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Association between the quality of plant-based diets and periodontitis in the U.S. general population

An Li[1,2] | Bingjiang Qiu[3,4] | Marjolein Goettsch[2] | Yuntao Chen[5,6] | Shaohua Ge[7] | Shulan Xu[1] | Geerten-Has E. Tjakkes[2]

[1]Center of Oral Implantology, Stomatological Hospital, School of Stomatology, Southern Medical University, Guangzhou, China

[2]Department of Periodontology, Center for Dentistry and Oral Hygiene, University Medical Center Groningen (UMCG), University of Groningen, Groningen, The Netherlands

[3]Department of Radiology and Guangdong Cardiovascular Institute and Guangdong Provincial Key Laboratory of Artificial Intelligence in Medical Image Analysis and Application, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, China

[4]Data Science Center in Health (DASH) and 3D Lab, UMCG, University of Groningen, Groningen, The Netherlands

[5]Department of Epidemiology and Public Health, University College London, London, UK

[6]Medical Statistics and Decision Making, Department of Epidemiology, UMCG, University of Groningen, Groningen, The Netherlands

[7]Department of Periodontology, School and Hospital of Stomatology, Cheeloo College of Medicine, Shandong University & Shandong Key Laboratory of Oral Tissue Regeneration & Shandong Engineering Laboratory for Dental Materials and Oral Tissue Regeneration & Shandong Provincial Clinical Research Center for Oral Diseases, Jinan, China

Correspondence
Shaohua Ge, Department of Periodontology, School and Hospital of Stomatology, Cheeloo College of Medicine, Shandong University & Shandong Key Laboratory of Oral Tissue Regeneration & Shandong Engineering Laboratory for Dental Materials and Oral Tissue Regeneration & Shandong Provincial Clinical Research Center for Oral Diseases,

Abstract

Aim: To investigate the relationship between plant-based diet indices (PDIs) and periodontitis and serum IgG antibodies against periodontopathogens in the U.S. population.

Materials and Methods: We analysed cross-sectional data on 5651 participants ≥40 years of age from the Third National Health and Nutrition Examination Survey. Food frequency questionnaire data were used to calculate the overall PDI, healthy plant-based diet index (hPDI), and unhealthy plant-based diet index (uPDI). Periodontitis was defined using a half-reduced Centers for Disease Control and Prevention and American Academy of Periodontology case definition. Serum antibodies against 19 periodontopathogens were used to classify the population into two subgroups using hierarchical clustering. Survey-weighted multivariable logistic regressions were applied to assess the associations of PDI/hPDI/uPDI *z*-scores with periodontitis and hierarchical clusters after adjusting for potential confounders.

Results: A total of 2841 (50.3%) participants were defined as having moderate/severe periodontitis. The overall PDI *z*-score was not significantly associated with the clinical and bacterial markers of periodontitis. By considering the healthiness of plant foods, we observed an inverse association between hPDI *z*-score and periodontitis (odds ratio [OR] = 0.925, 95% confidence interval [CI]: 0.860–0.995). In contrast, higher uPDI *z*-score (adherence to unhealthful plant foods) might increase the risk of periodontitis (OR = 1.100; 95% CI: 1.043–1.161). Regarding antibodies against periodontopathogens, the participants in cluster 2 had higher periodontal antibodies than those in cluster 1. The hPDI *z*-score was positively associated with cluster 2 (OR = 1.192; 95% CI: 1.112–1.278). In contrast, an inverse association between uPDI *z*-score and cluster 2 was found (OR = 0.834; 95% CI: 0.775–0.896).

Conclusions: Plant-based diets were associated with periodontitis, depending on their quality. A healthy plant-based diet was inversely related to an increased risk of periodontitis but positively related to elevated antibody levels against periodontopathogens. For an unhealthy plant-based diet, the opposite trends were observed.

An Li and Bingjiang Qiu share the first authorship.

No. 44-1 West Wenhua Road, Jinan, 250012, China.
Email: shaohuage@sdu.edu.cn

Shulan Xu, Center of Oral Implantology, Stomatological Hospital, School of Stomatology, Southern Medical University, No. 366 Jiangnan S Avenue, Guangzhou, 510280, China.
Email: xushulan_672588@smu.edu.cn

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KEYWORDS
bacterial antibodies, cluster analysis, immune response, periodontitis, plant-based diet index

Clinical Relevance

Scientific rationale for study: Healthy diets, such as plenty of fruits, vegetables, whole grain cereals, lean protein, and a fat-restricted diet, might positively affect the pathogenesis of periodontitis by modulating the host's immune function. We examined the relationship between plant-based diet indices and the clinical and bacterial markers of periodontitis.

Principal findings: We did not observe any significant association between overall plant-based diets and periodontitis and serum antibodies against periodontopathogens. However, higher adherence to healthful plant foods was associated with a lower risk of periodontitis and elevated antibody levels. In contrast, unhealthful plant-based dietary patterns might increase periodontitis risk and reduce periodontal antibody levels.

Practical implications: As an adjunct to periodontal therapy, dentists could provide dietary guides and recommendations to patients with periodontitis in the day-to-day clinical practice. Increasing the intake of healthy plant foods (e.g., whole grains, fruits, and vegetables) while reducing the intake of less healthy plant foods (e.g., refined grains, fried potatoes, sugary products, and sugar-sweetened beverages) may be beneficial for preventing periodontitis.

1 | INTRODUCTION

Over a billion people were affected by severe periodontitis globally in 2019 (Chen et al., 2021). In addition to the main aetiological factor for tooth loss, periodontitis is closely associated with several systemic diseases, leading to a considerable economic burden on the healthcare system and society (Genco & Sanz, 2020). Periodontal therapy commonly aims to remove biofilms and calculi using mechanical debridement and oral hygiene measures. Treatment success is affected by the stage of periodontitis, and early preventive measures can prevent deterioration and extensive treatment (Chapple et al., 2015). From a public health perspective, dietary intervention might also be a promising non-pharmacological strategy to prevent periodontitis (Dommisch et al., 2018). Population-based studies have revealed a significant association between pro-inflammatory dietary patterns measured by the dietary inflammatory index and an increased risk of periodontitis (Li, Chen, Schuller, et al., 2021; Machado et al., 2021). A randomized controlled trial (RCT) suggested that an anti-inflammatory diet rich in fibres and plant nitrates but low in processed foods reduces gingival bleeding (Woelber et al., 2019). Of note, vegetarian or vegan diets, partially or wholly excluding animal foods, have become increasingly popular. Lower probing pocket depth (PPD) and less gingival bleeding have been reported in vegetarians compared to omnivores (Staufenbiel et al., 2013). In a 14-year follow-up study, a higher intake of whole grains was found to be less likely to lead to periodontitis (Merchant et al., 2006), although not all plant foods are beneficial to periodontal health. A higher intake of added sugars may increase periodontitis risk in the young population (Lula et al., 2014). Therefore, investigating the quantity and quality of plant-based diets would lead to a better understanding of the relationship between plant foods and periodontitis.

Three distinct indices were developed to describe the quantity and quality of plant-based dietary patterns in the Nurses' Health Study and the Health Professionals Follow-Up Study (Satija et al., 2016, 2017). Specifically, the plant-based diet index (PDI) reflects a higher intake of plant foods and a lower intake of meat. The healthful plant sources of whole foods (e.g., fruits, vegetables, plant proteins, and whole grains) were scored as healthful PDI (hPDI). In contrast, the unhealthful plant-derived processed foods (e.g., refined grains, fried potatoes, sugar-sweetened beverages, sweets, and desserts) were considered unhealthful PDI (uPDI). However, few population-based studies have investigated the association between plant-based diets and periodontitis.

Elevated serum immunoglobulin G (IgG) levels against periodontopathogens can persist for up to 15 years, protecting against periodontal infections (Papapanou et al., 2004; Lakio et al., 2009). Therefore, serum IgG level was regarded as an alternative marker for immune response to oral bacteria (Papapanou et al., 2001). Merchant et al. applied Ward's minimum variance method to classify 19 periodontal antibodies into four clusters using the Third National Health and Nutrition Examination Survey (NHANES III) data (Merchant et al., 2014). Four clustering scores were calculated to reflect different periodontopathogens in the oral cavity and then colour-coded according to Socransky's classification scheme (Socransky & Haffajee, 2002). The rationale for forming these IgG clusters was based on their relevance to the aetiopathogenesis of periodontitis. Nevertheless, it is difficult to reflect the characteristics of the population with this method. Unsupervised clustering techniques were recently used to identify subgroups of patients with similar clinical features (Woolley et al., 2021). In this context, the subgroups represent individuals with similar immune responses to periodontopathogens.

Therefore, this study aimed (1) to investigate the association between PDIs and periodontitis measured by clinical parameters in

U.S. adults ≥40 years of age, and (2) to assess the relationship between the diet indices and serum periodontal antibody clusters.

2 | MATERIALS AND METHODS

2.1 | Study design and population

The present cross-sectional study used NHANES III data from 1988 through 1994 in the United States, as these years included information on serum antibodies against periodontopathogens (Figure 1a). NHANES III was conducted by the National Center for Health Statistics (NCHS) to obtain data on the health and nutritional status of the non-institutionalized U.S. population. NHANES used a complex, multi-stage, stratified, clustered sampling design to achieve a nationally representative sample (Ezzati et al., 1992). This nationwide survey included demographic and basic health data, standardized medical examinations, and laboratory tests. The NCHS Research Ethics Review Board approved all the data collection procedures. In addition, the participants signed informed consent forms. The present study used publicly available data sources; therefore, it did not require ethics review. NHANES III determined IgG antibodies in adults ≥40 years of age. In this study, of the 8153 participants from NHANES III who were ≥40 years of age and had clinical periodontal measurements and data on bacteria, 2312 were not eligible because of edentulism ($n = 1593$) and missing data on periodontal examination ($n = 719$). Thus, this study included participants having data on clinical and bacterial markers of periodontitis and at least one tooth. In addition, participants with incomplete dietary data were excluded ($n = 190$). In total, 5651 participants of NHANES III were included (Figure S1).

2.2 | Dietary assessment

PDI, hPDI, and uPDI were defined as the exposure variables in all analyses (Figure 1b) and calculated based on the food frequency questionnaire (FFQ) data as a previously used method (Satija et al., 2016; Kim et al., 2018). The participants from NHANES III completed an 81-item FFQ to assess the frequencies of specified food items they had consumed over the past month without considering the portion size. The average daily intake of each food item was calculated and assigned to 17 food groups classified into three food categories: animal foods, healthful plant foods, and unhealthful plant foods (Table S1). The 17 food groups were ranked into quintiles and scored 1–5 (Figure 1b). The scores of these 17 food groups were summed to obtain the PDI/hPDI/uPDI. The indices ranged from 17 to 85 and were divided into quintiles for statistical analyses (Figure 2a for PDI, Figure 2b for hPDI, and Figure 2c for uPDI). The detailed scoring methods and intake of foods were as follows:

1. To calculate PDI, the participants received a score of 5 when they fell within the highest quintile of plant food groups (positive

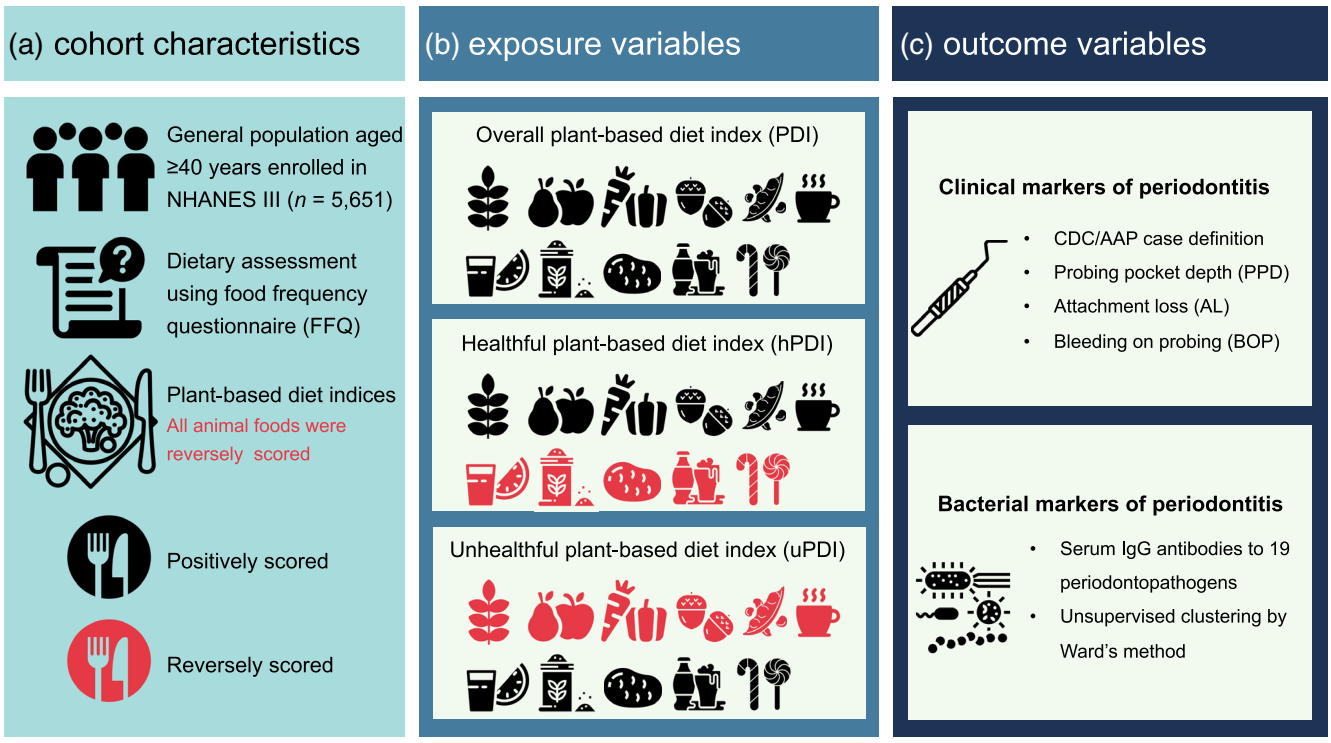

FIGURE 1 Graphical overview of cohort characteristics and study design. CDC/AAP, Centers for Disease Control and Prevention/American Academy of Periodontology; IgG, immunoglobulin G; NHANES III, The Third National Health and Nutrition Examination Survey.

scores). In contrast, those in the highest quintile of animal food groups received a score of 1 (reverse scores), with higher PDI scores indicating a higher intake of plant foods but a lower intake of animal foods (PDI quintile 5 vs. 1, Figure 2d).

2. To calculate hPDI, only the healthful plant foods received positive scores, whereas animal foods and unhealthful plant foods were given reverse scores, with higher hPDI scores representing a higher intake of healthy plant foods but a lower intake of animal foods and unhealthful plant foods (hPDI quintile 5 vs. 1, Figure 2e).
3. To calculate uPDI, only the unhealthful plant foods were given positive scores; however, animal foods and healthful plant foods were given reverse scores, with higher uPDI scores indicating a higher intake of unhealthful plant foods but a lower intake of animal foods and healthy plant foods (uPDI quintile 5 vs. 1, Figure 2f).

2.3 | Clinical parameters of periodontitis

Periodontal assessment included clinical and bacterial markers of periodontitis (Figure 1c). Trained and calibrated examiners selected two random quadrants (one maxillary and one mandibular) to determine periodontal parameters using a partial-mouth periodontal examination protocol. PPD, attachment loss (AL), and bleeding on probing (BOP)

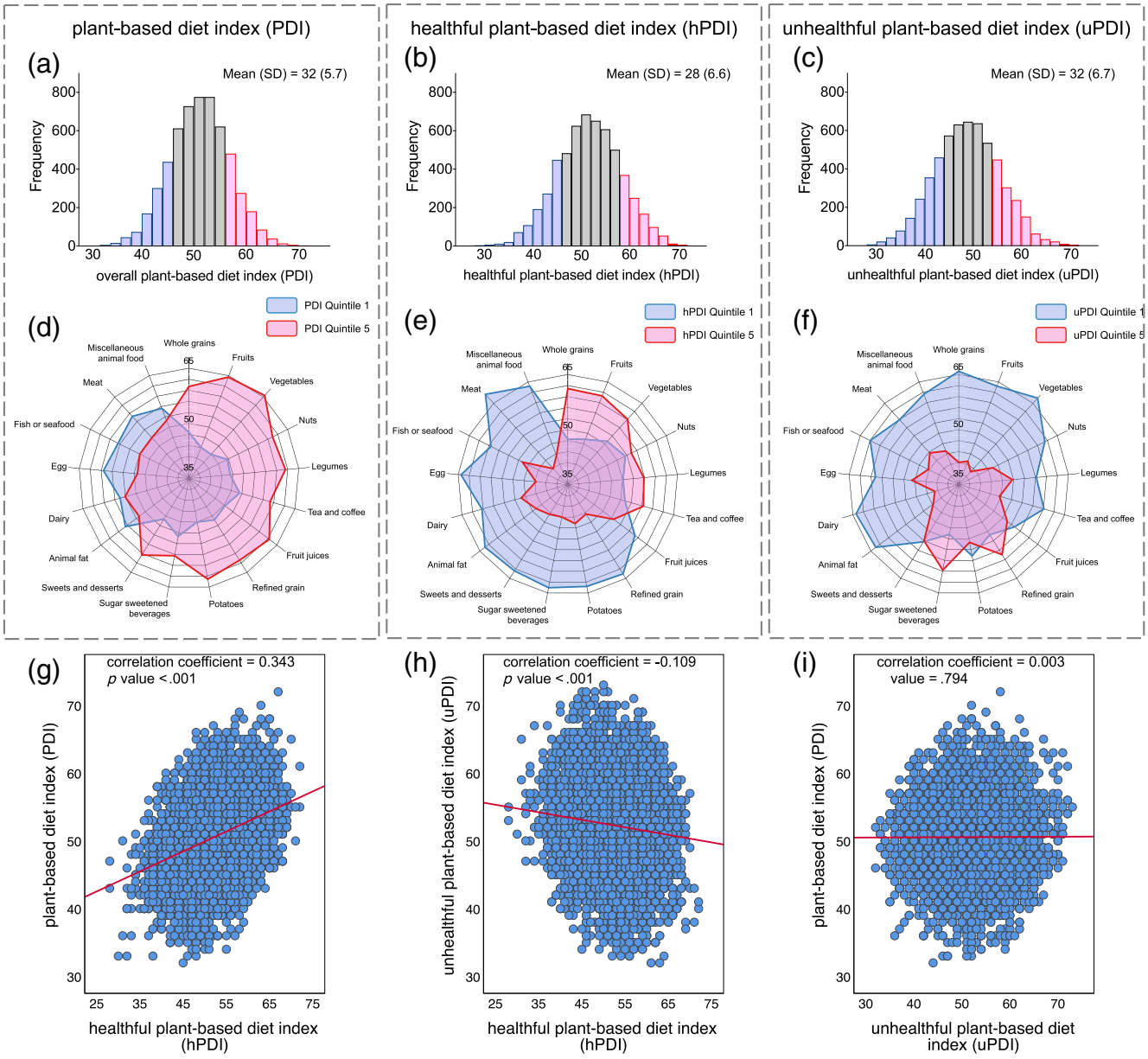

FIGURE 2 Characteristics for plant-based diet indices. Distributions of PDI (a), hPDI (b), and uPDI (c) in Third National Health and Nutrition Examination Survey population. Percentage differences in 17 food items of the lowest and highest quintile of PDI (d), hPDI (e), and uPDI (f). Pearson correlations between PDI, hPDI, and uPDI scores (g, h, i).

were assessed at mid-buccal and mesio-buccal sites per tooth (Winn et al., 1999). The number of missing teeth was also recorded during the examinations. Since NHANES III applied the partial-mouth periodontal examination protocol, we used a half-reduced case definition by the Centers for Disease Control and Prevention (CDC)/American Academy of Periodontology (AAP) to assess the severity of periodontitis (Tran et al., 2014). The half-reduced definition has been applied to NHANES participants in our previous works (Li, Chen, van der Sluis, et al., 2021; Li et al., 2022). When a participant was defined as a case, (s)he was assigned to the moderate/severe periodontitis group (moderate: ≥1 interproximal site with ≥4 mm AL, or ≥1 interproximal site with ≥5 mm PPD; severe: ≥1 interproximal site with ≥6 mm AL and ≥1 interproximal site with ≥5 mm PPD). In the absence of moderate/severe signs of periodontitis, the participant was assigned to the no/mild periodontitis group (control). In brief, the participants were categorized into two groups (no/mild periodontitis vs. moderate/severe periodontitis). The groups were treated as the binary outcome in the logistic regression analysis.

2.4 | Antibacterial antibodies in periodontitis

Serum IgG antibodies against 19 periodontopathogens were determined using stored serum samples of NHANES III participants through a rapid checkerboard immunoblotting technique as previously described (Sakellari et al., 1997; Papapanou et al., 2001). In Supplemental Methods, the bacterial strains used to prepare whole-cell antigenic extracts are described. In brief, bacterial extracts were diluted in PBS to the optical density of 1 using a spectrophotometer (wavelength = 600 nm). The antigenic extracts and protein A standards (5 mg/ml) were immobilized on nitrocellulose membranes. Each subject's serum and human IgG standards were loaded into the bacterial extracts and were allowed to interact. After washing, membranes were incubated with Fab fragments of anti-human IgG and a horseradish peroxidase substrate. The chemiluminescent signal was assessed and compared with those generated by protein A and human IgG standards. Sera from NHANES III phase 2 (1992–1994) were tested first, followed by phase 1 (1988–1991) samples. Discrepancies were observed in the titre levels between samples from the two phases since different protein A standards were used (Dye et al., 2009). Specifically, the antibody levels to periodontopathogens in phase 1 were lower than in phase 2 (Goh et al., 2016).

The present study used the unsupervised clustering approach to classify the NHANES III population into several subgroups based on antibody levels. First, Spearman's rank correlation analysis was performed to assess the correlations between 19 periodontopathogen IgG titers. Second, an attempt was made to reduce the effect of nonlinearity using kernel principal component analysis with a radial basis function kernel on all the 19 periodontopathogens using the *sklearn* package in Python (Pedregosa et al., 2011). A hierarchical clustering algorithm was then used on the NHANES dataset using a bottom-up approach called agglomerative clustering. The linkage criteria of Ward were used to determine the merge strategy of the agglomerative clustering metric, and the Euclidean distance metric was used to compute the linkage. Finally, silhouette analysis was used to select the optimum number of clusters. The silhouette score plot in Figure S2 shows that a cluster number of 2 is the best pick for the dataset. We then regarded two hierarchical clustering subgroups as a binary outcome in the logistic regression analysis.

2.5 | Potential confounders used for adjustment

We pre-defined as confounders for adjustment in multivariable regression models mainly known or suspected risk factors for diets and periodontitis (Kotsakis et al., 2018; Wright et al., 2020; Li, Chen, Schuller, et al., 2021). In addition, potential confounders were further selected using a directed acyclic graph (Figure S3) (Schipf et al., 2011). Potential confounders included age, sex, race/ethnicity, annual family income, educational attainment, smoking status, physical activity, dental visit, total energy intake, and diabetes. Age (years), sex (male and female), and race/ethnicity (White, Black, and others) were collected by trained interviewers from in-person household interviews. Annual family income (<$20,000 and ≥$20,000) and educational attainment (≤primary school, middle/high school graduate, ≥college or higher) were regarded as indicators of socio-economic status. Concerning healthy lifestyles, physical activity, smoking status (never, former, and current), and time since the last dental visits (<1 year and ≥1 year) were also obtained from the interviews. The total energy intake was assessed based on data from a 24-h dietary recall questionnaire. Table S2 presents the detailed definitions and categories of systemic diseases, including diabetes, heart diseases, dyslipidaemia, abdominal adiposity, and obesity.

2.6 | Statistical analyses

Statistical analyses were performed using survey-weighting, accounting for the complex sampling design of the NHANES III. Weighted proportions, means, and standard deviations (SDs) were used to describe participant characteristics. Pearson's correlation coefficient was used to assess the correlation between PDI, hPDI, and uPDI. In addition, survey-weighted multivariable logistic regression models were used to investigate the relationship between PDIs (*z*-score) and periodontitis and hierarchical cluster 2 of serum antibodies against periodontopathogens. Data are presented as model 1 (unadjusted), model 2 (adjusted for socio-demographic variables [age, sex, race/ethnicity, educational attainment, and annual family income]), and model 3 (adjusted for smoking status, physical activity, dental visits, the total energy intake, and diabetes). In addition, we computed the *E*-value to assess whether an unmeasured confounder could completely explain the associations between plant-based diets and periodontitis and elevated antibodies (VanderWeele & Ding, 2017). With higher *E*-values, the observed association is less likely to be explained by unmeasured confounding. In contrast, lower *E*-values indicate that a relatively weak unmeasured confounder can render the observed association a

TABLE 1 Characteristics for the participants of The Third National Health and Nutrition Examination Survey (1988–1994).

Variables	Total study population ($n = 5651$)
Socio-demographic variables	
Age (year), mean (SD)	57.73 (13.06)
Sex, *n* (%)	
Male	2670 (47.2)
Female	2981 (52.8)
Race/ethnicity, *n* (%)	
Non-Hispanic White	2623 (46.4)
Non-Hispanic Black	1368 (24.2)
Mexican-American	1420 (25.1)
Others	240 (4.2)
Education, *n* (%)[a]	
<High school	1461 (26.1)
High school	2502 (44.6)
≥College	1645 (29.3)
Annual family income, *n* (%)[a]	
<$20,000	2360 (42.5)
≥$20,000	3194 (57.5)
Lifestyle variables	
Smoking habit, *n* (%)	
Non-smoker	2659 (47.1)
Former smoker	1766 (31.3)
Current smoker	1226 (21.7)
Physical activity level, *n* (%)	
Low	1979 (35.0)
Moderate	2650 (46.9)
High	1022 (18.1)
Time since the last dental visit, *n* (%)[a]	
<2 years	2748 (49.7)
≥2 years	2779 (50.3)
Health-related factors	
Body mass index (kg/m^2), mean (SD)	27.96 (5.61)
Waist circumference (cm), mean (SD)	96.93 (13.45)
Serum cholesterol (mg/dl), mean (SD)	216.99 (43.72)
Serum HDL cholesterol (mg/dl), mean (SD)	50.92 (16.29)
Glycated haemoglobin (%), mean (SD)	5.78 (1.24)
Diabetes, *n* (%)[a]	
No physician's diagnosis	5058 (89.6)
Physician's diagnosis	588 (10.4)
Heart diseases, *n* (%)[a]	
No physician's diagnosis	5215 (93.1)
Physician's diagnosis	385 (6.9)
Obesity, *n* (%)[a]	
Normal	1766 (31.3)
Overweight	2222 (39.3)
Obese	1654 (29.3)
Abdominal adiposity, *n* (%)	
No abdominal adiposity	1867 (33.0)
Moderate abdominal adiposity	1897 (33.6)
Severe abdominal adiposity	1887 (33.4)
Dyslipidemia, *n* (%)[a]	
Normal	2958 (52.3)
Intermediate dyslipidaemia	1508 (26.7)
Dyslipidaemia	1118 (19.8)
Clinical and bacterial markers of periodontitis	
CDC/AAP case definition, *n* (%)	
No/mild periodontitis	2810 (49.7)
Moderate/severe periodontitis	2841 (50.3)
Mean PPD (mm), mean (SD)	1.59 (0.61)
Mean AL (mm), mean (SD)	1.75 (1.42)
BOP (%), median (25%–75%)	4.6 (0.0–18.2)
Number of the teeth present, median (25%–75%)	24 (18–27)
Hierarchical clustering subgroups, *n* (%)	
Cluster 1	1137 (20.1)
Cluster 2	4514 (79.9)

Abbreviations: AAP, American Academy of Periodontology; AL, attachment loss; BOP, bleeding on probing; CDC, Centers for Disease Control and Prevention; HDL, high-density lipoprotein; PPD, probing pocket depth; SD, standard deviation.

[a]Missing value for total population: education ($n = 43$; <1%), income ($n = 97$; 1.7%), dental visit ($n = 124$; 2.2%), diabetes ($n = 5$; <1%), obesity ($n = 9$; <1%), dyslipidaemia ($n = 67$; 1.2%), and heart diseases ($n = 51$; < 1%).

null estimate. Scripts to generate this study's *E*-value results are publicly available on the GitHub (https://github.com/qbingjiang/E-Value-python).

The following sensitivity analyses were performed to test the robustness of the results. First, we used mean PPD, mean AL, and BOP as clinical markers of periodontitis. Multivariable linear regression models were used to estimate the relationship between PDIs and the clinical markers (continuous outcomes). Second, PDI, hPDI, and uPDI were treated as quintile groups (categorical exposures). Third, periodontal status was also assessed using the 2018 periodontitis classification (Papapanou et al., 2018) (See Data S1 for more details). Fourth, we applied the previously reported clustering method in the NHANES III study (Merchant et al., 2014). Four clustering scores were computed, namely Orange-Red, Red-Green, Yellow-Orange, and Orange-Blue clusters (Figure S4). Multivariable linear regression models were used to estimate the relationship between PDIs and four clustering scores (continuous outcomes). Fifth, we applied inverse probability of treatment weighting (IPTW) to adjust for potential

TABLE 2 Association of plant-based diet indices with periodontitis and serum antibodies against periodontopathogens among participants of The Third National Health and Nutrition Examination Survey.

OR (95% CI)[b]	PDI[a]	hPDI[a]	uPDI[a]
Periodontitis			
Model 1[b]	1.068 (0.993–1.138)	**0.957 (0.934–0.984)**	**1.092 (1.033–1.155)**
Model 2[b]	1.036 (0.982–1.092)	**0.919 (0.855–0.988)**	**1.108 (1.045–1.175)**
Model 3[b]	0.995 (0.938–1.054)	**0.925 (0.860–0.995)**	**1.100 (1.043–1.161)**
Hierarchical cluster 2			
Model 1[b]	1.000 (0.933–1.071)	**1.196 (1.116–1.282)**	**0.917 (0.856–0.983)**
Model 2	1.005 (0.937–1.078)	**1.201 (1.120–1.288)**	**0.839 (0.781–0.902)**
Model 3	1.014 (0.947–1.087)	**1.192 (1.112–1.278)**	**0.834 (0.775–0.896)**

Note: Bold indicates *p*-value <.05.

Abbreviations: CI, confidence interval; hPDI, healthful plant-based diet index; OR, odds ratio; PDI, plant-based index; uPDI, unhealthful plant-based diet index.

[a]Plant-based diet indices include PDI, hPDI, and uPDI. The continuous dietary scores were transformed to *z*-score as exposure variables.

[b]Data are presented as model 1 (unadjusted), model 2 (adjusted for age, sex, race/ethnicity, educational attainment, and annual family income), and model 3 (adjusted for smoking status, physical activity level, and dental visits, the total energy intake, and diabetes).

selection bias (Chesnaye et al., 2022). The highest quintile (Q5) of PDIs representing the highest level of consumption was defined as the treatment group; other quintiles (Q1–Q4) were defined as the control group. Propensity scores were calculated based on the differences between the two groups. The inverse of the propensity scores was set as the weights. We used the weights to create a weighted population to account for selection bias. In the weighted population, the characteristics were equally distributed between the highest level of consumption (Q5) and the other (Q1–Q4) groups. Sixth, effect modification was tested for age or smoking status by including a multiplicative interaction term in the model. A *p*-value of <.05 suggested a significant interaction.

Variables with missing value for total study are education ($n = 43$; <1%), income ($n = 97$; 1.7%), dental visit ($n = 124$; 2.2%), diabetes ($n = 5$; <1%), and heart diseases ($n = 51$; <1%). We therefore carried out a complete case analysis since missing data were rare (<3%). All analyses used a cut-off *p*-value = .05 for statistical significance. Statistical analyses were performed using Python (Python Language Reference, version 3.9.7) and R Project for Statistical Computing (version 4.2.1).

3 | RESULTS

3.1 | Population characteristics

Table 1 presents the participant characteristics ($n = 5651$). The mean age was 57.73 (SD = 13.06) years, and 52.8% of the subjects were female. A total of 2841 (50.3%) participants were defined as having moderate/severe periodontitis. A positive correlation was found between PDI and hPDI scores ($r = 0.343$, Figure 2g). In addition, hPDI scores were negatively correlated to uPDI scores ($r = -0.109$, Figure 2h). However, there was no significant correlation between PDI and uPDI scores (Figure 2i). When the NHANES III population was grouped using the PDI quintiles (Table S3), a significantly graded decrease was observed in the body mass index, waist circumference, serum HDL cholesterol level, and serum glucose with increasing PDI scores (greater adherence to plant-based diets). Lower PDI scores were observed in older adults, males, African-American participants, current smokers, and those with low activity, no frequent dental visits, and diabetes. Individuals with higher PDI scores had less periodontal compromise and less gingival bleeding ($p_{trend} < .05$). In addition, the prevalence of periodontitis and antibody levels against periodontopathogens did not differ significantly between participants with different PDI quintiles. Tables S4 and S5 show the characteristics of participants in terms of hPDI and uPDI quintiles in the NHANES III dataset.

3.2 | Plant-based diet indices and clinical markers of periodontitis

In model 1, unadjusted odds ratio (OR) of periodontitis was 1.068 per one-unit increment in PDI *z*-score (95% confidence interval [CI]: 0.993–1.138). After multivariable adjustment (model 3), the PDI *z*-score was not statistically associated with periodontitis (Table 2). Moreover, the healthful degree of plant-based diets was measured by hPDI. The hPDI *z*-score exhibited a decreased risk of periodontitis (adjusted OR = 0.925; 95% CI: 0.860–0.995; see Table 2). In addition, higher uPDI represented less healthful plant-based diets. There was a positive association between uPDI *z*-score and periodontitis (adjusted OR = 1.100; 95% CI: 1.043–1.161; see Table 2). An unmeasured confounder was evaluated by *E*-values (Table S6). To explain the association between plant-based diets and periodontitis, an unmeasured confounder should have risk ratios ranging from 1.053 to 1.275.

3.3 | Hierarchical clustering antibodies of periodontopathogens

Unsupervised clustering analyses were performed separately because of a potential systematic difference in antibody levels between phase

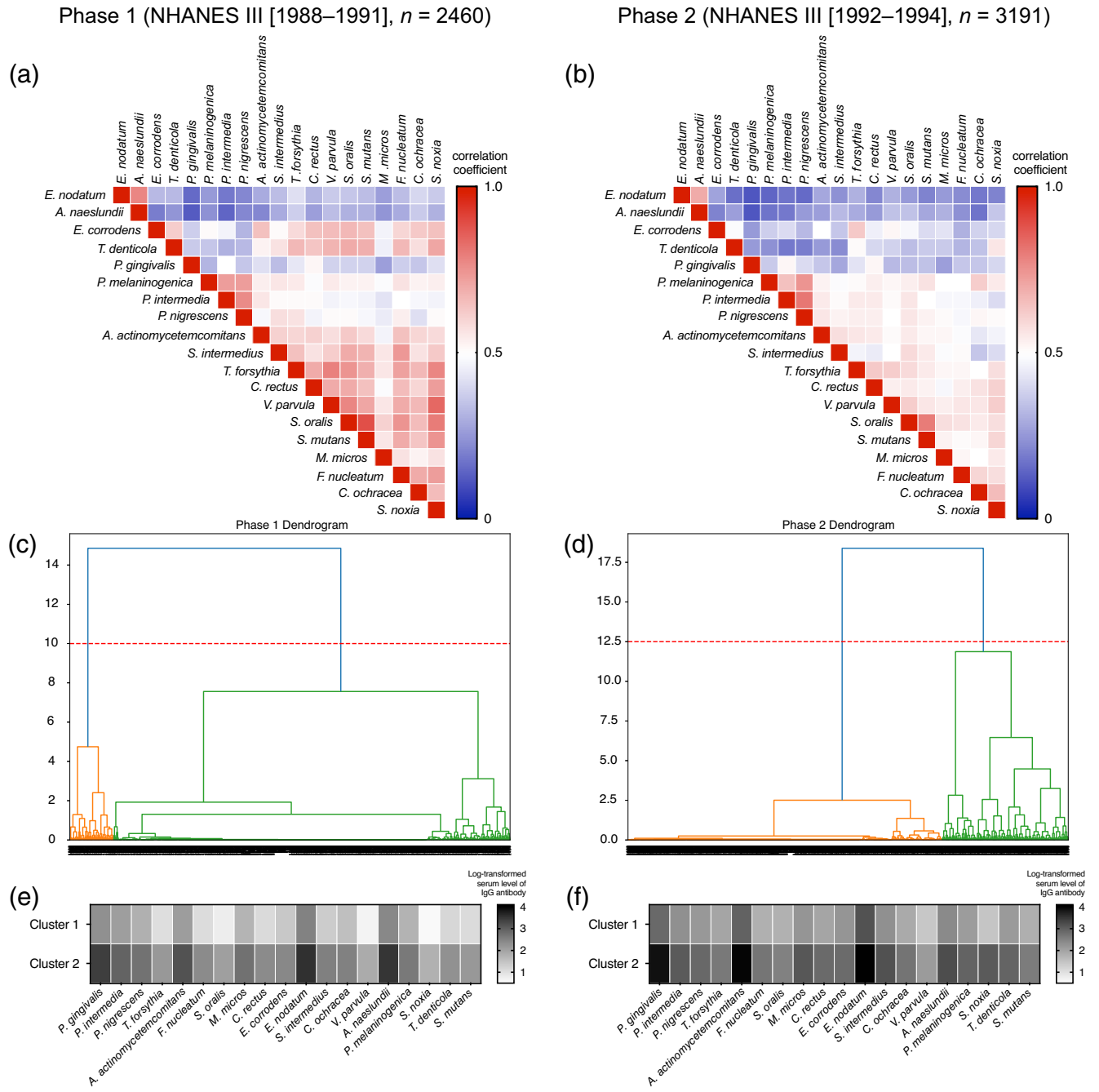

FIGURE 3 Unsupervised clustering periodontal bacterial markers. Spearman rank correlation matrices presenting the correlation coefficients of antibody levels against 19 periodontopathogens in The Third National Health and Nutrition Examination Survey (NHANES III) phase 1 (a) and phase 2 (b). Dendrogram of hierarchical clustering for NHANES III phase 1 (c) and phase 2 (d) participants based on antibody levels against periodontopathogens. Heatmap displaying antibody levels against periodontopathogens across two clusters among participants of NHANES III phase 1 (e) and phase 2 (f). IgG, immunoglobulin G. *P. melaninogenica*, *Prevotella melaninogenica*; *P. intermedia*, *Prevotella intermedia*; *P. nigrescens*, *Prevotella nigrescens*; *P. gingivalis*, *Porphyromonas gingivalis*; *T. forsythia*, *Tannerella forsythia*; *T. denticola*, *Treponema denticola*; *A. actinomycetemcomitans*, *Aggregatibacter actinomycetemcomitans*; *E. corrodens*, *Eikenella corrodens*; *S. noxia*, *Selenomonas noxia*; *V. parvula*, *Veillonella parvula*; *C. rectus*, *Campylobacter rectus*; *S. intermedius*, *Streptococcus intermedius*; *S. oralis*, *Streptococcus oralis*; *S. mutans*, *Streptococcus mutans*; *F. nucleatum*, *Fusobacterium nucleatum*; *P. micra*, *Parvimonas micra*; *C. ochracea*, *Capnocytophaga ochrace*; *E. nodatum*, *Eubacterium nodatum*; *A. naeslundii*, *Actinomyces naeslundii*.

1 and 2 samples. Spearman's rank correlation matrices showed positive correlations between antibodies to 19 periodontopathogens in phase 1 (Figure 3a) and phase 2 (Figure 3b). We obtained the dendrogram depicted in Figure 3c,d based on the hierarchical clustering. The

serum IgG antibody levels in cluster 2 were significantly higher than in cluster 1 in participants from either phase 1 or phase 2 (Figure 3e,f). Table S7 presents the detailed values. Thus, we pooled two hierarchical clustering subgroups together (cluster 1: $n = 1137$; cluster 2: $n = 4514$). These two clustering subgroups were regarded as binary outcomes in the following regression models.

3.4 | Plant-based diet indices and periodontal antibodies

Table 2 also shows the association between PDI/hPDI/uPDI *z*-scores and the clustering subgroups based on periodontal antibodies. In the unadjusted and adjusted models, the ORs for the PDI *z*-score were not statistically significant. In contrast, the hPDI *z*-score was positively associated with hierarchical cluster 2 (adjusted OR = 1.192; 95%CI: 1.112–1.278). An inverse association of the uPDI *z*-score with cluster 2 was found (adjusted OR = 0.834; 95% CI: 0.775–0.896; see Table 2). Based on the E-values, an unmeasured confounder would need to be associated with both plant-based diets and periodontal antibodies by a risk ratio of 1.091–1.418 (Table S6).

3.5 | Sensitivity analyses

First, we observed the inverse association of hPDI *z*-score with mean PPD, mean AL, and BOP (Table S8). In contrast, uPDI *z*-score was positively associated with these clinical markers of periodontitis (Table S8). No statistically significant association between PDI and the clinical markers was found. Second, the sensitivity analysis showed consistent results in terms of bacterial markers of periodontitis when hPDI and uPDI were treated as quintile groups (Table S9). Participants in the highest hPDI quintile had a higher likelihood of belonging to cluster 2 than those in the lowest quintile (adjusted OR = 1.579; 95% CI: 1.270–1.964). Compared with quintile 1, quintile 5 of uPDI was inversely associated with elevated antibodies against periodontopathogens (adjusted OR = 0.561; 95% CI: 0.442–0.711). Third, similar findings were observed using the 2018 periodontitis classification. These findings were consistent when dietary indices were treated as quintiles (Table S10). Fourth, we used Merchant's method to cluster 19 periodontal antibodies and generated four clustering scores in the sensitivity analyses (Table S11). There were positive associations of PDI and hPDI *z*-scores with the Yellow-Orange cluster, which loaded highly on *Streptococcus intermedius*, *S. oralis*, *S. mutans*, *Fusobacterium nucleatum*, *Parvimonas micra*, and *Chremistica ochracea* titers (adjusted β-coefficient = 0.060 [0.011–0.110] for PDI; 0.112 [0.062–0.161] for hPDI). In contrast, the uPDI *z*-score was inversely associated with the Yellow-Orange cluster (adjusted β-coefficient = −0.052 [−0.103 to −0.001]). Fifth, the results of the IPTW adjustment were largely similar to those of multivariable regression models (shown in Table S12). Sixth, the uPDI *z*-score was significantly associated with hierarchical cluster 2 in the elderly rather middle-aged adults (p for interaction = 0.012, Table S13). No significant smoking–plant-based diets interaction was found (Table S14).

4 | DISCUSSION

We found that greater adherence to healthful plant-based diets was associated with a lower risk of periodontitis in the U.S. population aged ≥40 years (OR = 0.925; 95% CI: 0.860–0.995). Conversely, adherence to unhealthful plant-based diets was associated with a higher periodontitis risk (OR = 1.100; 95% CI: 1.043–1.161). We did not observe any significant association for overall plant-based diets. The present study used an unsupervised approach to identify distinct clusters based on serum IgG antibodies against 19 periodontopathogens. Healthful plant-based diets were positively associated with elevated levels of periodontal antibodies (OR = 1.192; 95% CI: 1.112–1.278). In contrast, an inverse association between unhealthful plant-based diets and periodontal antibody levels was found (OR = 0.834; 95% CI: 0.775–0.896). Similar to clinical markers, overall plant-based diets were not significantly related to periodontal antibodies.

The protective effect of healthy plant-based dietary patterns on periodontal health can be explained by healthy whole-food components such as fibres, fruits, vegetables, whole grains, tea, and coffee. The food components of hPDI are generally similar to those of other plant-predominant diets such as the Mediterranean diet and dietary approaches to treat hypertension (Aleksandrova et al., 2021). Similar results were obtained concerning the impact of a Mediterranean diet on gingivitis (Bartha et al., 2022). In addition, a posteriori derived dietary patterns (characterized by high micronutrients and fibres) were inversely associated with periodontitis risk (Watson et al., 2022). A Mediterranean diet could reduce the bacterial abundance of periodontopathogens (*P. gingivalis*, *P. intermedia*, and *T. denticola*) in overweight subjects (Laiola et al., 2020). Khocht et al. showed differences in the levels of bacterial species between vegetarians and non-vegetarians in periodontally healthy individuals (Khocht et al., 2021). The species associated with gingival health were prominent in vegetarians. Increased levels of periodontal-health-related bacterial species were positively correlated with the anti-inflammatory cytokine IL-10 in vegetarians (Khocht et al., 2021). Nevertheless, immunomodulation by plant-based diets to promote periodontal health should be clarified through RCTs.

We grouped up serum IgG antibodies against periodontopathogens using cluster analyses. From a statistical perspective, analysing single IgG antibodies was prone to increase in the likelihood of type 1 error and false-positive results because of multiple comparisons (Wang et al., 2007). A European cohort study revealed no association between dietary factors and the total antibody levels against oral bacteria (Michaud et al., 2013). To this end, the total antibody level was calculated by summing up the antibody titers against 25 oral bacterial species. The conventional method assumes that all oral bacteria affect systemic outcomes similarly, instead of considering complex interactions between bacteria. In the present study, Spearman's rank correlation analysis showed positive interactions between 19 periodontal antibodies, which is consistent with a previous study (Shrestha et al., 2015) indicating that a sub-population might exist with a higher or lower overall antibody level. Although bacterial species have cooperation (or mutualism) and competition (or parasitism) (Palmer &

Foster, 2022), antibodies against periodontopathogens exhibit moderately positive interactions in terms of the immune response.

This study showed a positive association between adherence to healthful plant-based diets and higher overall antibodies. Conversely, unhealthful plant-based diets showed a reverse trend. Our findings suggest that the quality of plant-based diets might change the protective immune responses to the microbial challenge in periodontitis. We did not observe significant associations between overall plant-based diets and hierarchical clustering. However, caution should be exercised in interpreting the findings because higher antibody levels could also reflect an elevated bacterial burden (Goh et al., 2016). Moreover, healthful plant-based diets were positively associated with the Yellow-Orange cluster, with adherence to unhealthful plant-based diets being inversely associated with this cluster. This cluster contains *C. ochracea* related to periodontal health (Riep et al., 2009), indicating that unhealthy diets might decrease the protective effect of the Yellow-Orange cluster against periodontal lesions. A similar inverse association has been reported with alcohol intake (Merchant et al., 2017). Briefly, plant-based diets promote an immune response against periodontopathogens in the general population, possibly depending on the quality of plant foods.

Our findings have significant clinical relevance and public health implications. We applied dietary pattern analyses rather than individual nutrients or foods. Index-based dietary patterns are highly recommended to investigate the potential synergistic and interactive effects of foods (Hu, 2002). Of note, PDIs focus on the amount and healthiness of plant foods. PDI negatively scored all animal foods (e.g., dairy products, poultry, and fish) that could benefit periodontal health (Lee & Kim, 2019; O'Connor et al., 2020; Ottosson et al., 2022). Higher protein intake might improve healing after periodontal treatment in non-smoking patients (Dodington et al., 2021). Excluding animal foods may lead to vitamin B_{12} deficiency (Rizzo et al., 2016), increasing the progression and risk of periodontitis (Zong et al., 2016). Adjunctive use of fish-derived omega-3 fatty acids would promote periodontal wound healing in the treatment of periodontitis (Chee et al., 2016; Kruse et al., 2020). At the same time, vegetarian/vegan diets can be supplemented by essential nutrients (e.g., carnosine, creatine, vitamin B12, and omega-3 fatty acids). From a macroscopic perspective of planetary health, plant-based diets tend to have less environmental pollution than animal-based diets (Hemler & Hu, 2019). Meat is the food with the most significant impact on land usage and greenhouse gas (GHG) emissions (Nelson et al., 2016). In the present study, the association of plant-based diets with periodontal antibodies was more substantial in the elderly. These people might be an optimal target population for dietary intervention to prevent the onset and progression of periodontitis. In summary, plant-based diets tend to incorporate abundant fruits, vegetables, nuts, and legumes and limit sugar and processed meat. Such diets could provide adequate nutrients, improve periodontal and general health, and protect the environment by reducing GHG emissions and the use of cropland and freshwater.

The present study had several strengths. To the best of our knowledge, this is the first population-based study to reveal that the quality or healthiness of plant-based diets significantly improves the clinical and bacterial markers of periodontitis. In addition, the observed relationship persisted after comprehensive adjustment for potential confounders. Several sensitivity analyses also made the findings robust and strengthened our analyses. However, several limitations should be considered. First, the NHANES III data were not the latest (i.e., 1988–1994); however, this did not affect the aetiological plausibility of the relationship between dietary patterns and serum antibodies. Second, NHANES III used a partial-mouth periodontal examination protocol, which has been reported to underestimate periodontitis prevalence (Eke et al., 2010). Although we used the half-reduced CDC/AAP case definition to minimize bias, the findings warrant further replication in future studies using full-mouth periodontal examinations. Third, PDIs, as a priori dietary patterns, are limited by the current knowledge of the diet–health association. For example, not all potato meals are unhealthy; chilling and reheating potatoes can increase the amount of resistant starch that can promote health, similar to insoluble dietary fibres (Alzaabi et al., 2020). Moreover, the quintiles of food groups in the PDI scoring system are somewhat arbitrary, and percentiles might capture more details and differences in PDI/hPDI/uPDI. Although the FFQ has been reported to highly correlate with the probability of consumption on 24-h recalls in the NHANES dataset (Subar et al., 2006), the absence of portion size in the FFQ might result in the misclassification of dietary intake. Future studies should validate the calculation of PDIs. Fourth, the cross-sectional study design for this study was not the best design for determining temporal and causal relationships. It is reported that a cross-sectional study is not inferior to a prospective or retrospective cohort study when using causal diagrams and controlling bias well (Shahar & Shahar, 2013). A cross-sectional study may provide insights into inferring causality (Savitz & Wellenius, 2022). Hence, this study used the IPTW method to control selection bias. Certainly, dietary intervention studies with long-term follow-ups are necessary to confirm the protective effect of healthful plant-based diets on periodontitis. Fifth, there is a possibility of residual confounding factors. Given that the *E*-values were less than two, unmeasured confounders could explain away the observed associations.

5 | CONCLUSION

Overall, PDI was not associated with the clinical parameters and antibacterial antibodies of periodontitis in U.S. adults aged ≥40 years. There was an inverse association between healthy plant-based diets and periodontitis. In contrast, periodontitis risk increased with a diet containing less healthy plant foods. Our findings support dietary guidelines emphasizing a higher intake of healthy plant foods (whole foods) and fewer unhealthy plant foods (processed foods) for periodontal health. Further interventional studies and experimental research are warranted to identify the impact of high-quality plant-based diets on periodontopathogens and explore the biological mechanisms of promoting periodontal health.

AUTHOR CONTRIBUTIONS

An Li was responsible for study conception and design, statistical analyses, data interpretation, and drafting the manuscript. Bingjiang Qiu contributed to study conception, study design and statistical analyses and critically reviewed manuscript. Marjolein Goettsch contributed to study conception and design and critically reviewed manuscript. Yuntao Chen, a statistical consultant, contributed to statistical analyses and critically reviewed manuscript. Shaohua Ge contributed to the study conception, study design and data interpretation and critically reviewed manuscript. Shulan Xu contributed to the study conception and design, data interpretation and drafting manuscript.s Geerten-Has E. Tjakkes contributed to the study conception and design, data interpretation, and critically reviewing manuscript. All authors gave final approval and agreed to be accountable for all aspects of this work to ensure integrity and accuracy.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in National Health and Nutrition Examination Survey (NHANES) at https://www.cdc.gov/nchs/nhanes/index.htm. These data were derived from the following resources available in the public domain: - NHANES III, https://wwwn.cdc.gov/nchs/nhanes/nhanes3/default.aspx

ETHICS STATEMENT

Ethical approval was not required.

ORCID

An Li https://orcid.org/0000-0001-5750-526X
Shaohua Ge https://orcid.org/0000-0003-3821-5480
Shulan Xu https://orcid.org/0000-0002-5706-3526

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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