgroup (26). Respondents with severe (≥ 2 interproximal sites with loss of attachment of ≥ 6 mm and ≥ 1 interproximal sites with a pocket depth of ≥ 5 mm) or moderate (≥ 2 interproximal sites with loss of attachment of ≥ 4 mm or ≥ 2 interproximal sites with a pocket depth of ≥ 5 mm) periodontitis were classified as having periodontal disease in our analysis. Reported loss-of-attachment values were based on two measurements taken at each site: the distance between the cemento–enamel junction and the free gingival margin; and the distance from the bottom of the sulcus (pocket depth) to the free gingival margin. Diagnostic criteria were intentionally conservative to ensure inter-rater reliability. When a classification of periodontal disease was not agreed upon, the classification of milder disease was selected (25).

Physiological mechanisms

In order to examine links between oral health and physiological mechanisms, the levels of three indicators of physiological status – CRP, glycated hemoglobin (HbA1c) and CMV – were included in the analysis. Serum CRP was used as a nonspecific indicator of general levels of inflammation. For NHANES III, high-sensitivity CRP assays were performed on blood samples using a Behring Nephelometer (24). HbA1c, which is often used to screen for and measure control of diabetes, was measured using a Diamat Analyzer System. CMV antibody testing was performed on stored sera specimens from NHANES III, and IgG optical density values were reported. CMV optical density was top-coded at 3.01 by NHANES III.

Sociodemographic characteristics

Age, race/ethnicity, income and sex were self-reported and were included as independent predictors of oral health status. Age was top-coded at 90 in the data set of NHANES III to protect the confidentiality of the respondents. Dummy variables were created to classify the subjects into three race/ethnicity categories: non-Hispanic white people; non-Hispanic black people; and Hispanic people, most of whom were Mexican Americans. In the analyses, non-Hispanic white people were used as the reference category. SES was indicated by the poverty income ratio (PIR). The PIR

is calculated as the ratio of the midpoint of a subject's reported annual family income category to the current federal poverty threshold for a family of the reported size and composition (Bureau of the Census, US Department of Commerce). It is categorized into four categories: below poverty (PIR < 1); low income (PIR = 1–1.99); normal income (PIR $\geq$ 2); and unknown income. The last category includes those who did not disclose their annual family income and was included in order to avoid a sample selection effect resulting from eliminating those who did not report income. Lastly, sex was indicated with a dichotomous variable, with female subjects coded as 1 and male subjects coded as 0.

Statistical analysis

SAS statistical software package version 9.2 (SAS Institute Inc., Cary, NC, USA) was used for all analyses. Three logistic-regression models were used to examine whether demographic factors, including SES and race/ethnicity (Model 1), and biomarkers (Model 2) were associated with periodontal disease, and whether the power of such relationships could be attributed to associations between demographic variables and physiological measures of systemic health (Model 3). All analyses controlled for age and sex, and utilized sample weights to make the results representative of the US noninstitutionalized population and SAS survey procedures to account for the complex sampling procedures in NHANES III.

Results

Sample description

Just over half of the sample was female (51.2%) (Table 1). Most subjects were non-Hispanic white (79.1%); non-Hispanic black subjects made up 10.8% of the sample and Mexican American subjects made up 10.1%. Approximately two-thirds of the sample (64.4%) had an annual family income that was at least two times the poverty level, while 18.9% were just above the poverty level (PIR = 1–1.99) and 11% were below the poverty level. The age of subjects ranged from 20 to 90 years, with a mean of 42 years. Periodontal disease was present in 10.1% of subjects. The mean CRP level for the sample was 3.9 mg/L (standard deviation = 0.8); the mean CMV optical density was 1.7 (standard deviation = 1.6); and the mean HbA1c was 5.3% (standard deviation = 1.2).

Table 1. Weighted sample characteristics for subjects

Characteristics	
Age (years)	42.0 ± 21.9
Sex (female)	51.2
Race/ethnicity	
Non-Hispanic white	79.1
Non-Hispanic black	10.8
Mexican American	10.1
PIR	
Below poverty (PIR < 1)	11.0
Low income (PIR = 1–1.99)	18.9
Adequate income (PIR $\geq$ 2)	64.5
Nonresponse	5.6
Has periodontal disease	10.1
CRP	3.9 ± 0.8
CMV OD	1.7 ± 1.6
HbA1c (%)	5.3 ± 1.2

Values are given as mean ± standard deviation or per cent.CMV OD, cytomegalovirus optical density; CRP, C-reactive protein (mg/L); HbA1c, glycated hemoglobin; PIR, poverty income ratio.

As shown in Table 2, periodontal disease, and the levels of CRP, CMV and HbA1c, were highest in non-Hispanic black subjects followed by Hispanic subjects and non-Hispanic white subjects. Mean comparisons using a Bonferroni adjustment revealed that, for CRP and HbA1c, all three race/ethnicity groups had significantly different means. Non-Hispanic white subjects had a significantly lower mean CMV optical density value than did Hispanic subjects and non-Hispanic black subjects. However, the means for the two minority groups did not differ significantly from each other.

Those below the poverty level had the highest CMV optical density value and the highest level of periodontal disease, while those who did not disclose their income had the highest levels of CRP and HbA1c. (Table 3). Subjects with incomes at least twice the poverty limit had a significantly lower mean CRP level and CMV optical density value than did those with lower incomes or who did not disclose income. Subjects in the highest income group also had a significantly lower HbA1c level than both the groups with income below the poverty limit and those with unknown income. Subjects with no PIR score also had a significantly higher HbA1c level than did subjects with a PIR of 1–1.99; however, the values in neither of those groups differed significantly from those of subjects below the poverty level.

Associations among periodontal disease, demographic characteristics and biomarkers

Table 4 illustrates the results from the three logistic regression models. In Model 1, increased age, being male, being non-Hispanic black or having a household income that was either low or below poverty, was linked to a significantly increased likelihood of having periodontal disease. For every 10-year increase in age, subjects were 60% more likely to have periodontal disease [odds ratio (OR) = 1.06; 95% confidence interval (CI): 1.06–1.07], while being female decreased the

Table 2. Biomarkers and frequency of periodontal disease by race/ethnicity

Race/ethnicity	CRP(mg/L)	CMV OD	HbA1c(%)	Periodontal disease(%)
Non-Hispanic white	3.7	1.53	5.26	9.46
Non-Hispanic black	4.8	2.19	5.58	15.03
Hispanic	4.1	2.15	5.42	9.57

CMV OD, cytomegalovirus optical density; CRP, C-reactive protein; HbA1c, glycated hemoglobin.

Table 3. Biomarker means and frequency of periodontal disease by poverty income ratio (pir)

PIR	CRP(mg/L)	CMV OD	HbA1c(%)	Periodontal disease(%)
Below poverty	4.5	1.92	5.40	15.17
Low income	4.3	1.85	5.33	12.06
Income two or more times poverty	3.6	1.55	5.28	8.33
Unknown income	4.9	1.88	5.44	13.35

CMV OD, cytomegalovirus optical density; CRP, C-reactive protein; HbA1c, glycated hemoglobin.

likelihood of periodontal disease by 54% (OR = 0.46; 95% CI: 0.39–0.56). Non-Hispanic black subjects were 87% more likely than non-Hispanic white subjects to have periodontal disease (OR = 1.87; 95% CI: 1.52–2.31). Relative to individuals with higher income, low-income individuals (PIR = 1–1.99) were 65% more likely to have periodontal disease (OR = 1.65; 95% CI: 1.34–2.03), and those below the poverty level were over two and a half times as likely to have periodontal disease (OR = 2.74; 95% CI: 2.16–3.47).

In Model 2, having a higher CRP level, a higher CMV optical density value and a higher HbA1c level were significantly related to the likelihood of having periodontal disease. One-unit increases in the CMV optical density value and in CRP and HbA1c levels were associated with an increased likelihood of periodontal disease of 25% (OR = 1.25; 95% CI: 1.14–1.36), 13% (OR = 1.13; 95% CI: 1.03–1.24) and 19% (OR = 1.19; 95% CI: 1.12–1.27), respectively. The effects of age and gender were only slightly lower than the values in Model 1 with the introduction of the biological markers.

When all predictor variables were included in the model, the size of the associations between periodontal disease and race/ethnicity, CRP, CMV optical density and HbA1c were reduced (Model 3). The association between periodontal disease and being non-Hispanic black was decreased by 23.6%, while the association between periodontal disease and being below the poverty level was reduced by 10%. The association between CRP and periodontal disease decreased by 31.9% and was no longer significant. Additionally, although they remained significant, the power of CMV optical density and HbA1c to predict periodontal disease decreased by 27.9 and 19.4%, respectively.

Discussion

Our findings suggest that the risk of periodontal disease is increased in individuals who are non-Hispanic black or of low SES; however, these associations are caused partly by the propensity of elevated levels of CRP, CMV optical density, and HbA1c to be more common among these subgroups. Given the differences in the onset and prevalence of comorbid diseases and exposures among individuals with varying sociodemographic characteristics, differences in oral health problems, such as periodontal disease, may be reflective of a multitude of complex health changes.

The simultaneous presence of periodontal disease and other adverse health conditions, such as diabetes, impaired immune response and systemic inflammation, are thought to be the result of underlying physiological mechanisms, which are more adverse among racial minorities and those with a low SES (27–29). In addition to oral health problems, many chronic conditions, such as hypertension, diabetes and stroke, are significantly higher among black subjects (30). Furthermore, individuals with lower income and lower education, and those who are black, have been found to have an earlier age at onset of biological risk factors, diseases and mortality (30–32). The increased prevalence of oral disease within particular segments of the population may also be reflective of a tendency towards "earlier aging" within disadvantaged segments of the population (33).

The racial disparities in health may reflect multifactorial biological, as well as environmental, mechanisms.

Table 4. Regression of periodontal disease on socio-economic, demographic and health indicators: odds ratios and 95% confidence interval (95% CI)

	Model 1		Model 2		Model 3	
	β Coefficient (SE)	Odds ratio (95% CI)	β Coefficient (SE)	Odds ratio (95% CI)	β Coefficient (SE)	Odds ratio (95% CI)
Below poverty	1.01 (0.121)	2.74 (2.16–3.47)			0.947 (0.122)	2.58 (2.03–3.28)
Low income	0.500 (0.106)	1.65 (1.34–2.03)			0.450 (0.105)	1.57 (1.28–1.93)
Unknown income	0.323 (0.1935)	1.38 (0.95–2.02)			0.299 (0.197)	1.35 (0.92–1.98)
Black	0.628 (0.106)	1.87 (1.52–2.31)			0.480 (0.107)	1.62 (1.31–1.99)
Hispanic	0.072 (0.164)	1.08 (0.78–1.48)			−0.041 (0.171)	0.96 (0.69–1.34)
Age	0.060 (0.003)	1.06 (1.06–1.07)	0.050 (0.003)	1.05 (1.05–1.06)	0.054 (0.003)	1.06 (1.05–1.06)
Sex (female)	−0.772 (0.093)	0.46 (0.39–0.56)	−0.758 (0.098)	0.47 (0.39–0.57)	−0.816 (0.097)	0.44 (0.37–0.53)
CRP			0.119 (0.047)	1.13 (1.03–1.24)	0.081 (0.049)	1.08 (0.99–1.19)
HbA1c			0.175 (0.033)	1.19 (1.12–1.27)	0.141 (0.034)	1.15 (1.08–1.23)
CMV OD			0.222 (0.045)	1.25 (1.14–1.36)	0.160 (0.049)	1.17 (1.07–1.29)

CMV OD, cytomegalovirus optical density; CRP, C-reactive protein; HbA1c, glycated hemoglobin; SE, standard error.

These disparities have implications for the functioning of various physiological systems that affect inflammation, immunity and insulin regulation (34–36). While we have emphasized the links between race and income and biological factors in this paper, differential access and utilization of healthcare and dental care may account for the disparities in both oral and overall health among racial/ethnic and SES subpopulations.

There are limitations in the present study that should be acknowledged. First, the use of cross-sectional data hindered our ability to test for the temporality of our associations. Second, the data from NHANES III was collected between 1988 and 1994 and may not reflect current conditions. However, more recent nationally representative data that incorporate the biomarker measures used in the present study are not available. Despite these limitations, the present study is strengthened by the use of reliable techniques for measuring oral health and physiological markers, and inclusion of a large representative random sample.

The current study demonstrated that differences in physiological health are important factors to consider when examining the associations between oral health and SES or race/ethnicity. Furthermore, Black people and individuals below the poverty level were found to have a significantly higher prevalence of periodontal disease, reaching 15%, as well as poorer overall biological health markers. Given that increased prevalence of many chronic conditions, including periodontal disease, may reflect a tendency towards early aging, more research is needed to uncover the physiological and environmental mechanisms linking differences in multiple co-morbid conditions in disadvantaged populations.

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