RESEARCH



Association of periodontitis, tooth loss, and self-rated oral health with circadian syndrome in US adults: a cross-sectional population study

Yibo Li^{1,2†}, Yuhao Liu^{3†}, Tao Yin⁴, Mi He⁵, Changyun Fang⁵, Xiong Tang⁶, Shifang Peng^{7*} and Yundong Liu^{8*}

Abstract

Background This study was to investigate associations of periodontitis, tooth loss and self-rated oral health with circadian syndrome.

Methods Data regarding periodontitis, dentition, oral health questionnaire and circadian syndrome of 30–85 years old participants from US National Health and Nutrition Examination Survey 2005–2020 were analyzed. Periodontitis questions for periodontitis and dentition status were validated. Weighted multivariable logistic regression analyses were used.

Results Weighted prevalence of circadian syndrome and stage II-IV periodontitis was 33.29% and 88.87%, respectively. When compared with stage I periodontitis, stage II periodontitis was significantly associated with greater circadian syndrome prevalence after adjustment (odds ratio (OR) and 95% confidence interval (CI): Stage II: 1.35 (1.03, 1.76), P=0.032; Stage III: 1.30 (0.97, 1.73), P=0.069; Stage IV: 1.17 (0.82, 1.65), P=0300). Stage II periodontitis was significantly associated with greater prevalence of lower high-density lipoprotein cholesterol (HDL) and elevated triglycerides and stage III and stage IV periodontitis were significantly associated with greater hypertension prevalence. A 1 tooth increase in the number of missing teeth was associated with a 1% increase in circadian syndrome and its components of obesity, elevated fasting plasma glucose (FPG) and short sleep. Poor or fair self-rated oral health showed a specificity of > 70% for periodontitis and lack of functional dentition. Meanwhile, poor or fair self-rated oral health had relatively higher levels of sensitivity for stage II-IV periodontitis (35%), stage III-IV periodontitis (46%), stage IV periodontitis (60%) and lacking functional dentition (56%). When compared to excellent self-rated oral health, good, fair and poor self-rated oral health were significantly associated with higher circadian syndrome prevalence (OR and 95% CI: Very good: 1.13 (0.97, 1.32), P=0.120; Good: 1.34 (1.14, 1.57), P<0.001; Fair: 1.41 (1.16, 1.71), P=0.001; Poor: 1.63 (1.32, 2.03), P<0.001). Additionally, participants with worse self-rated oral health had significantly higher prevalence of elevated FPG, hypertension, low HDL, elevated triglycerides, short sleep and depression.

[†]Yibo Li and Yuhao Liu contributed equally to this work.

*Correspondence: Shifang Peng pengsfxy@sina.com Yundong Liu Iydxjtu@163.com Full list of author information is available at the end of the article



© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

Conclusions Periodontitis, tooth loss and worse self-rated oral health were associated with circadian syndrome in US adults. Self-rated oral health may be a simple question to indicate oral and systemic health.

Keywords Circadian syndrome, Periodontitis, Tooth loss, Self-rated oral health, Sleep hour, Depression, National Health and Nutrition Examination Survey (NHANES)

Introduction

The circadian clock is a timekeeper molecular system found in all cells and organs [1, 2]. Recently, the circadian rhythm alteration was recognized to be closely associated with chronic neuropsychiatric diseases of anxiety, depression and sleep disorders as well as type 2 diabetes and cardiovascular disease [2, 3]. The well-known concept of metabolic syndrome included five components: central obesity, high blood pressure, increased fasting plasma glucose (FPG), elevated triglycerides (TG), and lower high-density lipoprotein cholesterol (HDL) [4]. Individuals with \geq 3 above-mentioned components were diagnosed as metabolic syndrome patients. Considering the tight connection between circadian disruption and sleep disorder, depression and the various components of metabolic syndrome [3], some researchers have proposed the new concept of circadian syndrome [5, 6]. Circadian syndrome added another two components of depression and short sleep to represent a cluster of circadian disruption associated risk factors for cardiovascular disease [6]. Consequently, recent investigations have suggested that circadian syndrome is a good predictor for cardiovascular disease [6-8], stroke [9] and cognition impairment [10]. Furthermore, circadian syndrome is even better to predict cardiovascular diseases than the previous metabolic syndrome [6, 8].

Dental caries and periodontitis are the most common oral diseases and the main causes of tooth loss [11, 12]. Chronic periodontitis and apical periodontitis could destruct epithelial barrier and thus permit oral microbiome to spread to blood and the distant organs [13-15]. Consequently, recent investigations indicated periodontitis, apical periodontitis and tooth loss were associated with elevated systemic inflammation, components of metabolic syndrome and cardiovascular diseases [16-27]. Even though there were some controversies about the association between periodontitis and short sleep [28–31], the majority of reports found the close relationship between tooth loss and short sleep [29, 31–35]. Moreover, several researches have suggested the tight link between periodontitis, root canal Endotoxin, tooth loss and depressive symptoms [36-48]. Particularly, longitudinal studies suggested tooth loss causally increased depression prevalence [37, 39, 40]. Recently, Yu et al. reported that self-rated oral health status was as good as periodontal disease in predicting systemic comorbidities [49]. They further found fair or poor self-reported oral health was associated with increased cardiovascular diseases [49]. Self-rated oral health questionnaire is straightforward means to measure oral health status in large population studies. However the association of periodontitis, tooth loss and self-rated oral health with circadian syndrome has not been sufficiently reported.

The present study therefore aimed to investigate the associations of periodontitis, tooth loss and self-rated oral health with circadian syndrome in a nationally representative sample by analyzing data from the National Health and Nutrition Examination Survey (NHANES) 2005–2020 cycles. The hypothesis was that having more severe periodontitis, more missing teeth, and worse self-rated oral health would be associated with higher circadian syndrome prevalence.

Material and methods

Study design and population

The Centers for Disease Control and Prevention examined the health and nutrition condition of a representative United States population in 2-year cycles using a complex multistage sampling design. As the NHANES 2005-2020 cycles had all the components of circadian syndrome assessment, dentition examination and self-rated oral questionnaire, the data of the NHANES 2005-2020 cycles were extracted for the current crosssectional study. Figure 1 shows the screening process of the two subsamples. Because NHANES 2009-2014 cycles had periodontal data and six periodontitis questions for >30 year old participants but did not have work schedule data, the first subsample was extracted from NHANES 2009-2014 cycles to validate the periodontitis questions and to investigate the association of periodontitis with circadian syndrome. The inclusion criteria for the first subsample were participants aged ≥ 30 years with all the components of circadian syndrome and complete periodontal parameters. The exclusion criteria for the first subsample were participants aged <30 and those without complete circadian syndrome and periodontal data (Fig. 1). Because NHANES 2005-2010 and NHANES 2017-2020 cycles had work schedule data, dentition examination, self-rated oral health question, and circadian syndrome data, so the second subsample was extracted from NHANES 2005-2010 and NHANES 2017–2020 cycles. The inclusion criteria for the second



Fig. 1 Flow diagram of the screening of study participants. Abbreviation: NHANES, National Health and Nutrition Examination Survey

subsample were participants aged \geq 30 years with complete date regarding work schedule, dentition, selfrated oral health question, and circadian syndrome. The exclusion criteria for the second subsample were participants aged < 30 and those without complete data on work schedule, dentition, self-rated oral health question, and circadian syndrome (Fig. 1). The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines of the Enhancing the QUAlity and Transparency Of health Research (EQUA-TOR) network. This study adhered to the Declaration of Helsinki. Written informed consent was obtained from all NHANES participants, and all the data collection and procedures were approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board. In the present study, data collection included questionnaires, interviews, physical examinations, and laboratory tests. In general, questionnaire and interview were carried out in participant' home, while physical examinations and blood specimen collection were performed at mobile examination center (MEC). The original data and more details were accessed on the NHANES website (https://wwwn.cdc.gov/nchs/nhanes/Default.aspx).

Circadian syndrome assessment

MEC participants were eligible for the evaluation of all the components of circadian syndrome in the NHANES 2005–2020 cycles. According to the diagnostic criteria reported in the previous studies [6, 8, 50], circadian syndrome was diagnosed if the participant had ≥ 4 of the following components: (1). Decreased sleep duration was defined as self-reported sleep duration <6 h/ day; (2). Depression symptom was defined as the score of Patient Health Questionnaire (PHQ-9) \geq 5; (3). Central obesity was defined as waist circumference ≥ 102 cm for males and waist circumference ≥ 88 cm for females; (4). Hypertension was defined as systolic blood pressure \geq 130 mmHg or diastolic blood pressure \geq 85 mmHg or the use of antihypertension drugs; (5). Increased FPG was defined as FPG $\geq 100 \text{ mg/dL}$ or the use of antidiabetic drugs; (6). Increased TG was defined as TG \geq 150 mg/dL or the use of lipid-lowering drugs; (7). Decreased HDL was defined as HDL <50 mg/dL for females and HDL <40 mg/dL for males or the use of lipid-lowering drugs. Sleep duration was extracted from the question: "How much sleep do you usually get at night on weekdays or workdays?" (Supplemental file 1). PHQ-9 included 9 questions to assess the depression status (Supplemental file 1). The scores for each question were: 0 for not at all, 1 for several days, 2 for more than half the days and 3 for nearly every day. The total PHQ-9 score of \geq 5 was defined as the presence of depressive symptoms. Central obesity was determined by waist circumference measurement. Elevated FPG, elevated TG and lower HDL were based on laboratory test and past history.

Periodontal examination

In NHANES 2009–2014, \geq 30 years old adults were eligible for full-mouth six sites periodontal examination. The current study adopted the 2018 World Workshop Classification of Periodontal and Peri-implant Diseases to determine periodontitis stages [51, 52]. According to this algorithm, periodontitis stages were determined from clinical attachment loss (CAL), periodontal pocket depth

(PPD) and the number of lost teeth. First, periodontitis was diagnosed if the interdental CAL was $\geq 1 \text{ mm in} \geq 2$ non-adjacent teeth or if CAL was $\geq 3 \text{ mm}$ and PPD was > 3 mm in the buccal/lingual sites of ≥ 2 teeth. Then, the maximum CAL of 1–2 mm was diagnosed as stage I periodontitis; 3–4 mm as stage II periodontitis; $\geq 5 \text{ mm}$ as stage III/IV periodontitis. Lastly, PPD and the number of lost teeth were further taken into consideration. Stage II periodontitis with maximum PPD $\geq 6 \text{ mm}$ was classified into stage III periodontitis. Stage III periodontitis with remaining teeth < 20 was classified into stage IV.

Dental examination

Participants were eligible to undergo dental examination in the 2005–2020 cycles of NHANES. All oral examinations were conducted by trained dentists in the MEC. Data regarding the third molars were excluded. "Tooth not present" was defined as missing tooth. The retention of \geq 20 teeth was deemed as a functional dentition, whereas the loss of >8 teeth was deemed as lack of functional dentition [53].

Oral health questionnaire

NHANES collected some periodontitis questions including gum disease, self-rated oral health status, periodontal treatment, loose teeth, bone loss and teeth not right (Supplemental file 1) [49]. The questionnaire was performed by trained interviewers using Computer-Assisted Personal Interview (CAPI) system. Gum disease was extracted from the answer to the question: "Gum disease is a common problem with the mouth. People with gum disease might have swollen gums, receding gums, sore or infected gums or loose teeth. Do you think you might have gum disease?" Self-reported oral health status was extracted from the answer to the question: "Overall, how would you rate the health of your teeth and gums?" Periodontal treatment was extracted from the answer to the question: "Have you ever had treatment for gum disease such as scaling and root planing, sometimes called "deep cleaning"?" Loose tooth was extracted from the answer to the question: "Have you ever had any teeth become loose on their own, without an injury?" Bone loss was extracted from the answer to the question: "Have you ever been told by a dental professional that you lost bone around your teeth?" Teeth not right was extracted from the answer to the question: "During the past three months, have you noticed a tooth that doesn't look right?" (Supplemental file 1).

Covariate assessments

Participants' demographic data including age, gender, race, family Poverty income ratio (PIR), marital status and education levels were obtained by standardized questionnaires. PIR was defined as the total family income divided by the threshold set by the Department of Health and Human Services poverty guideline, which is specific to family size, calendar year, and state. Current smokers were defined as smoking cigarettes now. Former smokers were defined as having smoked at least 100 cigarettes in life but not smoking cigarettes now. Never smokers were defined as having not smoked at least 100 cigarettes in life. Drinking status were extracted from the question: "During the past 12 months, about how often did you drink any type of alcoholic beverage?" The assessment of dietary quality adopted Healthy Eating Index-2020 (HEI-2020) using the two set of 24-h dietary questionnaire data in NHANES. In the present study, high dietary quality was defined as respondent's Healthy Eating Index-2020 score greater than the 60 th percentile [54]. Participants' work and recreational activities were extracted from the Physical Activity questionnaire. Work condition, work schedule and working hours were extracted from the Occupation Questionnaire (Supplemental file 1). Work schedule was divided as regular daytime work and shift work. Regular daytime work was defined as "traditional 9 AM to 5 PM day" or "a regular daytime schedule". Shift work was defined as "a regular evening shift" or "a regular night shift" or "a rotating shift" or "early mornings" or "another schedule" or "Variable" (Supplemental file 1).

Statistics

Weights were used to consider the planned oversampling of specific groups according to NHANES. Descriptive data were shown as means ± standard deviation for continuous variables or frequencies (weighted proportions) for categorical variables. Weighted chi-square tests (categorical variables) and weighted linear regression models (continuous variables) were used to compare baseline clinical data. For missing data in covariates, a missing indicator category was coded for categorical variables, and the median was imputed for continuous variables. epiR package was used to determine the sensitivity and specificity between the six periodontitis questions and different clinical statuses including stage II-IV periodontitis, stage III-IV periodontitis, stage IV periodontitis and lack of functional dentition. Weighted multivariable logistic regression analyses were then used to analyze the associations of periodontitis stages, the number of missing teeth, and self-rated oral health with circadian syndrome and its seven components. Confounding variables were considered from three aspects: clinical relevance, P< 0.05 in the univariate analysis, and the sufficient event data to perform a regression model. Statistical software programs (RStudio 2023.12.1+402; Posit Software and

IBM SPSS Statistics for Windows, v21.0; IBM Corp) were used for statistical analyses ($\alpha = 0.05$).

Results

Baseline data

The present study finally included the first subsample of 9164 US 30-85 years old participants including periodontitis data and the second subsample of 15,966 US 30-85 years old participants including tooth loss and self-rated oral health data (Fig. 1). Table 1 and Supplemental Table 1 present the results of the comparison of the demographic, clinical, and dental characteristics according to circadian syndrome and periodontitis stage respectively. The weighted prevalence of circadian syndrome and stage II-IV periodontitis was 33.29% and 88.87%, respectively. The participants with circadian syndrome were more likely to be older, widowed/divorced/ separated, former smokers, and non-drinkers. These individuals were more likely to have lower levels of education, income, activities and dietary quality; moreover, the prevalence of taking medicines was higher in these participants. Furthermore, these individuals were less likely to had regular daytime work but were more likely to be retired and unable to work. Lastly, these individuals had fewer remaining teeth, and lower levels of self-rated oral health status (Table 1).

Validation of periodontitis questions

Tables 2 demonstrates the validations of the six periodontitis questions for stage II-IV periodontitis, stage III-IV periodontitis, stage IV periodontitis and lack of functional dentition. All the six periodontitis questions including gum disease, poor or fair self-rated oral health, periodontal treatment, loose teeth, bone loss and teeth not right showed a specificity of >70%. However, the sensitivity range for gum disease, periodontal treatment, loose teeth, bone loss and teeth not right was only 14% to 30%. The poor or fair self-rated oral health had relatively higher levels of sensitivity for stage II-IV periodontitis (35%), stage III-IV periodontitis (46%), stage IV periodontitis (60%) and not having functional dentition (56%) (Table 2). Notably, the sensitivity levels decreased with higher educational levels and increased with depression, but the specificity levels increased with higher educational levels and decreased with depression (Supplemental Table 2).

Association of periodontitis with circadian syndrome

Table 3 showed the analyses of the associations of periodontitis stage with circadian syndrome. When compared to participants with stage I periodontitis, stage II periodontitis was significantly associated with greater circadian syndrome prevalence in the fully adjusted multivariable logistic regression model (odds ratio (OR) and 95% confidence interval (CI): Stage II: 1.35 (1.03, 1.76), P = 0.032; Stage III: 1.30 (0.97, 1.73), P = 0.069; Stage IV: 1.17 (0.82, 1.65), P = 0300) (Table 3). Furthermore, stage II periodontitis was significantly associated with greater prevalence of lower HDL and elevated TG and stage III and stage IV periodontitis were significantly associated with hypertension prevalence in the fully adjusted model (Table 3).

Association of the number of missing teeth with circadian syndrome

Table 4 showed the analyses of the associations of the number of missing teeth with circadian syndrome. After adjusting confounders, a 1 tooth increase in the number of missing teeth was associated with a 1% increase in the prevalence of circadian syndrome and its components of obesity, elevated FPG and short sleep (OR and 95% CI: circadian syndrome: 1.01 (1.01, 1.02), P < 0.001; obesity: 1.01 (1.00, 1.02), P = 0.010; elevated FPG: 1.01 (1.01, 1.02), P < 0.001; obesity: 1.01 (1.00, 1.02), P = 0.010; elevated FPG: 1.01 (1.01, 1.02), P < 0.001; short sleep: 1.01 (1.01, 1.02), P = 0.001) (Table 4).

Association of self-rated oral health status with circadian syndrome

As the question of self-rated oral health had relatively higher levels of sensitivity and specificity for periodontitis and functional dentition, the association of self-rated oral health status with circadian syndrome were further studied (Table 5). When compared to the excellent self-rated oral health, very good self-rated oral health was not significantly associated with higher circadian syndrome prevalence but good self-rated oral health, fair self-rated oral health and poor self-rated oral health were significantly associated with greater circadian syndrome prevalence in the multivariable logistic regression model (OR and 95% CI: Very good: 1.13 (0.97, 1.32), P = 0.120; Good: 1.34 (1.14, 1.57), P< 0.001; Fair: 1.41 (1.16, 1.71), P = 0.001; Poor: 1.63 (1.32, 2.03), *P* < 0.001) (Table 5). In addition, when the excellent self-rated oral health participants were the reference group, participants with worse self-rated oral health had significantly higher prevalence of components of circadian syndrome including elevated FPG, hypertension, lower HDL, elevated TG, short sleep and depression (Table 5). Specifically, worse self-rated oral health was positively associated with higher depression prevalence after adjusting the confounders (OR and 95% CI: Very good: 1.35 (1.10, 1.65), *P* = 0.006; Good: 1.53 (1.27, 1.84), P < 0.001; Fair: 2.06 (1.70, 2.50), P < 0.001; Poor: 2.55 (2.06, 3.16), *P* < 0.001) (Table 5).

Variables	Overall (<i>N</i> = 15,966)	Without circadian syndrome (N= 9939)	Circadian syndrome (<i>n</i> = 6027)	Р
Sex				0.309
Female	7896 (50.95%)	4796 (50.52%)	3100 (51.80%)	
Male	8070 (49.05%)	5143 (49.48%)	2927 (48.20%)	
Age (years)	52.18 ± 13.98	49.50 ± 13.41	57.56 ± 13.55	< 0.001
Race				0.402
Non-Hispanic White	7501 (71.96%)	4623 (71.66%)	2878 (72.54%)	
Non-Hispanic Black	3374 (9.78%)	2093 (9.62%)	1281 (10.10%)	
Mexican American	2383 (7.11%)	1487 (7.32%)	896 (6.69%)	
Other Hispanic	1430 (4.89%)	873 (4.97%)	557 (4.73%)	
Other	1278 (6.26%)	863 (6.43%)	415 (5.93%)	
Education				< 0.001
< High school	3909 (15.71%)	2179 (13.85%)	1730 (19.45%)	
High school	3739 (24.42%)	2176 (22.12%)	1563 (29.03%)	
> High school	8304 (59.82%)	5578 (64,00%)	2726 (51.46%)	
Marital status				< 0.001
Married/Cohabiting	10.247 (69.72%)	6611 (71,72%)	3636 (65.70%)	
Never married	1652 (8.94%)	1127 (9.71%)	525 (7.39%)	
Widowed/Divorced/Separated	4058 (21 29%)	2196 (18 52%)	1862 (26.82%)	
Family PIR	1000 (2112970)	2190 (10.0270)	1002 (20102,0)	< 0.001
< 1 3	3912 (15 29%)	2203 (13 48%)	1709 (18 92%)	
1 3-3 5	5586 (32 54%)	3369 (30 76%)	2217 (36 12%)	
> 3 5	5052 (45 51%)	3478 (49 22%)	1574 (38.07%)	
Smoking status	5652 (15.5176)	5176(15.2270)	137 1 (30.0770)	< 0.001
Nonsmokers	8350 (52 58%)	5469 (55 15%)	2881 (47 42%)	< 0.001
Former smokers	4433 (28.18%)	2460 (25 76%)	1973 (33.02%)	
Current smokers	3178 (19 22%)	2007 (1907%)	1171 (19 52%)	
Drinking status	5170(15.2270)	2007 (19.0770)	1171 (19.5270)	< 0.001
Never drinking in the past year	5301 (27 38%)	2877 (23.86%)	2424 (34 43%)	. 0.001
Drinking in the past year	10.644 (72.54%)	7054 (76 11%)	3590 (65 39%)	
Vigorous activity	5385 (37 92%)	3882 (43.47%)	1503 (26 78%)	< 0.001
Moderate activity	9540 (65 48%)	6281 (68.67%)	3259 (59 11%)	< 0.001
High dietary quality	6144 (38 72%)	3894 (39.88%)	2250 (36 39%)	0.007
Working condition and schedule	0111(30.7270)	5051(55.0070)	2250 (50.5576)	< 0.002
Begular daytime work	5682 (44 64%)	4222 (50 59%)	1460 (32 71%)	< 0.001
Shift work	3202 (19.92%)	2222 (30.39%)	980 (17 39%)	
Betired	3721 (18 30%)	1735 (13 56%)	1986 (28.06%)	
Unable to work/Disabled	1464 (6 55%)	558 (3.82%)	906 (12 0.2%)	
Not working / ooking for work	1404 (0.55%)	1202 (10.84%)	605 (0.82%)	
Working bours	1057 (10.5070)	1202 (10.0470)	0,02,00	< 0.001
< 40 h	12724 (7360%)	7575 (70 98%)	51/19 (79 13%)	< 0.001
> 10 h	3235 (26 2006)	7373 (78.98%)	877 (20.87%)	
Zaking modicings	10 152 (62 0204)	2000 (20.99%)	5071 (20.07 <i>%</i>)	< 0.001
Solf-reported and health	10,155 (05.05%)	5002 (52.50%)	5071 (04.0170)	< 0.001
Evcollopt	10/3 (1/ 66%)	1318 (15 02%)	625 (12 15%)	< 0.001
Very good	3061 (22 0504)	2077 (2/ 4104)	023 (12.1370)	
Good	5760 (32 6104)	2077 (24.4170)	1085 (37 3704)	
Fair	3501 (12 6204)	2273 (JS.2370) 2154 (17 8704)	1/37 (20 1504)	
Poor	2111 (10.0200)	21JH (17.0770) 1115 (0 E00/)	(20.1370)	
1001	2111 (10.20%)	1113 (0,30%)	770 (IJ.0170)	

Table 1 Comparison of demographic and clinical characteristics of NHANES participants with and without circadian syndrome

Table 1 (continued)

Variables	Overall (<i>N</i> = 15,966)	Without circadian syndrome (N= 9939)	Circadian syndrome (<i>n</i> = 6027)	Ρ
Number of lost teeth	5.17 ± 7.80	4.03 ± 6.82	7.44 ± 9.03	< 0.001
Obesity	9864 (60.01%)	4605 (45.71%)	5259 (88.67%)	< 0.001
Elevated FPG	6191 (33.97%)	2086 (18.43%)	4105 (65.12%)	< 0.001
Hypertension	8527 (47.00%)	3584 (30.55%)	4943 (79.98%)	< 0.001
Low HDL	7252 (42.91%)	2197 (22.26%)	5055 (84.29%)	< 0.001
Elevated TG	8109 (49.07%)	2868 (29.41%)	5241 (88.47%)	< 0.001
Short sleep	2277 (12.05%)	935 (8.00%)	1342 (20.18%)	< 0.001
Depression	3838 (22.27%)	1563 (14.99%)	2275 (36.87%)	< 0.001

Data were shown as means ± standard deviation for continuous variables or frequencies (weighted proportions) for categorical variables. Weighted chi-square tests (categorical variables) and weighted linear regression models (continuous variables) were used to compare baseline clinical data. Missing data for variables: education levels (0.04%), marital status (0.06%), family PIR (6.66%), smoking status (0.03%), drinking status (0.08%), dietary quality (10.86%), physical activity (0.02%), working hours (0.02%) and taking medicines status (0.05%). Significant values are shown in bold

Abbreviations: NHANES National Health and Nutrition Examination Survey, PIR Poverty income ratio, FPG Fasting Plasma Glucose, HDL High-density lipoprotein cholesterol, TG triglycerides

Table 2 Question sensitivity and specificity

Questions	Stage II-IV	Stage III-IV	Stage IV	Without functional dentition
Gum disease ($N = 897$)	3)			
Sensitivity	0.20 (0.19, 0.21)	0.27 (0.26, 0.28)	0.27 (0.25, 0.30)	0.24 (0.22, 0.26)
Specificity	0.92 (0.90, 0.94)	0.87 (0.86, 0.88)	0.82 (0.81, 0.83)	0.82 (0.81, 0.83)
Self-rated oral health ^a	(N=9088)			
Sensitivity	0.35 (0.34, 0.36)	0.46 (0.44, 0.47)	0.60 (0.57, 0.63)	0.56 (0.53, 0.58)
Specificity	0.85 (0.82, 0.87)	0.77 (0.75, 0.78)	0.70 (0.69, 0.71)	0.97 (0.97, 0.98)
Periodontal treatment	(N = 9071)			
Sensitivity	0.25 (0.24, 0.26)	0.29 (0.27, 0.30)	0.27 (0.25, 0.30)	0.26 (0.24, 0.28)
Specificity	0.84 (0.82, 0.87)	0.79 (0.78, 0.80)	0.76 (0.75, 0.77)	0.76 (0.75, 0.77)
Loose teeth ($N = 9094$)			
Sensitivity	0.16 (0.16, 0.17)	0.25 (0.24, 0.27)	0.40 (0.37, 0.43)	0.34 (0.32, 0.37)
Specificity	0.94 (0.92, 0.95)	0.93 (0.92, 0.93)	0.88 (0.87, 0.89)	0.89 (0.88, 0.89)
Bone loss (<i>N</i> = 9049)				
Sensitivity	0.14 (0.13, 0.15)	0.18 (0.17, 0.20)	0.23 (0.21, 0.26)	0.21 (0.19, 0.23)
Specificity	0.95 (0.94, 0.97)	0.91 (0.90, 0.92)	0.88 (0.88, 0.89)	0.89 (0.88, 0.89)
Teeth not right ($N = 90$	091)			
Sensitivity	0.18 (0.17, 0.19)	0.24 (0.22, 0.25)	0.30 (0.27, 0.33)	0.27 (0.25, 0.29)
Specificity	0.90 (0.88, 0.92)	0.88 (0.87, 0.89)	0.84 (0.84, 0.85)	0.85 (0.84, 0.85)

^a indicates the sensitivity and specificity test between fair and poor self-rated oral health status and different clinical statuses including stage II-IV periodontitis, stage III-IV periodontitis, stage III-IV periodontitis, stage IV periodontitis and lack of functional dentition

Discussion

In this study, more severe periodontitis was associated with higher circadian syndrome prevalence and its components of lower HDL, elevated TG and hypertension, while the number of missing teeth was associated with greater prevalence of circadian syndrome and its components of obesity, elevated FPG and short sleep. The question of self-rated oral health had relatively higher levels of sensitivity and specificity for periodontitis and functional dentition. Participants with worse self-rated oral health had significantly higher prevalence of circadian syndrome and circadian syndrome components including elevated FPG, hypertension, lower HDL, elevated TG, short sleep and depression. The hypotheses were therefore accepted.

Periodontitis stage	Model 1		Model 2		Model 3	
	OR (95% CI)	Р	OR (95% CI)	Р	OR (95% CI)	Р
Circadian syndrome						
Stage I (<i>n</i> = 806)	1.00		1.00		1.00	
Stage II (<i>n</i> = 4224)	1.38 (1.10, 1.73)	0.006	1.30 (1.03, 1.64)	0.030	1.35 (1.03, 1.76)	0.032
Stage III (<i>n</i> = 2944)	1.42 (1.12, 1.80)	0.005	1.19 (0.92, 1.55)	0.200	1.30 (0.97, 1.73)	0.069
Stage IV (n = 1190)	1.71 (1.27, 2.31)	< 0.001	1.14 (0.84, 1.54)	0.400	1.17 (0.82, 1.65)	0.300
Obesity						
Stage I (<i>n</i> = 806)	1.00		1.00		1.00	
Stage II (n = 4224)	1.23 (0.98, 1.54)	0.070	1.21 (0.95, 1.53)	0.110	1.21 (0.94, 1.57)	0.120
Stage III (<i>n</i> = 2944)	1.24 (1.00, 1.55)	0.054	1.16 (0.93, 1.46)	0.200	1.20 (0.94, 1.54)	0.130
Stage IV (n = 1190)	1.22 (0.93, 1.60)	0.140	0.96 (0.73, 1.26)	0.800	0.97 (0.72, 1.32)	0.800
Elevated FPG						
Stage I (<i>n</i> = 806)	1.00		1.00		1.00	
Stage II (n = 4224)	1.06 (0.83, 1.34)	0.600	1.03 (0.80, 1.33)	0.800	1.04 (0.79, 1.37)	0.800
Stage III (<i>n</i> = 2944)	1.34 (1.04, 1.74)	0.027	1.24 (0.93, 1.65)	0.120	1.29 (0.94, 1.75)	0.100
Stage IV (n = 1190)	1.46 (1.15, 1.86)	0.003	1.20 (0.92, 1.58)	0.200	1.22 (0.90, 1.65)	0.200
Hypertension						
Stage I (<i>n</i> = 806)	1.00		1.00		1.00	
Stage II (n = 4224)	1.36 (1.05, 1.76)	0.023	1.32 (1.00, 1.74)	0.050	1.35 (0.99, 1.84)	0.054
Stage III (<i>n</i> = 2944)	1.42 (1.11, 1.82)	0.007	1.30 (0.98, 1.73)	0.065	1.39 (1.01, 1.92)	0.044
Stage IV (n = 1190)	1.76 (1.31, 2.36)	< 0.001	1.44 (1.01, 2.05)	0.044	1.49 (1.01, 2.20)	0.047
Low HDL						
Stage I (<i>n</i> = 806)	1.00		1.00		1.00	
Stage II (n = 4224)	1.28 (1.06, 1.55)	0.013	1.24 (1.01, 1.52)	0.041	1.27 (1.02, 1.59)	0.036
Stage III (n = 2944)	1.32 (1.08, 1.61)	0.009	1.18 (0.94, 1.47)	0.140	1.25 (0.98, 1.60)	0.068
Stage IV (n = 1190)	1.53 (1.15, 2.05)	0.005	1.16 (0.86, 1.57)	0.300	1.19 (0.86, 1.66)	0.300
Elevated TG						
Stage I (<i>n</i> = 806)	1.00		1.00		1.00	
Stage II (n = 4224)	1.28 (1.08, 1.52)	0.006	1.25 (1.05, 1.48)	0.017	1.28 (1.05, 1.56)	0.022
Stage III (<i>n</i> = 2944)	1.30 (1.03, 1.64)	0.027	1.17 (0.91, 1.50)	0.200	1.24 (0.93, 1.64)	0.120
Stage IV (n = 1190)	1.57 (1.22, 2.01)	< 0.001	1.24 (0.95, 1.61)	0.110	1.27 (0.94, 1.70)	0.100
Short sleep						
Stage I (<i>n</i> = 806)	1.00		1.00		1.00	
Stage II (n = 4224)	1.08 (0.78, 1.51)	0.600	0.96 (0.68, 1.34)	0.800	0.97 (0.67, 1.38)	0.800
Stage III (<i>n</i> = 2944)	1.42 (1.03, 1.96)	0.032	1.05 (0.75, 1.47)	0.700	1.08 (0.76, 1.54)	0.600
Stage IV (n = 1190)	1.70 (1.19, 2.45)	0.005	0.96 (0.65, 1.42)	0.800	0.96 (0.64, 1.44)	0.800
Depression						
Stage I (<i>n</i> = 806)	1.00		1.00		1.00	
Stage II (<i>n</i> = 4224)	1.15 (0.93, 1.42)	0.200	0.95 (0.75, 1.21)	0.700	1.00 (0.75, 1.32)	> 0.900
Stage III (<i>n</i> = 2944)	1.25 (0.97, 1.62)	0.086	0.80 (0.59, 1.07)	0.120	0.87 (0.62, 1.23)	0.400
Stage IV (n = 1190)	1.75 (1.23, 2.49)	0.003	0.76 (0.51, 1.13)	0.200	0.75 (0.47, 1.17)	0.200

Table 3 Weighted multivariate logistic regression analyses of associations of periodontitis stage with circadian syndrome

In the weighted multivariable logistic regression models, the reference group was participants with stage I periodontitis. The outcome variables were circadian syndrome and the seven components of circadian syndrome. Model 1: adjusting periodontitis stage, age, sex and race. Model 2: adjusting periodontitis stage, age, sex, race, educational levels, family income, marital status, smoking status, drinking status, physical activity, and dietary quality. Model 3: adjusting periodontitis stage, age, sex, race, educational levels, family income, marital status, smoking status, drinking status, physical activity, dietary quality, working condition, working hours and taking medicines status. Data are shown as OR and 95% Cl. Significant values are shown in bold

Abbreviations: CI Confidence interval, OR Odds ratio, FPG Fasting Plasma Glucose, HDL High-density lipoprotein cholesterol, TG triglycerides

Number of missing teeth	Model 1		Model 2		Model 3	
	OR (95% CI)	Р	OR (95% CI)	Р	OR (95% CI)	Р
Circadian syndrome						
Missing teeth	1.03 (1.02, 1.04)	< 0.001	1.01 (1.01, 1.02)	< 0.001	1.01 (1.01, 1.02)	< 0.001
Obesity						
Missing teeth	1.02 (1.01, 1.02)	< 0.001	1.01 (1.00, 1.02)	0.003	1.01 (1.00, 1.02)	0.010
Elevated FPG						
Missing teeth	1.02 (1.02, 1.03)	< 0.001	1.02 (1.01, 1.02)	< 0.001	1.01 (1.01, 1.02)	< 0.001
Hypertension						
Missing teeth	1.02 (1.01, 1.02)	< 0.001	1.01 (1.00, 1.01)	0.019	1.01 (1.00, 1.01)	0.069
Low HDL						
Missing teeth	1.02 (1.01, 1.03)	< 0.001	1.01 (1.00, 1.01)	0.017	1.01 (1.00, 1.01)	0.073
Elevated TG						
Missing teeth	1.01 (1.01, 1.02)	< 0.001	1.01 (1.00, 1.01)	0.110	1.00 (1.00, 1.01)	0.300
Short sleep						
Missing teeth	1.04 (1.03, 1.05)	< 0.001	1.02 (1.01, 1.02)	< 0.001	1.01 (1.01, 1.02)	0.001
Depression						
Missing teeth	1.04 (1.03, 1.04)	< 0.001	1.01 (1.00, 1.02)	0.002	1.00 (1.00, 1.01)	0.120

Table 4 Weighted multivariate logistic regression analyses of associations of number of missing teeth with circadian syndrome

In the weighted multivariable logistic regression models, the outcome variables were circadian syndrome and the seven components of circadian syndrome. Model 1: adjusting the number of missing teeth, age, sex and race. Model 2: adjusting the number of missing teeth, age, sex, race, educational levels, family income, marital status, smoking status, drinking status, physical activity, and dietary quality. Model 3: adjusting the number of missing teeth, age, sex, race, educational levels, family income, marital status, smoking status, drinking status, physical activity, dietary quality, working condition, working hours and taking medicines status. Data are shown as OR and 95% CI. Significant values are shown in bold

Abbreviations: CI Confidence interval, OR Odds ratio, FPG Fasting Plasma Glucose, HDL High-density lipoprotein cholesterol, TG triglycerides

Circadian syndrome is a comprehensive concept to indicate risks for cardiovascular disease and has been reported to be influenced by multiple factors [5, 54]. In the present study, we comprehensively studied the association between oral health and circadian syndrome using 2018 World Workshop Classification of Periodontal and Peri-implant Diseases, tooth loss and self-rated oral health status. Self-rated oral health status had relatively higher sensitivity and specificity for periodontitis and functional dentition. Furthermore, worse self-rated oral health status was positively associated with circadian syndrome and its most components. Additionally, these components covered the components of circadian syndrome which were associated with periodontitis and the number of missing teeth. Oral health questionnaire could be simply performed without specific dental instruments or performed by any medical professionals, so they could be conveniently used in daily practice and population based investigations. This study used the strict sampling strategies to represent US general adult population. The present study also have considered the extensive covariates in the weighted multivariable analyses. The large sample size further ensured the validity of the results.

This study found that more severe periodontitis was associated with lower HDL, elevated TG and hypertension but not associated with depression and short sleep, suggesting periodontitis may be associated with the metabolic syndrome components but not with the key components of circadian syndrome. Previous reports suggested periodontitis was closely associated with metabolic syndrome and cardiovascular diseases [49, 55–57]. The prospective investigations have reported that childhood periodontal disease was associated with number of metabolic syndrome components and carotid artery intima-media thickness in adulthood [58, 59]. Recently, a longitudinal investigation reported that persistent or progressive periodontitis was positively associated with number of metabolic syndrome components but improved periodontitis was negatively associated with number of metabolic syndrome components in the follow-up, which suggested periodontitis improvements may play positive roles in decreasing the number of metabolic syndrome components [60]. The recent metaanalysis and Mendelian randomization study indicated that short sleep was not associated with periodontal disease [28]. Furthermore, Aldosari et al. reported that only severe depressive symptoms were associated with mild periodontitis. These findings indicated there may be no association or week association between periodontitis and short sleep and depression.

Furthermore, the present study found the number of missing teeth was positively associated with circadian

Table 5 Weighted multivariate logistic regression analyses of associations of self-rated oral health status with circadian syndrome

Self-rated oral health	Model 1		Model 2		Model 3	
	OR (95% CI)	Р	OR (95% CI)	Р	OR (95% CI)	Р
Circadian syndrome						
Excellent (n = 1943)	1.00		1.00		1.00	
Very good (n = 3591)	1.11 (0.96, 1.29)	0.150	1.15 (0.99, 1.33)	0.072	1.13 (0.97, 1.32)	0.120
Good (n = 5260)	1.46 (1.26, 1.69)	< 0.001	1.36 (1.18, 1.58)	< 0.001	1.34 (1.14, 1.57)	< 0.001
Fair (n = 2111)	1.65 (1.39, 1.96)	< 0.001	1.42 (1.19, 1.70)	< 0.001	1.41 (1.16, 1.71)	0.001
Poor (n = 3061)	2.21 (1.84, 2.65)	< 0.001	1.66 (1.36, 2.04)	< 0.001	1.63 (1.32, 2.03)	< 0.001
Obesity						
Excellent (n = 1943)	1.00		1.00		1.00	
Very good (n = 3591)	1.02 (0.87, 1.20)	0.800	1.03 (0.87, 1.21)	0.700	1.01 (0.85, 1.20)	0.900
Good (n = 5260)	1.15 (0.97, 1.36)	0.110	1.09 (0.92, 1.29)	0.300	1.08 (0.90, 1.28)	0.400
Fair (n = 2111)	1.22 (1.03, 1.44)	0.020	1.15 (0.96, 1.37)	0.130	1.13 (0.95, 1.36)	0.200
Poor (n = 3061)	1.30 (1.07, 1.58)	0.008	1.22 (0.98, 1.52)	0.077	1.20 (0.96, 1.50)	0.100
Elevated FPG						
Excellent (n = 1943)	1.00		1.00		1.00	
Very good (n = 3591)	1.04 (0.88, 1.23)	0.600	1.06 (0.89, 1.26)	0.500	1.05 (0.89, 1.25)	0.600
Good (n = 5260)	1.24 (1.05, 1.47)	0.011	1.19 (1.01, 1.40)	0.042	1.17 (0.99, 1.39)	0.060
Fair (n = 2111)	1.31 (1.12, 1.54)	0.001	1.21 (1.02, 1.43)	0.026	1.20 (1.02, 1.42)	0.034
Poor (n = 3061)	1.47 (1.19, 1.82)	< 0.001	1.27 (1.02, 1.58)	0.030	1.25 (1.00, 1.56)	0.047
Hypertension						
Excellent (n = 1943)	1.00		1.00		1.00	
Very good (n = 3591)	1.11 (0.93, 1.32)	0.200	1.12 (0.94, 1.34)	0.200	1.11 (0.92, 1.34)	0.300
Good (n = 5260)	1.28 (1.09, 1.51)	0.004	1.21 (1.03, 1.41)	0.023	1.20 (1.01, 1.42)	0.037
Fair (n = 2111)	1.32 (1.10, 1.58)	0.003	1.18 (0.99, 1.40)	0.061	1.18 (0.98, 1.42)	0.084
Poor (n = 3061)	1.39 (1.14, 1.70)	0.002	1.15 (0.93, 1.41)	0.200	1.13 (0.90, 1.42)	0.300
Low HDL						
Excellent (n = 1943)	1.00		1.00		1.00	
Very good (n = 3591)	1.07 (0.92, 1.24)	0.400	1.08 (0.93, 1.25)	0.300	1.08 (0.93, 1.25)	0.300
Good (n = 5260)	1.25 (1.08, 1.44)	0.003	1.17 (1.01, 1.35)	0.034	1.17 (1.01, 1.35)	0.034
Fair (n = 2111)	1.29 (1.09, 1.53)	0.004	1.13 (0.96, 1.34)	0.130	1.13 (0.96, 1.34)	0.130
Poor (n = 3061)	1.49 (1.26, 1.76)	< 0.001	1.17 (0.98, 1.40)	0.086	1.17 (0.98, 1.40)	0.086
Elevated TG						
Excellent (n = 1943)	1.00		1.00		1.00	
Very good (n = 3591)	1.10 (0.96, 1.26)	0.200	1.12 (0.97, 1.29)	0.120	1.10 (0.95, 1.29)	0.200
Good (n = 5260)	1.20 (1.04, 1.38)	0.014	1.14 (0.98, 1.33)	0.079	1.13 (0.96, 1.33)	0.130
Fair (n = 2111)	1.22 (1.06, 1.40)	0.005	1.11 (0.96, 1.28)	0.150	1.10 (0.94, 1.28)	0.200
Poor (n = 3061)	1.48 (1.26, 1.73)	< 0.001	1.25 (1.05, 1.49)	0.013	1.23 (1.03, 1.47)	0.021
Short sleep						
Excellent (n = 1943)	1.00		1.00		1.00	
Very good (n = 3591)	1.00 (0.78, 1.28)	> 0.900	1.01 (0.78, 1.29)	> 0.900	0.99 (0.77, 1.27)	> 0.900
Good (n = 5260)	1.50 (1.17, 1.93)	0.002	1.38 (1.07, 1.77)	0.014	1.34 (1.05, 1.73)	0.023
Fair (n = 2111)	2.10 (1.61, 2.74)	< 0.001	1.71 (1.30, 2.24)	< 0.001	1.66 (1.27, 2.17)	< 0.001
Poor (n = 3061)	3.17 (2.41, 4.17)	< 0.001	2.16 (1.64, 2.84)	< 0.001	2.08 (1.58, 2.74)	< 0.001
Depression						
Excellent (n = 1943)	1.00		1.00		1.00	
Very good (n = 3591)	1.32 (1.09, 1.59)	0.006	1.34 (1.10, 1.63)	0.005	1.35 (1.10, 1.65)	0.006
Good (n = 5260)	1.74 (1.44, 2.09)	< 0.001	1.55 (1.29, 1.86)	< 0.001	1.53 (1.27, 1.84)	< 0.001
Fair (n = 2111)	2.73 (2.25, 3.30)	< 0.001	2.07 (1.70, 2.52)	< 0.001	2.06 (1.70, 2.50)	< 0.001
Poor (n = 3061)	4.44 (3.65, 5.39)	< 0.001	2.67 (2.17, 3.27)	< 0.001	2.55 (2.06, 3.16)	< 0.001

In the weighted multivariable logistic regression models, the reference group was participants with excellent self-rated oral health status. The outcome variables were circadian syndrome and the seven components of circadian syndrome. Model 1: adjusting self-rated oral health status, age, sex and race. Model 2: adjusting self-rated oral health status, age, sex, race, educational levels, family income, marital status, smoking status, drinking status, physical activity, and dietary quality. Model 3: adjusting self-rated oral health status, age, sex, race, educational levels, family income, marital status, smoking status, drinking status, physical activity, dietary quality. Model 3: adjusting self-rated oral health status, age, sex, race, educational levels, family income, marital status, smoking status, drinking status, physical activity, dietary quality, working condition, working hours and taking medicines status. Data are shown as OR and 95% CI. Significant values are shown in bold

Abbreviations: CI Confidence interval, OR Odds ratio, FPG Fasting Plasma Glucose, HDL High-density lipoprotein cholesterol, TG triglycerides

syndrome and its components of obesity, elevated FPG and short sleep. Tooth extraction is indicated when the tooth suffers from severe caries or periodontal damage, which often reflected the long-term and accumulative dental diseases. Similarly, the meta-analysis reported that a 2-tooth increase in lost teeth was associated with a 3% increase in coronary heart disease and stroke risk [27]. Recently, tooth loss had been found to be associated with circadian disruption and systemically chronic diseases. Yang et al. reported loss of 8-28 teeth and dental pain were independently associated with anxiety/ depression prevalence in Korea population [61]. Several recent studies have shown the close associations of tooth missing with short sleep [29, 31-35]. Even though in the fully adjusted model taking considerations of medication use and work shift, the association between the number of missing teeth with depression (PHQ score \geq 5) was not significant, several longitudinal studies indicated tooth missing causally increased depression risk [37, 39, 40]. These findings further suggested the possible link between oral diseases and circadian syndrome.

In the current study, worse self-rated oral health status were found to be associated with a higher prevalence of circadian syndrome. Even though the sensitivity and specificity levels were influenced by different educational levels and depression status, the self-rated oral health question had relatively high sensitivity and specificity. Similar with previous literature, the other periodontitis questions had higher specificity but had lower sensitivity [62, 63]. Interestingly, Yu et al. recently reported that self-rated oral health status had the similar magnitude of associations with systemic comorbidities when compared to periodontal disease [49]. They further found fair and poor self-reported oral health was associated with increased cardiovascular diseases [49]. These result were in consistence with our findings, as we found population with worse self-reported oral health had significantly higher prevalence of circadian syndrome and its most components as compared with population with excellent self-reported oral health. Moreover, these components covered the components associated with periodontitis and the number of missing teeth. Similarly, Pereira et al. found that self-reported tooth pain, worsen self-perceived oral health, and gingival bleeding were significantly associated with self-reported sleep disorders in Brazilian population [64]. Self-rated oral health status is therefore a simple indicator to represent oral health and could be used in the evaluation of the link between oral health and systemic health. Moreover, circadian syndrome is even better to predict cardiovascular diseases than metabolic syndrome [6, 8], so self-rated oral health and circadian syndrome are useful comprehensive indicators and are recommended to be used in the future researches of oral health and systemic health. In summary, self-rated oral health was a simple question to indicate oral and systemic health.

Although we found the close association of periodontitis, tooth loss and worse self-rated oral health with circadian syndrome, the mechanisms were not clear. Chronic periodontitis and caries are the main oral diseases. Firstly, chronic periodontitis and apical periodontitis could destruct epithelial barrier and permit oral microbiome to spread to blood and the distant organs. Porphyromonas gingivalis is one of the important pathogen in apical periodontitis and chronic periodontitis, which could be found in the brain of Alzheimer's disease participants [14] and atherothrombotic carotid plaques of patients with periodontitis [65]. The animal study demonstrated that Porphyromonas gingivalis from infected tooth pulp could be identified in mouse liver and played roles in steatohepatitis [15]. Secondly, apical periodontitis, periodontal disease and tooth loss were associated with elevated systemic inflammation levels [19, 26, 66]. In contrast, Caribe found periodontal interventional therapy decreased serum C-reactive protein and increased serum levels of sirtuin 1 (SIRT1), a deacetylase that acts as an important molecular effector in the circadian epigenetic regulation of the environment changes [1, 67]. Recently, Ma et al. demonstrated rat periodontitis could elevate reactive oxygen species and decrease circadian clock protein Bmal1 in renal tissues, suggesting the possible mechanism of Bmal1 in the involvement of periodontitis in the renal injury [68]. However, we did not found the association of periodontitis with short sleep and depression. Similarly, Hiratsuka et al. reported that nutritional status other than systemic inflammation may mediate the association between tooth loss and mortality [69]. Recently, Wei et al. showed that impaired functional tooth units were associated with premature death through diet-related diseases [70]. Furthermore, there was a close association between dietary pattern and circadian syndrome [5]. Whether dietary changes brought by poor oral health could influence the circadian clock system need more basic investigations and prospective clinical trials.

Limitations of the present study should be noted. Because the nature of self-reported oral questionnaire, there are some inaccuracies. The sensitivity and specificity of self-rated oral health were influenced by educational and depression status. The regional or cultural factors may also impact the accuracy of the question, and hence these results should be validated in different regions and could not be generalized into the other countries and cultures. In addition, this was a cross-sectional study, which could not permit causal inferences. It is possible that circadian syndrome could lead to more severe periodontitis, tooth loss and worse self-rated oral health, indicating"reverse causality". Whether maintaining excellent oral health would be beneficial for lowering circadian syndrome and improving systemic health should be validated by more long-term prospective studies. Although the extensive covariates were adjusted, there were some unknown psychological factors such as stress. These factors should be kept in mind when one interprets the current findings.

Conclusion

In summary, periodontitis, tooth loss and worse selfrated oral health were associated with circadian syndrome in US adults. Self-rated oral health may be a simple question to indicate oral and systemic health. However, prospective studies were needed to confirm the cause-effect relationship.

Supplementary Information

The online version contains supplementary material available at https://doi. org/10.1186/s12903-025-06078-z.

Additional file 1.

Additional file 2: Supplemental Table 1. Comparison of demographic and clinical characteristics of NHANES participants with Stage I and Stage II-IV periodontitis. Data were shown as means \pm standard deviation for continuous variables or frequenciesfor categorical variables. Weighted chi-square testsand weighted linear regression modelswere used to compare baseline clinical data. Missing data for variables: education levels (0.06%), marital status (0.06%), family PIR (6.17%), smoking status (0.01%), drinking status (0.09%), dietary quality (10.00%), vigorous activity (0.01%), moderate activity (0.04%), working condition (0.04%), working hours (0.07%), taking medicines status (0.01%), gum disease (1.53%), self-rated oral health status (0.51%), periodontal treatment (0.71%), loose teeth (0.50%), bone loss (0.85%) and teeth not right (0.49%). Significant values are shown in bold. Abbreviations: NHANES, National Health and Nutrition Examination Survey; PIR, Poverty income ratio; FPG, Fasting Plasma Glucose; HDL Highdensity lipoprotein cholesterol; TG triglycerides.

Additional file 3: Supplemental Table 2. Self-rated oral health sensitivity and specificity in different education and depression subgroups. The sensitivity and specificity test between fair and poor self-rated oral health status and different clinical statuses including stage II-IV periodontitis, stage III-IV periodontitis, stage IV periodontitis and lack of functional dentition was shown in different education and depression subgroups.

Acknowledgements

The authors thank all the staff, investigators and participants involved in the National Health and Nutrition Examination Survey for their contributions.

Authors' contributions

Yibo Li: Investigation, Formal analysis and Funding acquisition; Yuhao Liu: Investigation and Formal analysis; Tao Yin: Investigation, Formal analysis and Validation; Mi He: Formal analysis and Funding acquisition; Changun Fang: Methodology; Xiong Tang: Funding acquisition; Shifang Peng: Conceptualization and Methodology; Yundong Liu: Conceptualization, Methodology, Investigation, Formal analysis, Funding acquisition, Writing- Original draft preparation, Writing- Reviewing and Editing, and Funding acquisition.

Funding

This work was supported by Natural Science Foundation of Hunan Province (No. 2025JJ80535), the National Natural Science Foundation of China (No. 8170041519), Fundamental Research Funds for the Central Universities of Central South University (No. 2021zzts1035) and the Graduate Innovation Project of Central South University (No. 1053320220341).

Data availability

The original data are available on the website of NHANES (https://www.cdc. gov/nchs/nhanes/index.htm). The processed data in this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study adhered to the Declaration of Helsinki. All investigations and study procedures were approved by the NCHS Research Ethics Review Board. Written informed consent was obtained from all participants.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

Author details

¹Department of Orthodontics, Changsha Stomatological Hospital, Changsha, Hunan 410004, P. R. China. ²School of Stomatology, Hunan University of Chinese Medicine, Changsha, Hunan 410208, P. R. China. ³Changjun Bilingual School of Changsha, Changsha, Hunan 410013, P. R. China. ⁴Changsha Health Vocational College, Changsha, Hunan 410605, P. R. China. ⁵Department of Stomatology, Xiangya Hospital, Central South University, Changsha, Hunan 410008, P. R. China. ⁶Department of General Medicine, Xiangya Hospital, Central South University, Changsha, Hunan 410008, P. R. China. ⁷Department of Infectious Diseases, Xiangya Hospital, Central South University, 87 Xiangya Road, Changsha, Hunan 410008, P. R. China. ⁸Health Management Center, Xiangya Hospital, Central South University, 87 Xiangya Road, Changsha, Hunan 410008, P. R. China.

Received: 4 November 2024 Accepted: 29 April 2025 Published online: 13 May 2025

References

- 1. Orozco-Solis R, Sassone-Corsi P. Epigenetic control and the circadian clock: linking metabolism to neuronal responses. Neuroscience. 2014;264:76–87.
- Panda S. The arrival of circadian medicine. Nat Rev Endocrinol. 2019;15(2):67–9.
- Russell KL, Rodman HR, Pak VM. Sleep insufficiency, circadian rhythms, and metabolomics: the connection between metabolic and sleep disorders. Sleep Breath. 2023;27(6):2139–53.
- Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA. 2001;285(19):2486–97.
- Akbar Z, Shi Z. Dietary Patterns and Circadian Syndrome among Adults Attending NHANES 2005–2016. Nutrients. 2023;15(15):3396.
- Shi Z, Tuomilehto J, Kronfeld-Schor N, Alberti GK, Stern N, El-Osta A, Bilu C, Einat H, Zimmet P. The circadian syndrome predicts cardiovascular disease better than metabolic syndrome in Chinese adults. J Intern Med. 2021;289(6):851–60.
- Tian H, Zhao X, Zhang Y, Xia Z. Research progress of circadian rhythm in cardiovascular disease: A bibliometric study from 2002 to 2022. Heliyon. 2024;10(7):e28738.
- Shi Z, Tuomilehto J, Kronfeld-Schor N, Alberti G, Stern N, El-Osta A, Chai Z, Bilu C, Einat H, Zimmet P. The Circadian Syndrome Is a Significant and Stronger Predictor for Cardiovascular Disease than the Metabolic Syndrome-The NHANES Survey during 2005–2016. Nutrients. 2022;14(24):5317.
- Wang Y, Yang L, Zhang Y, Liu J. Relationship between circadian syndrome and stroke: A cross-sectional study of the national health and nutrition examination survey. Front Neurol. 2022;13:946172.
- 10. Shi Z, Stern N, Liu J, Tuomilehto J, Kronfeld-Schor N, El-Osta A, Alberti G, Chai Z, Bilu C, Einat H, et al. The circadian syndrome is a predictor

for cognition impairment in middle-aged adults: Comparison with the metabolic syndrome. Diabetes Metab Res Rev. 2024;40(5):e3827.

- Petersen PE, Ogawa H. The global burden of periodontal disease: towards integration with chronic disease prevention and control. Periodontol 2000. 2012;60(1):15–39.
- Sun R, Xu X, Dong Y, Li J, Guan W, Huang Y, Li S, Wang Y, Li J. Global and regional trends in prevalence of untreated caries in permanent teeth: Age-period-cohort analysis from 1990 to 2019 and projections until 2049. J Dent. 2024;147:105122.
- Zhang J, Huang X, Lu B, Zhang C, Cai Z. Can apical periodontitis affect serum levels of CRP, IL-2, and IL-6 as well as induce pathological changes in remote organs? Clin Oral Investig. 2016;20(7):1617–24.
- Dominy SS, Lynch C, Ermini F, Benedyk M, Marczyk A, Konradi A, Nguyen M, Haditsch U, Raha D, Griffin C, et al. Porphyromonas gingivalis in Alzheimer's disease brains: Evidence for disease causation and treatment with small-molecule inhibitors. Sci Adv. 2019;5(1):eaau3333.
- Furusho H, Miyauchi M, Hyogo H, Inubushi T, Ao M, Ouhara K, Hisatune J, Kurihara H, Sugai M, Hayes CN, et al. Dental infection of Porphyromonas gingivalis exacerbates high fat diet-induced steatohepatitis in mice. J Gastroenterol. 2013;48(11):1259–70.
- Berlin-Broner Y, Febbraio M, Levin L. Association between apical periodontitis and cardiovascular diseases: a systematic review of the literature. Int Endod J. 2017;50(9):847–59.
- Liljestrand JM, Mantyla P, Paju S, Buhlin K, Kopra KA, Persson GR, Hernandez M, Nieminen MS, Sinisalo J, Tjaderhane L, et al. Association of Endodontic Lesions with Coronary Artery Disease. J Dent Res. 2016;95(12):1358–65.
- Garrido M, Cardenas AM, Astorga J, Quinlan F, Valdes M, Chaparro A, Carvajal P, Pussinen P, Huaman-Chipana P, Jalil JE, et al. Elevated Systemic Inflammatory Burden and Cardiovascular Risk in Young Adults with Endodontic Apical Lesions. J Endod. 2019;45(2):111–5.
- Gomes MS, Blattner TC, Sant'Ana Filho M, Grecca FS, Hugo FN, Fouad AF, Reynolds MA. Can apical periodontitis modify systemic levels of inflammatory markers? A systematic review and meta-analysis. J Endod. 2013;39(10):1205–17.
- Sun J, Wang W, Li D, Song J, Chen Z, Chen L, Smeets R, Beikler T, Strenge J, Yang Z, et al. Association between C-Reactive protein and periodontitis in an obese population from the NHANES 2009–2010. BMC Oral Health. 2023;23(1):512.
- Meisel P, Pink C, Pitchika V, Nauck M, Volzke H, Kocher T. Competing interplay between systemic and periodontal inflammation: obesity overrides the impact of oral periphery. Clin Oral Investig. 2021;25(4):2045–53.
- Ioannidou E, Swede H, Dongari-Bagtzoglou A. Periodontitis predicts elevated C-reactive protein levels in chronic kidney disease. J Dent Res. 2011;90(12):1411–5.
- Lee JH, Mun SJ. Relationship between C-reactive protein level and periodontitis and systemic diseases. J Periodontol. 2024;95(5):494–501.
- Slade GD, Ghezzi EM, Heiss G, Beck JD, Riche E, Offenbacher S. Relationship between periodontal disease and C-reactive protein among adults in the Atherosclerosis Risk in Communities study. Arch Intern Med. 2003;163(10):1172–9.
- Bretz WA, Weyant RJ, Corby PM, Ren D, Weissfeld L, Kritchevsky SB, Harris T, Kurella M, Satterfield S, Visser M, et al. Systemic inflammatory markers, periodontal diseases, and periodontal infections in an elderly population. J Am Geriatr Soc. 2005;53(9):1532–7.
- Paraskevas S, Huizinga JD, Loos BG. A systematic review and meta-analyses on C-reactive protein in relation to periodontitis. J Clin Periodontol. 2008;35(4):277–90.
- Cheng F, Zhang M, Wang Q, Xu H, Dong X, Gao Z, Chen J, Wei Y, Qin F. Tooth loss and risk of cardiovascular disease and stroke: A dose-response meta analysis of prospective cohort studies. PLoS ONE. 2018;13(3):e0194563.
- Zhou F, Liu Z, Guo Y, Xu H. Association of short sleep with risk of periodontal disease: A meta-analysis and Mendelian randomization study. J Clin Periodontol. 2021;48(8):1076–84.
- Muniz F, Pola NM, Silva CFE, Silva FGD, Casarin M. Are periodontal diseases associated with sleep duration or sleep quality? A systematic review. Arch Oral Biol. 2021;129:105184.
- Singh VP, Gan JY, Liew WL, Kyaw Soe HH, Nettem S, Nettemu SK. Association between quality of sleep and chronic periodontitis: A case-control study in Malaysian population. Dent Res J (Isfahan). 2019;16(1):29–35.
- Liu M, Wu Y, Song J, He W. Association of Sleep Duration with Tooth Loss and Periodontitis: Insights from the National Health and Nutrition Examination Surveys (2005–2020). Sleep Breath. 2024;28(2):1019–33.

- 32. Al-Zahrani MS, Alhassani AA, Zawawi KH. Tooth loss as a potential risk factor for deficient sleep: an analysis of a nationally representative sample of adults in the USA. Sleep Breath. 2021;25(2):1101–7.
- Vago EL, Frange C. G DAPO, Juliano ML, Machado MA, Coelho FMS: The association between sleep disturbances and tooth loss among poststroke patients. Arq Neuropsiquiatr. 2022;80(2):173–9.
- 34. Han K, Park JB. Evaluation of the association between sleep duration and tooth loss among Korean adults: data from the Korean National Health and Nutrition Examination Survey (KNHANES 2012–2014). BMJ Open. 2018;8(5):e018383.
- Koyama S, Aida J, Cable N, Tsuboya T, Matsuyama Y, Sato Y, Yamamoto T, Kondo K, Osaka K. Sleep duration and remaining teeth among older people. Sleep Med. 2018;52:18–22.
- Fukuhara S, Asai K, Kakeno A, Umebachi C, Yamanaka S, Watanabe T, Yamazaki T, Nakao K, Setoh K, Kawaguchi T, et al. Association of Education and Depressive Symptoms with Tooth Loss. J Dent Res. 2021;100(4):361–8.
- Matsuyama Y, Jurges H, Dewey M, Listl S. Causal effect of tooth loss on depression: evidence from a population-wide natural experiment in the USA. Epidemiol Psychiatr Sci. 2021;30:e38.
- Ortuno D, Martinez C, Caneo C, Paredes F, Soto M, Gonzalez MI, Vargas JP, Koller G. Tooth loss and depression in Chilean participants of the National Health Survey 2016–2017: Oral and social functions mediation analysis. J Affect Disord. 2024;358:19–27.
- Ehrenthal JC, Graetz C, Plaumann A, Dorfer CE, Herzog W. Number of teeth predict depressive symptoms in a longitudinal study on patients with periodontal disease. J Psychosom Res. 2016;89:16–9.
- 40. Kunrath I, Silva AER. Oral health and depressive symptoms among older adults: longitudinal study. Aging Ment Health. 2021;25(12):2265–71.
- Gluszek-Osuch M, Ciesla E, Suliga E. Relationship between the number of lost teeth and the occurrence of depressive symptoms in middle-aged adults: a cross-sectional study. BMC Oral Health. 2024;24(1):559.
- 42. Takahashi S, Naganuma T, Kurita N, Omae K, Ohnishi T, Yoshioka T, Ito F, Takeshima T, Fukuma S, Hamaguchi S, et al. Social Isolation/Loneliness and Tooth Loss in Community-Dwelling Older Adults: The Sukagawa Study. Innov Aging. 2023;7(6):igad065.
- Shah RJ, Diwan FJ, Diwan MJ, Chauhan VJ, Agrawal HS, Patel GC. A study of the emotional effects of tooth loss in an edentulous Gujarati population and its association with depression. J Indian Prosthodont Soc. 2015;15(3):237–43.
- Cademartori MG, Gastal MT, Nascimento GG, Demarco FF, Correa MB. Is depression associated with oral health outcomes in adults and elders? A systematic review and meta-analysis. Clin Oral Investig. 2018;22(8):2685–702.
- Ortuno D, Martinez C, Caneo C. Association between number of remaining teeth and incident depression in a rural Chilean cohort. BMC Oral Health. 2023;23(1):633.
- 46. Okoro CA, Strine TW, Eke PI, Dhingra SS, Balluz LS. The association between depression and anxiety and use of oral health services and tooth loss. Community Dent Oral Epidemiol. 2012;40(2):134–44.
- Aldosari M, Helmi M, Kennedy EN, Badamia R, Odani S, Agaku I, Vardavas C. Depression, periodontitis, caries and missing teeth in the USA, NHANES 2009–2014. Fam Med Commun Health. 2020;8(4):e000583.
- Gomes C, Martinho FC, Barbosa DS, Antunes LS, Povoa HCC, Baltus THL, Morelli NR, Vargas HO, Nunes SOV, Anderson G, et al. Increased Root Canal Endotoxin Levels are Associated with Chronic Apical Periodontitis, Increased Oxidative and Nitrosative Stress, Major Depression, Severity of Depression, and a Lowered Quality of Life. Mol Neurobiol. 2018;55(4):2814–27.
- 49. Yu YH, Steffensen B, Chasman DI, Buring JE. Self-reported oral health is associated with systemic health outcomes and all-cause mortality. J Am Dent Assoc. 2024;155(3):233–243.e8.
- Sun L, Huo X, Jia S, Chen X. The Association between Circadian Syndrome and Frailty in US adults: a cross-sectional study of NHANES Data from 2007 to 2018. Aging Clin Exp Res. 2024;36(1):105.
- 51. Liu Y, Yin T, He M, Fang C, Peng S. The association of reproductive health factors with periodontitis in 45–80 years old US women from NHANES 2009–2014. Clin Oral Investig. 2024;28(11):623.
- Papapanou PN, Sanz M, Buduneli N, Dietrich T, Feres M, Fine DH, Flemmig TF, Garcia R, Giannobile WV, Graziani F, et al. Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. J Clin Periodontol. 2018;45(Suppl 20):S162–70.

- Tsai SJ, Lin MS, Chiu WN, Jane SW, Tu LT, Chen MY. Factors associated with having less than 20 natural teeth in rural adults: a cross-sectional study. BMC Oral Health. 2015;15:158.
- Arabi A, Nasrallah D, Mohsen S, Abugharbieh L, Al-Hashimi D, AlMass S, Albasti S, Al-Ajmi SA, Khan MN, Zughaier SM. Association between Serum Vitamin D Status and Circadian Syndrome: A Cross-Sectional Study. Nutrients. 2024;16(13):2111.
- Kim OS, Shin MH, Kweon SS, Lee YH, Kim OJ, Kim YJ, Chung HJ. The severity of periodontitis and metabolic syndrome in Korean population: The Dong-gu study. J Periodontal Res. 2018;53(3):362–8.
- Ngoude JXE, Moor VJA, Nadia-Flore TT, Agoons BB, Marcelle GGC, Mac-Brain EE, Tcheutchoua DN, Nkeck JR. Relationship between periodontal diseases and newly-diagnosed metabolic syndrome components in a sub-Saharan population: a cross sectional study. BMC Oral Health. 2021;21(1):326.
- Watanabe K, Cho YD. Periodontal disease and metabolic syndrome: a qualitative critical review of their association. Arch Oral Biol. 2014;59(8):855–70.
- Pussinen PJ, Paju S, Viikari J, Salminen A, Taittonen L, Laitinen T, Burgner D, Kahonen M, Lehtimaki T, Hutri-Kahonen N, et al. Childhood Oral Infections Associate with Adulthood Metabolic Syndrome: A Longitudinal Cohort Study. J Dent Res. 2020;99(10):1165–73.
- Pussinen PJ, Paju S, Koponen J, Viikari JSA, Taittonen L, Laitinen T, Burgner DP, Kahonen M, Hutri-Kahonen N, Raitakari OT, et al. Association of Childhood Oral Infections With Cardiovascular Risk Factors and Subclinical Atherosclerosis in Adulthood. JAMA Netw Open. 2019;2(4):e192523.
- Sakurai SI, Yamada SI, Karasawa I, Sakurai A, Kurita H. A longitudinal study on the relationship between dental health and metabolic syndrome in Japan. J Periodontol. 2019;90(7):728–46.
- Yang SE, Park YG, Han K, Kim SY. Association between dental pain and tooth loss with health-related quality of life: the Korea national health and nutrition examination survey: A population-based cohort study. Medicine (Baltimore). 2016;95(35):e4707.
- Abbood HM, Hinz J, Cherukara G, Macfarlane TV. Validity of Self-Reported Periodontal Disease: A Systematic Review and Meta-Analysis. J Periodontol. 2016;87(12):1474–83.
- Lertpimonchai A, Tuntrakul S, Rattanasiri S, Sutthiboonyapan P, Vathesatogkit P, Udomsak A, Tavedhikul K. Validity of Simple Self-Reported Periodontal Status Questions. Int Dent J. 2023;73(1):121–7.
- Pereira D, Progiante P, Pattussi M, Grossi P, Grossi M. Study on the association between sleep disorders versus oral health related variables. Med Oral Patol Oral Cir Bucal. 2021;26(2):e164–71.
- Brun A, Nuzzo A, Prouvost B, Diallo D, Hamdan S, Meseguer E, Guidoux C, Lavallee P, Amarenco P, Leseche G, et al. Oral microbiota and atherothrombotic carotid plaque vulnerability in periodontitis patients A crosssectional study. J Periodontal Res. 2021;56(2):339–50.
- Luo H, Wu B, Kamer AR, Adhikari S, Sloan F, Plassman BL, Tan C, Qi X, Schwartz MD. Oral Health, Diabetes, and Inflammation: Effects of Oral Hygiene Behaviour. Int Dent J. 2022;72(4):484–90.
- Caribe PMV, Villar CC, Romito GA, Pacanaro AP, Strunz CMC, Takada JY, Cesar LAM, Mansur AP. Influence of the treatment of periodontal disease in serum concentration of sirtuin 1 and mannose-binding lectin. J Periodontol. 2020;91(7):900–5.
- Ma H, Li Q, Shang Y, Xin X, Liu X, Wu Z, Yu W. Impact of circadian clock protein Bmal1 on experimentally-induced periodontitis-associated renal injury. Hua Xi Kou Qiang Yi Xue Za Zhi. 2024;42(2):163–71.
- 69. Hiratsuka T, Komiyama T, Ohi T, Tanji F, Tomata Y, Tsuji I, Watanabe M, Hattori Y. Contribution of systemic inflammation and nutritional status to the relationship between tooth loss and mortality in a community-dwelling older Japanese population: a mediation analysis of data from the Tsurugaya project. Clin Oral Investig. 2020;24(6):2071–7.
- Wei X, Zhang X, Chen R, Zhang X, Liu S, Lai H, Shi J. Diet-related diseases mediate the effect of masticatory function on premature death in older adults. J Periodontal Res. 2024. https://doi.org/10.1111/jre.13335.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.