Periodontitis and Prevalence of Elevated Aminotransferases in the Hispanic Community Health Study/Study of Latinos

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Abstract

Objective—NAFLD prevalence is greater among Hispanics/Latinos than other racial/ethnic groups and is reported to vary among Hispanic/Latino groups. Experimental animal and human studies demonstrate associations between periodontitis and non-alcoholic fatty liver disease (NAFLD), not yet reported among Hispanics/Latinos. This study examined periodontitis as a novel risk factor that may contribute to the burden of NAFLD among Hispanics/Latinos.

Methods—Data came from 11,914 participants of the Hispanic Community Health Study/Study of Latinos. Periodontitis was defined as the extent (none, <30%, ≥30%) of periodontal sites with clinical attachment level (CAL) of ≥3mm or probing pocket depth (PD) of ≥4mm. Elevated serum

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transaminases indicative of suspected NAFLD were defined as having alanine aminotransferase levels (ALT) >40 IU/L or aspartate aminotransferase (AST) >37 IU/L for men and ALT >31 IU/L or AST >31 IU/L for women. Survey-logistic regression models estimated prevalence odds ratios (POR) and 95% confidence intervals (CI) of the association between periodontitis and suspected NAFLD.

Results—The overall age standardized percentage of study participants with <30% of sites with CAL ⩾3mm or PD ⩾4mm was 53.5% and 58.6% respectively, while those with ⩾30% sites with CAL ⩾3mm or PD ⩾4mm comprise 16% and 5.72% respectively. The overall age-standardized prevalence (95% CI) of suspected NAFLD was 18.1% (17.1%–19.0%). Within the entire cohort, we observed a dose-response association between PD ⩾4mm and the prevalence odds of suspected NAFLD, whereby participants with <30% affected had a crude POR =1.19 (95% CI: 1.03, 1.38) while those with ⩾30% affected had a crude POR =1.39 (95% CI: 1.02, 1.90). These crude estimates were attenuated towards the null and rendered non-significant upon covariate adjustment. No differences were found by Hispanic/Latino background group.

Conclusion—Previously reported associations between periodontitis and NAFLD were marginal to null in this study of a diverse group of Hispanics/Latinos.

Introduction

Non-alcoholic fatty liver disease (NAFLD) is the most common type of liver disease and the hepatic component of the metabolic syndrome.[1, 2] Estimated to affect 17–33% of U.S. adults,[1–4] NAFLD is associated with higher healthcare costs and mortality.[1, 5, 6] Insulin resistance and obesity, both characterized by chronic low-grade systemic inflammation[1, 7, 8] are identified as NAFLD risk factors. Indeed, epidemiologic studies have reported associations between pro-inflammatory cytokines and components of the metabolic syndrome[9] including NAFLD.[10, 11] Thus, chronic health conditions that elicit systemic inflammatory response potentially represent unrecognized but potentially modifiable factors in the etiology of NAFLD. Specific to the Hispanic/Latino population, NAFLD prevalence is reported to be greater compared to estimates reported for non-Hispanic Whites and African-Americans.[12, 13] Furthermore, there is heterogeneity in reported NAFLD prevalence among Hispanics/Latinos, and risk factors such as genetics, lifestyle and environment as well acculturation do not completely account for the burden of disease in this population.[12, 13] Therefore, it is important to identify novel modifiable risk factors for NAFLD.

Periodontitis, a major cause of tooth loss[14, 15] is a chronic inflammatory disease of the oral cavity, involving the gingiva, connective tissue and alveolar bone supporting the teeth. Affecting about 45% of the adult U.S. population,[16, 17] periodontitis has been shown in rat models to be causally related to[18, 19] and in epidemiologic studies to be associated[20–24] with insulin resistance. Periodontitis has also been linked to low-grade systemic inflammation in experimental animal[25, 26] and epidemiologic[20, 27–30] studies. Recently, periodontitis was linked to NAFLD in both mice models[31, 32] and human studies,[31, 33] but the relationship has

not been investigated in an ethnically diverse population group. Because NAFLD disproportionately affects Hispanics/Latinos and previous studies on the association between periodontitis and NAFLD have mostly focused on Caucasians[33] and Asians,[31] the objective of this study was to examine associations between periodontitis and indicators of NAFLD in a diverse group of Hispanic/Latino men and women who participated in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL).

Materials and Methods

Study population

The HCHS/SOL is a multicenter community based cohort study of 16,415 self-identified Hispanic/Latino men and women, designed to investigate risk and protective factors for chronic health conditions. Eligible 18–74-year-olds of Cuban, Dominican, Mexican, Puerto Rican, Central and South-American background were recruited between March 2008 and June 2011 from randomly selected households in 4 U.S. communities (Bronx, New York; Chicago, Illinois; Miami, Florida; and San Diego, California) using a stratified two-stage area probability sampling.[34, 35] Oversampling of 45–74-year olds was conducted, and sampling weights were calculated to reflect this disproportionate sampling. At baseline, study participants completed interviewer-administered questionnaires, underwent clinical assessments including dental examination, and a sample of whole blood was collected for laboratory analysis.[34–36] Institutional Review Boards of all participating institutions approved the study and all participants gave informed consent.

This study was restricted to participants who completed dental examinations with serum transaminase measurements, who did not have detectable serum levels of hepatitis B surface antigen or hepatitis C antibody. Furthermore, restricted to participants who did not report excessive alcohol consumption (consuming >70 g of ethanol/week for women and >140 g/week for men), and had transferrin saturation levels of 50%.

Exposure of interest

Study participants not requiring antibiotic prophylaxis received a full-mouth periodontal examination following a standardized protocol. Measurements of probing pocket depth (PD) and gingival recession were recorded on 6 sites (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, disto-lingual, and lingual) per tooth except third molars. PD is the distance from the free gingival margin to the bottom of the sulcus while gingival recession is the distance from the cementoenamel junction to the free gingival margin. Clinical attachment level (CAL) was calculated as sum of PD and gingival recession. Examiners were recalibrated annually to a gold standard examiner, with very good to excellent agreement.[37] This investigation defined periodontitis as the proportion of periodontal sites (none, <30%, 30%) affected by CAL 3mm or PD 4mm.[38] Because this definition takes into consideration measurements made at all periodontal sites, it permits comparison to previous prevalence studies and is preferred to alternative classification systems that only uses the "worst score".[38]

Outcome of interest

Elevated serum transaminase levels indicative of suspected NAFLD were defined as having alanine aminotransferase (ALT) >40 IU/L or aspartate aminotransferase (AST) >37 IU/L for men and ALT >31 IU/L or AST >31 IU/L for women.[39]

The presence of NAFLD was also assessed with the fatty liver index (FLI),[40] an algorithm based on BMI, waist circumference, triglycerides and gamma glutamyl-transferase levels (GGT) to indicate the likelihood of having NAFLD. This index based on the equation below is reported to be 84% accurate and a FLI score of 60% indicates a high likelihood of NAFLD.[40]

$$FLI = 100 *$$

$$(\frac{e^{(0.953 * \log_e (\text{triglycerides}) + 0.139 * \text{BMI} + 0.718 * \log_e (\text{ggt}) + 0.053 * \text{waist circumference} - 15.745)}}{1 + e^{(0.953 * \log_e (\text{triglycerides}) + 0.139 * \text{BMI} + 0.718 * \log_e (\text{ggt}) + 0.053 * \text{waist circumference} - 15.745)}})$$

Study participants with a FLI score 60%[40] were classified as having a high likelihood of NAFLD.

Covariates

Age and gender were self-reported. Waist circumference measured in centimeters (cm) was dichotomized as >88 cm for women and >102 cm for men indicating the presence of abdominal obesity as part of the National Cholesterol Education Program, Adult Treatment Panel (NCEP ATP) III definition of the metabolic syndrome. Smoking was categorized into non-smoker, former and current smokers based on current and previous use of at least 100 cigarettes in a lifetime. Diabetes status was based on the American Diabetes Association definition,[41] namely participants with normal and impaired fasting glucose or impaired glucose tolerance (fasting glucose between 100–125 mg/dl or post oral glucose tolerance test (OGTT) between 140–199 mg/dl or HbA1C between 5.7 and <6.5%) were categorized as not having diabetes. Acculturation was evaluated using the six-item language subscale of the Short Acculturation Scale for Hispanics that characterizes language on a 5-point Likert scale.[42] The scale is interpreted as 1 -Spanish only speakers, 2-speaks Spanish better than English, 3- speaks Spanish and English equally, 4- speaks English better than Spanish, and 5- English only speaker.[42, 43] Physical activity (PA) was calculated as the average of the total amount of time per week engaged in work or recreational physical activity and the total metabolic energy expenditure based on the Global Physical Activity Questionnaire.[44] This variable was categorized into high [(vigorous work and recreational PA 3 days and total metabolic expenditure (MET) 1,500) or (moderate and vigorous PA 7 days and MET 3,000)], moderate [(vigorous work and recreational PA 3 days and total vigorous activity level of 60 minutes for 7 days or moderate work, transportation and recreational PA for 5 days and total moderate activity level of 150 minutes for 7 days or moderate and vigorous PA level for 5 days and total activity level of 600 minutes for 7 days)] and low physical activity level for those not meeting the criteria for high and moderate PA. Educational attainment was categorized as: <high school, high school, or >high school.

Statistical analysis

Of the 16,415 HCHS/SOL participants, 11,914 were eligible for this study. Reasons for exclusions include: excessive alcohol consumption (n=828), missing ALT/AST (n=169), hepatitis B surface antigen and hepatitis C antibody in blood samples (n=356), transferrin saturation >50% (n=690), no dental examination and/or edentulous (n=1,275) and report of 'other' as Hispanic/Latino background (n=503). Also excluded were participants with missing data on the following covariates: diabetes (n=21), alcohol use (n=65), education (n=91), acculturation score (n=102), physical activity (n=140), smoking (n=93), and waist circumference (n=74).

Weighted proportions and standard errors (SE) for the study population characteristics were estimated for all groups combined and according to Hispanic/Latino background. In addition, the distributions of study population characteristics age-standardized to the 2010 US census age distribution[45] were estimated for periodontitis (CAL 3mm and PD 4mm) and suspected NAFLD using weighted least squares survey regression. Design-adjusted Wald chi-square tests assessed the associations of categorical variables with periodontitis (CAL 3mm and PD 4mm) and suspected NAFLD. Potential effect measure modification (EMM) of the association between periodontitis and suspected NAFLD was assessed using design-adjusted Wald chi-square tests comparing models with and without product interaction terms between periodontitis and Hispanic/Latino background, and between periodontitis and gender. Threshold for statistically significant interaction was set at p <0.10. Separate survey logistic regression models for suspected NAFLD based serum transaminases (AST and ALT) thresholds and the FLI 60% were used to estimate prevalence odds ratios (POR) and 95% confidence intervals (CI). The first model was stratified by Hispanic/Latino background but did not include other covariates. Subsequent stratified models sequentially adjusted for age and gender and then for NAFLD risk factors (i.e., abdominal obesity, diabetes), smoking, physical activity, educational attainment and acculturation score. Statistical tests were 2-sided and significance was set at p <0.05. Statistical tests and data analysis were conducted in SAS v. 9.4 (SAS Institute Cary, NC) accounting for the complex sampling design and applying weights to account for the unequal sampling probabilities.

Results

The overall mean age (SE) was 40.4 (0.26) years and was greater for Cuban background participants [mean (SE)=44.9 (0.61) years] than for any other Hispanic/Latino background groups. The mean acculturation score was highest for Puerto Rican background group (mean=3.15) in comparison to all groups combined (mean=2.07) and about half of the Cuban background group and South-American background group had more than a high school education. A majority of the study participants were never smokers (65.5%) and a sizable proportion (44.9%) engaged in some form of moderate physical activity (Table 1).

The overall age standardized percentage of study participants with <30% of sites with CAL 3mm or PD 4mm was 53.5% and 58.6% respectively while 16% and 5.72% respectively had 30% of sites with CAL 3mm or PD 4mm. The distribution of extent of sites with CAL 3mm and PD 4mm was similar for each of the covariates explored in this report. For

example, having <30% of sites affected by CAL 3mm and PD 4mm was most common for these covariates (Table 2).

The overall age-standardized prevalence (95% CI) of suspected NAFLD was 18.1% (17.1%– 19.0%) while 47.1% (45.5%–48.7%) met the criteria for FLI 60%. The age-standardized prevalence of suspected NAFLD was greatest among Puerto Ricans and Dominicans background groups at approximately 20% in each group and, lowest among participants 65 years, [10.4% (95% CI: 7.48%, 13.4%)]. While there was no difference in prevalence of suspected NAFLD (based on serum transaminase levels) according to education and physical activity level, the prevalence of FLI 60% differed significantly according to levels of these covariates (Table 3).

There was no significant effect measure modification between periodontitis and gender (p=0.2) with respect to suspected NAFLD prevalence, hence results were not stratified according to gender. There was no statistically significant difference in the unadjusted and covariate-adjusted associations between periodontitis and suspected NAFLD within each Hispanic/Latino background groups (p=0.7). For all groups combined, there was a marginal but statistically non-significant association between the proportion of sites with CAL 3mm and suspected NAFLD but this association was attenuated upon adjusting for covariates (Table 4). When periodontitis was defined as the proportion of sites with PD 4mm, there was a dose-response association with suspected NAFLD for all groups combined, whereby participants with 30% of sites affected had an unadjusted POR of 1.39 (95% CI: 1.02, 1.90), while those with <30% had an unadjusted POR of 1.19 (95% CI: 1.03, 1.38). However, these crude estimates were likewise attenuated towards the null upon covariate adjustment (Table 5). Similar patterns in unadjusted and covariate-adjusted estimates for CAL 3mm were observed overall among all study participants, when the FLI was used as the outcome (see supplementary Table 1 in online *Journal of Periodontology*). For PD 4mm, the observed positive unadjusted dose-response relationship persisted upon covariate adjustment but was statistically non-significant in the fully adjusted model (see supplementary Table 2 in online *Journal of Periodontology*).

Discussion

This cross-sectional study of Hispanic/Latino adults found no meaningful association between extent of periodontitis and indicators of NAFLD. These findings are inconsistent with previous studies in animal models[31, 32] and human studies[31, 33, 46] that have reported positive associations. While the unadjusted estimates of this association were greater for the fatty liver index than for serum transaminases, these estimates were attenuated upon covariate adjustment. The FLI was developed and tested for accuracy in a population of Europeans[40] and may not be optimal for a population of Hispanics/Latinos. Furthermore, the algorithm for the FLI includes waist circumference, which was adjusted for as a NAFLD risk factor and thus adjusted estimates for the FLI may represent a form of over-adjustment bias. A sensitivity analysis removing waist circumference as a covariate from the fully-adjusted model for the FLI resulted in POR within the entire study population of 1.13 (95% CI: 1.01, 1.27) and 1.31 (95% CI: 1.03, 1.68) for PD <30% and 30% respectively and POR of 0.98 (95% CI: 0.84, 1.14) and 0.98 (95% CI: 0.79, 1.21) for CAL <30% and 30%

respectively. Given that the prevalence of suspected NALFD of 18.1% based on transaminases differs significantly from the 47.1% for FLI   60% (Table 3), a threshold of FLI   60% may not be optimal for this population.

NAFLD is a heterogeneous condition and while its risk factors appear universal, the contribution of these risk factors to the burden of NAFLD might differ among population groups. Specifically, while the prevalence of NAFLD is reported to be greater among Hispanic/Latino populations compared to other racial/ethnic groups,[47] factors such as periodontitis investigated in this study represents an upstream (i.e. distal) risk factor whose effects were likely rendered non-significant by more proximal risk factors, hence the appearance of a null association in this study.

Other likely reasons for the discrepancies between current and prior findings include the method for characterizing the outcome. While liver ultrasound is the preferred method for characterizing NAFLD in epidemiologic settings, this investigation unlike prior studies, relied primarily on serum transaminases (AST, ALT) and the FLI for characterizing NAFLD. Serum transaminases are non-specific markers on hepatocellular injury and are not always elevated when NAFLD is present. Therefore, potential for misclassification of true NAFLD status is possible in this study. If this misclassification was non-differential according to periodontitis status, the reported estimates were likely biased towards the null, however, if misclassification was differential, then the direction of bias may be hard to predict. Furthermore, the FLI was developed for predicting the likelihood of having NAFLD and may be unsuitable for epidemiologic studies.

While we attempted to minimize misclassification of NAFLD cases by excluding individuals who reported excessive alcohol consumption, due of the non-specific nature of serum transaminases, it is also possible that other hepatic conditions might be responsible for elevated serum transaminase levels. Given the self-reported nature of alcohol use, potential for misreporting and misclassification of alcohol use status is also likely and could have biased these findings.

Lastly, possible racial/ethnic differences may exist with regards to the relationship between periodontitis and NAFLD, whereby the profile of NAFLD risk factors, such as lifestyle and diet, genetics or the intestinal microbiome may differ in their associations with periodontitis among groups who self-identified by race or ethnicity. Within the constraints of our characterization of NAFLD, it is thus important to report on the lack of an association between periodontitis and NAFLD among individuals of Hispanic/Latino background.

Study limitations include the cross-sectional design that is subject to incidence-prevalence bias. Serum transaminases are not always elevated when NAFLD is present and so outcome definition may have been underestimated and/or misclassified. The FLI does not accurately capture NAFLD because it only states the likelihood of having the condition. In spite of these limitations, study strengths include the large study sample and the first report to investigate this question of concerning public health in a diverse group of Hispanics/Latinos. Furthermore, the population of Hispanics/Latinos studied here also sets this study apart from

previous epidemiologic studies that have investigated periodontitis and NAFLD in Japanese[31] and German[33] populations.

Conclusions

Previously reported associations between periodontitis and NAFLD were not replicated in this study of a diverse group of Hispanic/Latino men and women. One reason for this discrepancy might be the use of transaminases to characterize NAFLD in this study compared to liver ultrasounds and biopsies used in prior studies.[31]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Distribution of baseline characteristics, overall and by Hispanic/Latino Background, in the target population of the Hispanic Community Health Study/ Study of Latinos, 2008–2011

	Mexican [unweighted n=5,195]	Cuban [unweighted n=1,669]	Puerto Rican [unweighted n=1,742]	Dominican [unweighted n=1,089]	Central American [unweighted n=1,365]	South American [unweighted n=854]	All [unweighted n=11,914]
Age, in yrs., mean [SE]	38.2 [0.37]	44.9 [0.61]	41.4 [0.62]	38.8 [0.69]	39.3 [0.52]	41.9 [0.84]	40.4 [0.26]
Gender, Male [%]	43.3 [1.08]	49.1 [1.36]	48.9 [1.71]	39.5 [2.17]	45.2 [1.77]	45.1 [2.17]	45.1 [0.65]
Acculturation,[*] score mean [SE]	2.04 [0.03]	1.60 [0.03]	3.15 [0.05]	2.02 [0.06]	1.72 [0.05]	1.81 [0.04]	2.07 [0.02]
Education [%]							
<High school	35.2 [1.35]	19.4 [1.03]	33.5 [1.94]	34.7 [2.14]	37.4 [1.85]	21.5 [2.00]	31.2 [0.78]
High school	29.9 [1.05]	31.3 [1.73]	29.3 [1.44]	23.9 [2.33]	25.7 [1.56]	27.7 [1.86]	29.0 [0.65]
>High school	34.9 [1.54]	49.4 [1.70]	37.2 [1.99]	41.4 [2.28]	36.9 [1.84]	50.8 [2.24]	39.8 [0.89]
Abdominal obesity[†] [%]	54.6 [1.25]	50.4 [1.49]	55.5 [1.82]	51.4 [2.25]	47.7 [1.60]	40.0 [2.47]	52.2 [0.77]
Smoking [%]							
Never	66.9 [1.19]	59.8 [1.84]	54.6 [1.89]	79.2 [2.04]	73.8 [1.67]	67.2 [2.28]	65.5 [0.73]
Former	17.9 [0.94]	18.0 [1.18]	15.4 [1.13]	10.3 [1.11]	14.2 [1.17]	21.8 [1.89]	16.7 [0.51]
Current	15.2 [1.00]	22.2 [1.45]	30.0 [1.82]	10.5 [1.93]	12.0 [1.22]	11.0 [1.39]	17.8 [0.63]
Diabetes[‡] [%]	13.8 [0.71]	13.9 [1.15]	16.0 [1.15]	12.8 [1.09]	13.0 [1.19]	8.94 [1.18]	13.7 [0.46]
Moderate PA[§] [%]	46.7 [1.11]	37.6 [1.49]	47.2 [1.92]	45.6 [2.25]	46.3 [1.78]	48.4 [2.49]	44.9 [0.72]

[*] Acculturation score-based on the language subscale of the Short Acculturation Scale for Hispanics that characterizes language preference on a 5-point Likert scale

[†] Abdominal obesity [waist circumference >88cm for women and >102cm or men]

[‡] Defined based on the American Diabetes Association definition[41], those with normal and impaired glucose tolerance were categorized as not having diabetes

[§] PA- physical activity level

Estimates are presented as mean [SE] or % [SE]

All statistics were weighted except for the sample size

Table 2

Age-standardized prevalence [row percent [SE]] of periodontitis by selected study characteristics, Hispanic Community Health Study/Study of Latinos, 2008–2011

Characteristic	Periodontitis [CAL 3mm]*				Periodontitis [PD 4mm]†			
	No site [n=3,109]	<30% [n=6,985]	30% [n=1,820]	p-value‡	No site [n=3,872]	<30% [n=7,305]	30% [n=737]	p-value‡
All groups	30.5 [0.72]	53.5 [0.81]	16.0 [0.55]		35.7 [0.77]	58.6 [0.74]	5.72 [0.35]	
Hispanic/Latino background				<0.0001				<0.0001
Mexican	37.2 [1.66]	49.2 [1.93]	13.6 [1.40]		53.6 [2.26]	41.9 [2.15]	4.43 [0.86]	
Cuban	29.7 [1.62]	54.7 [1.95]	15.6 [1.40]		43.9 [1.92]	48.9 [1.94]	7.11 [1.14]	
Puerto Rican	26.0 [1.51]	57.0 [1.96]	17.0 [1.63]		29.6 [2.06]	64.8 [1.99]	5.65 [1.01]	
Dominican	28.7 [1.10]	58.7 [1.17]	12.6 [0.85]		25.9 [1.14]	67.3 [1.11]	6.81 [0.57]	
Central American	30.5 [1.50]	48.0 [1.52]	21.5 [1.32]		37.6 [1.44]	58.0 [1.49]	4.44 [0.57]	
South American	30.1 [2.35]	52.3 [2.53]	17.6 [1.73]		38.7 [2.43]	56.6 [2.58]	4.67 [1.38]	
Age group, [yrs.]				<0.0001				<0.0001
18–44	47.9 [1.07]	48.6 [1.03]	3.53 [0.33]		37.4 [1.11]	58.4 [1.09]	4.19 [0.46]	
45–64	15.7 [0.97]	62.3 [1.07]	22.0 [0.84]		29.7 [0.88]	62.4 [0.91]	7.93 [0.57]	
65	11.4 [1.59]	49.3 [2.59]	39.3 [2.37]		43.1 [2.74]	51.4 [2.75]	5.52 [0.98]	
Gender				<0.0001				<0.0001
Female	33.1 [0.88]	54.1 [0.99]	12.8 [0.66]		40.1 [1.00]	55.7 [0.97]	4.20 [0.42]	
Male	27.5 [0.94]	52.2 [1.12]	20.3 [0.93]		30.1 [1.09]	62.3 [1.10]	7.65 [0.52]	
Education				<0.0001				<0.0001
< High school	27.3 [1.11]	54.3 [1.18]	18.4 [0.82]		33.5 [1.18]	59.0 [1.19]	7.47 [0.62]	
High school	29.9 [1.13]	52.1 [1.52]	18.0 [1.22]		34.0 [1.45]	60.1 [1.49]	5.94 [0.89]	
> High school	32.9 [1.13]	54.1 [1.25]	13.0 [0.92]		38.0 [1.32]	57.8 [1.28]	4.28 [0.43]	
Smoking				<0.0001				<0.0001
Never	33.1 [0.85]	54.3 [0.93]	12.6 [0.70]		36.9 [0.92]	58.5 [0.88]	4.66 [0.39]	
Former	26.9 [1.78]	48.8 [2.01]	24.3 [1.69]		33.8 [1.87]	58.4 [1.91]	7.77 [0.95]	
Current	23.3 [1.39]	56.8 [1.58]	19.9 [1.09]		32.3 [1.58]	59.8 [1.66]	7.85 [1.03]	
Diabetes§				<0.0001				<0.0001
No	31.8 [0.82]	53.1 [0.94]	15.2 [0.67]		36.3 [0.91]	58.8 [0.88]	4.85 [0.33]	

Characteristic	Periodontitis [CAL ≥3mm]*				Periodontitis [PD ≥4mm]†		
	No site [n=3,109]	<30% [n=6,985]	30% [n=1,820]	p-value‡	No site [n=3,872]	<30% [n=7,305]	30% [n=737]	p-value‡
Yes	22.5 [1.66]	56.1 [1.98]	21.3 [1.32]		31.5 [1.80]	58.2 [1.86]	10.3 [1.18]	

*
CAL–Clinical attachment level;

†
PD–Probing pocket depth; SE–standard error

§
Defined based on the American Diabetes Association definition[41], those with normal and impaired glucose tolerance were categorized as non-diabetics.

‡
Survey design-adjusted Wald chi-square test

All estimates were age-standardized to the 2010 U.S. Census age distribution[43]

Table 3

Age-standardized prevalence [95% C.I] of suspected NAFLD by selected study characteristics, Hispanic Community Health Study/Study of Latinos, 2008–2011

Characteristic	Suspected NAFLD[*]			FLI 60%[†]		
	Row Percent	95% CI	p value[‡]	Row Percent	95% CI	p value[‡]
All groups	18.1	17.1–19.0		47.1	45.5–48.7	
Hispanic/Latino background			<0.0001			0.0002
Mexican	12.9	10.3–15.5		41.1	37.1–45.0	
Cuban	14.9	12.5–17.4		49.1	45.1–53.1	
Puerto Rican	20.0	17.3–22.7		47.2	43.4–51.0	
Dominican	20.4	18.6–22.1		49.5	46.9–52.1	
Central American	17.1	15.2–19.0		45.2	42.1–48.4	
South American	16.9	13.7–20.1		39.9	34.9–44.9	
Age groups, [yrs.]			<0.0001			<0.0001
18–44	19.6	18.1–21.1		39.8	37.9–41.8	
45–64	19.7	18.3–21.2		55.5	53.6–57.3	
65	10.4	7.48–13.4		50.8	45.7–55.8	
Gender			<0.0001			<0.0001
Female	15.0	13.8–16.1		42.4	40.4–44.5	
Male	21.7	19.9–23.5		52.8	50.6–55.0	
Education			0.7			<0.0001
< High school	18.1	16.5–19.7		51.1	48.8–53.4	
High school	17.6	15.8–19.5		46.9	44.0–49.7	
> High school	18.0	16.3–19.7		44.6	41.9–47.3	
Abdominal obesity			<0.0001			<0.0001
No	13.8	12.4–15.2		21.1	19.4–22.8	
Yes	21.8	20.4–23.1		68.8	67.0–70.7	
Smoking			0.02			<0.0001
Never	17.4	16.2–18.5		44.5	42.5–46.4	
Former	17.5	14.9–20.1		45.2	41.2–49.1	

Characteristic	Suspected NAFLD[*]			FLI 60%[†]		
	Row Percent	95% CI	p value[‡]	Row Percent	95% CI	p value[‡]
Current	21.4	18.8–24.0		56.9	53.5–60.2	
Physical activity			0.1			<0.0001
Low	17.9	16.5–19.2		43.0	40.6–45.4	
Moderate	17.7	16.3–19.2		50.3	48.2–52.4	
High	17.6	15.0–20.1		49.8	43.5–56.2	
Diabetes[§]			<0.0001			<0.0001
No	16.4	15.3–17.4		42.9	41.1–44.7	
Yes	28.6	25.2–32.0		71.5	68.2–74.8	

[*] Defined ALT >40 IU/L or AST >37 IU/L for men and ALT >31 IU/L or AST >31 IU/L for women [39]

[†] FLI [40]-based on Triglyceride levels, BMI, waist circumference and GGT levels

[‡] Survey design-adjusted Wald chi-square test

[§] Defined based on the American diabetes association definition[41], those with normal and impaired glucose tolerance were categorized as non-diabetics.

NAFLD-non-alcoholic fatty liver disease; FLI-fatty liver index; ALT-alanine aminotransferase; AST-Aspartate aminotransferase; GGT-gamma glutamyl transferase; BMI-body mass index

All estimates were age-standardized to the 2010 U.S. Census age distribution[43]

Table 4

Prevalence Odds Ratios (POR [95% CI]) for the association between Periodontitis (CAL ≥3mm) and suspected NALFD* in the Hispanic Community Health Study/Study of Latinos

	Unadjusted		Adjusted†		Adjusted‡	
			POR§ [95% CI] for CAL ≥3mm			
	<30%	30%	<30%	30%	<30%	30%
All groups	1.18 [1.01, 1.36]	1.04 [0.83, 1.30]	1.04 [0.89, 1.22]	0.93 [0.72, 1.21]	1.03 [0.87, 1.21]	0.91 [0.70, 1.18]
Mexican	1.06 [0.84, 1.34]	1.00 [0.69, 1.44]	0.97 [0.75, 1.25]	1.04 [0.69, 1.58]	0.95 [0.73, 1.24]	0.89 [0.58, 1.37]
Cuban	1.19 [0.84, 1.70]	1.15 [0.71, 1.87]	1.09 [0.74, 1.59]	0.98 [0.60, 1.61]	1.05 [0.71, 1.54]	0.98 [0.57, 1.71]
Puerto Rican	1.23 [0.80, 1.89]	1.21 [0.65, 2.27]	1.04 [0.62, 1.73]	1.07 [0.49, 2.23]	1.05 [0.63, 1.75]	0.99 [0.45, 2.18]
Dominican	1.13 [0.70, 1.82]	1.13 [0.54, 2.38]	0.86 [0.53, 1.41]	0.93 [0.38, 2.32]	0.83 [0.51, 1.36]	0.77 [0.29, 2.01]
Central American	1.69 [1.10, 2.59]	0.92 [0.52, 1.63]	1.42 [0.92, 2.19]	0.71 [0.37, 1.38]	1.52 [0.99, 2.32]	0.74 [0.38, 1.43]
South American	1.32 [0.78, 2.25]	1.35 [0.70, 2.61]	1.10 [0.65, 1.88]	1.20 [0.60, 2.39]	1.31 [0.77, 2.20]	1.45 [0.73, 2.88]

*
Defined ALT >40 IU/L or AST >37 IU/L for men and ALT >31 IU/L or AST >31 IU/L for women [39]

†
Adjusted for age, gender

‡
Additionally adjusted for abdominal obesity, smoking, diabetes, physical activity, education and acculturation score. NAFLD-non-alcoholic fatty liver disease; CAL-clinical attachment level

§
Prevalence odds ratio relative to subjects with no sites affected

Table 5

Prevalence Odds Ratios (POR [95% CI]) for the association between Periodontitis (PD ≥4mm) and suspected NALFD[*] in the Hispanic Community Health Study/Study of Latinos

	Unadjusted		Adjusted[†]		Adjusted[‡]	
			POR§ [95% CI] for PD ≥4mm			
	<30%	30%	<30%	30%	<30%	30%
All groups	1.19 [1.03, 1.38]	1.39 [1.02, 1.90]	1.07 [0.92, 1.25]	1.14 [0.83, 1.56]	1.03 [0.88, 1.20]	1.00 [0.72, 1.38]
Mexican	1.25 [0.96, 1.63]	1.56 [0.97, 2.51]	1.15 [0.86, 1.53]	1.34 [0.83, 2.18]	1.07 [0.81, 1.40]	1.16 [0.70, 1.91]
Cuban	0.79 [0.58, 1.09]	1.07 [0.56, 2.03]	0.72 [0.53, 0.97]	0.84 [0.45, 1.56]	0.73 [0.54, 0.99]	0.80 [0.41, 1.56]
Puerto Rican	1.01 [0.68, 1.49]	1.24 [0.60, 2.54]	0.85 [0.56, 1.30]	0.95 [0.45, 1.97]	0.88 [0.57, 1.37]	0.87 [0.41, 1.85]
Dominican	1.24 [0.77, 2.00]	2.22 [0.76, 6.51]	1.08 [0.66, 1.77]	1.77 [0.60, 5.26]	1.09 [0.67, 1.79]	1.58 [0.58, 4.31]
Central American	1.48 [0.99, 2.22]	0.84 [0.36, 1.99]	1.38 [0.92, 2.08]	0.73 [0.30, 1.77]	1.34 [0.89, 2.01]	0.60 [0.23, 1.59]
South American	1.08 [0.70, 1.67]	0.25 [0.08, 0.78]	0.93 [0.61, 1.43]	0.19 [0.06, 0.62]	1.02 [0.66, 1.57]	0.19 [0.05, 0.68]

[*] Defined ALT >40 IU/L or AST >37 IU/L for men and ALT >31 IU/L or AST >31 IU/L for women [39]

[†] Adjusted for age, gender

[‡] Additionally adjusted for abdominal obesity, smoking, diabetes, physical activity, education and acculturation score. NAFLD-non-alcoholic fatty liver disease; PD-probing pocket depth

§ Prevalence odds ratio relative to subjects with no sites affected