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Original Article

Association between periodontitis and anemia: Results from the National Health and Nutrition Examination Survey

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Abstract *Background/purpose:* Recently, the association between periodontitis and anemia has raised the attention, however there is still a lack of convincing evidence on the association between periodontitis and anemia. This study aimed to examine the association between periodontitis and anemia by analyzing a large population-based nationally representative sample in American.

Materials and methods: The study utilized data collected from 2009 to 2014 of the National Health and Nutrition Examination Survey (NHANES). Participants who had received periodontal examination and hemoglobin tests were enrolled, and the final sample size was 10,321. Participants were categorized as no, mild, moderate, or severe periodontitis. Associations between periodontitis and anemia were assessed using multiple logistic regression models.

Results: Overall, 49.57 % of participants were diagnosed with periodontitis, and 9.09 % had anemia. The prevalence of anemia in moderate periodontitis and severe periodontitis groups was 10.79 % and 11.19 %, respectively, compared to 8.00 % in the non-periodontitis participants. Moderate and severe periodontitis were associated with increased odds of anemia, and the adjusted odds ratios (AORs) were 1.27 (95 % CI: 1.04–1.55) and 1.46 (95 % CI: 1.02–2.10), respectively. Among participants aged 30–49 years old, moderate periodontitis was associated with increased odds of anemia (AOR:1.40, 95 % CI: 1.02–1.93).

Conclusion: Our findings indicated that the more severe periodontitis was associated with the increased odds of anemia by using a large nationally representative sample, especially for young adults aged 30–49 years. This study advances the understanding of periodontitis

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systemic implications, highlights the importance of preventing periodontitis progression, while meaningfully broadens the scope of recognized inflammatory conditions associated with anemia.

Introduction

Periodontitis is the sixth most prevalent condition worldwide, and the prevalence of severe periodontitis is approximately 10 % in the adult population.[1] Periodontitis, a chronic inflammatory disorder of periodontal tissues, represents the primary etiology of tooth loss in the adult population. Moreover, periodontitis is linked epidemiologically with various chronic disorders, including cardiovascular diseases,[2] type 2 diabetes mellitus, Alzheimer's disease, rheumatoid arthritis,[3] nonalcoholic fatty liver diseases,[4] and certain cancers.[5] Evidences have verified periodontitis could lead to a low-grade systemic inflammation.[6] Recent studies have reported that erythrocytes are affected by chronic inflammatory diseases, leading to "anemia of inflammation", which is ranked as the world's second most common form of anemia.[7] Anemia of inflammation develops in the context of systemic inflammation, while periodontitis could also activate the systemic immunity.[8] The association between periodontitis and anemia has raised the significant attention from researchers.

Several clinical studies[9–12] and meta-analyses[13,14] have reported tendencies toward periodontitis-related anemia. A recent meta-analysis of 1423 periodontitis patients reported the positive association between periodontitis and anemia.[14] Another study enrolled 471 periodontitis patients revealed the associations between periodontitis and decreased hemoglobin level.[12] Our previous studies also revealed that there was a tendency toward anemia in periodontitis patients and investigated the underlying pathological mechanisms.[15,16] These studies indicated that periodontal inflammation-activated immuno-inflammatory responses might increase the risk of anemia. However, currently, there are no large national population-level studies on the association between periodontitis and anemia.

Moreover, most of the existing studies were subject to several limitations. First, only a few studies focused on the severity or progression of periodontitis,[9,12,17] while other studies involved only chronic or aggressive periodontitis without severity.[10,11,18] Until now, the risk of anemia with periodontitis severity classified by broadly acceptable and commonly used definitions has not been reported. Second, previous studies simply conducted the regression analyses between periodontitis and the values of anemia-related hematological parameters,[11,12,17] rather than between periodontitis and the risk of anemia, which is more relevant and direct. Until now, the risk of anemia with different periodontitis severity has not been reported. Third, various confounding factors, including socioeconomic factors, lifestyle factors, and chronic and inflammatory diseases, have been found associated with periodontitis or anemia.[7,19,20] More diseases, such as rheumatoid arthritis, stomach or intestinal illness, and chronic bronchitis, have been found to be strongly associated with anemia in recent years.[7] Nevertheless, previous traditional studies adjusted for only common confounding factors (e.g., age, sex, ethnicity, smoking status, and BMI) and did not include these chronic and inflammatory diseases,[9,11,12,17] which may affect the reliability of the results. Given the above, there is still a lack of convincing evidence on the association between periodontitis and anemia.

Therefore, the aim of this study was to analyze the association between periodontitis and anemia by analyzing a large population-based sample in the United States. The findings will provide new evidence regarding the association between periodontitis and anemia, enhance comprehension of the impact of periodontitis on overall health, and highlight the importance of periodontitis prevention and treatment.

Materials and methods

Data sources and the study population

The study utilized data from the National Health and Nutrition Examination Survey (NHANES). The NHANES systematically collects cross-sectional data on health status, nutrition indicators, and health-related behavior data among the non-institutionalized U.S. civilian population. The NHANES is conducted every 2-year period, and this study included three consecutive 2-year cycles (2009–2010, 2011–2012, and 2013–2014), which were the only years that included the full-mouth periodontal examination. NHANES utilizes a complex, stratified, multistage probability cluster sampling design to achieve adequate nationally representation. The Centers for Disease Control and Prevention (CDC) and the National Center for Health Statistics (NCHS) Ethics Review Board approved the oral health data collection protocol. The present study was exempt from institutional review board approval by Peking University School of Stomatology as it exclusively utilized de-identified, publicly available NHANES database.

The study population enrolled individuals aged 30 years and above who had undergone periodontal examinations and serum hemoglobin testing. Information on the technical aspects, such as sample design, periodontal data collection techniques, and data usability, is available in the NHANES. In total, we included 10,321 participants in the present study (Fig. 1).

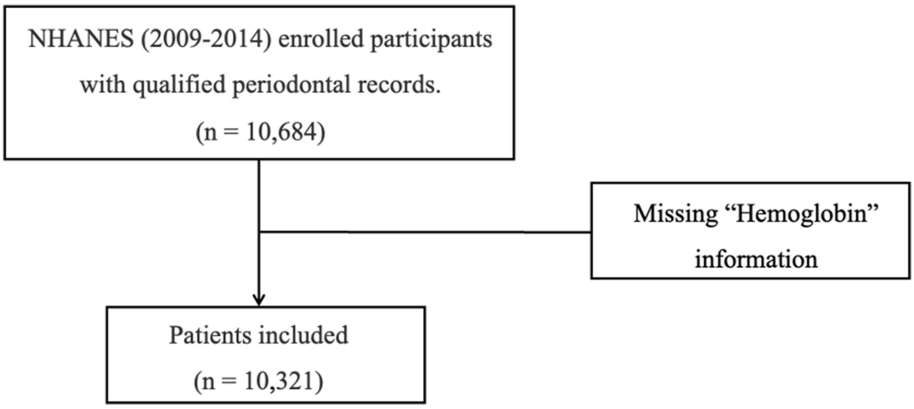

Figure 1 Flowchart for the selection of the eligible particpants.

Study variables

Periodontal measurements and periodontitis groups

According to the NHANES, periodontal examination were conducted to participants who were aged ≥30 years and retained at least one natural permanent tooth. Trained and calibrated examiners performed periodontal assessments, measuring six sites per tooth (buccal, mesiobuccal, distobuccal, lingual, mesiolingual, and distolingual). Periodontal parameters were assessed using a standardized HU-Friedy probe with 2-mm gradations. Probing pocket depth (PPD) and gingival recession measurements were recorded. Clinical attachment loss (CAL) was calculated as the difference between PPD and gingival recession.

Participants were classified into no, mild, moderate, or severe periodontitis groups according to periodontitis diagnostic criteria from the Centers for Disease Control/American Academy of Periodontology (CDC/AAP).[21] According to standard case definitions, mild periodontitis was characterized by either: interproximal CAL ≥3 mm at ≥2 sites or interproximal PPD ≥4 mm at ≥2 non-adjacent sites or any PPD ≥5 mm; moderate periodontitis was characterized by either: two or more interproximal sites with CAL ≥4 mm (not on the same tooth) or two or more interproximal sites with PPD ≥5 mm (not on the same tooth); severe periodontitis was characterized by either: two or more interproximal sites with CAL ≥6 mm (not on the same tooth) and one or more proximal sites with PPD ≥5 mm. Participants were classified into the no periodontitis group if they had no evidence of mild, moderate, or severe periodontitis.

Anemia

According to the American Society of Hematology diagnostic criteria, participants had anemia if the serum hemoglobin concentration was less than 13.5 g/dL for male adults or less than 12 g/dL for female adults (https://www.hematology.org/education/patients/anemia). Hemoglobin was measured using a Beckman Coulter DxH-800 Analyzer based on the Mobile Examination Center methodology.

Covariates

Potential confounding factors associated with both periodontitis and anemia were adjusted for in the analyses, including socioeconomic and lifestyle factors (i.e., age, race, sex, body mass index (BMI), education, marital status, annual household income, alcohol abuse, and smoking status), chronic diseases (i.e., high cholesterol, hypertension, cardiovascular disease, and diabetes), and other comorbidities (i.e., chronic kidney disease, rheumatoid arthritis, stomach or intestinal illness, asthma, chronic bronchitis, liver illness, cancer, and congestive heart failure).

Age was categorized as 30–49 years, 50–64 years, and ≥65 years. Race was categorized as: non-Hispanic White, Hispanic, non-Hispanic Black, and others. Education level was categorized as: less than 11th grade, high school, and college and above. The annual household income was classified as below $25,000, $25,000-$75,000 and above $75,000. Alcohol abuse was determined based on the question "Ever have 5 or more drinks every day?" (yes/no). Smoking status was assessed by the question "Do you now smoke cigarettes?" (yes: every day or someday smoke/no: not at all). BMI values were computed as weight divided by height squared (kg/m^2) and stratified into normal, overweight, and obese (normal: <25 kg/m^2; overweight: 25–30 kg/m^2; and obese: ≥30 kg/m^2). Health conditions were considered if the respond was "yes" to the questions "Have you ever been told by a doctor or other health professional that you had hypertension, high cholesterol, cardiovascular disease, diabetes, rheumatoid arthritis, chronic kidney disease, stomach or intestinal illness, asthma, chronic bronchitis, liver illness, cancer or malignancy, congestive heart failure?".

Data analysis

Demographic characteristics of participants were analyzed by descriptive statistics, stratified by periodontitis groups. The prevalence of anemia among the periodontitis groups was calculated. Chi-square tests were used to detect differences in categorical variables. Associations between periodontitis and anemia were assessed by multiple logistic regression models in the total sample and in the age or sex subgroup samples, respectively. All analyses accounted for NHANES's multistage sampling design and were conducted in R software (Version 4.3.0).[22] Weighted estimates were used for all prevalence and odds ratio results. Statistical significance was evaluated using two-sided tests with the threshold set at $\alpha = 0.05$.

Results

Characteristics of the study sample

Overall, the majority of the study sample were aged 30—49 years old (49.57 %), female (51.25 %), with college graduate or above education level (64.16 %), non-Hispanic white (69.13 %), married (63.72 %), with an annual household income of $25,000-$75,000 (39.37 %), non-alcohol abusers (86.50 %),non-smokers (82.67 %),obese (37.08 %), with no hypertension (65.70 %), with no high cholesterol (62.78 %), with no diabetes (90.39 %), and with cardio-health (83.67 %). These characteristics were significantly different among the periodontitis groups (Table 1). The percentages of higher white blood cell count (>11 cells/μL) in mild, moderate, and severe periodontitis groups were significantly higher than in the non-periodontitis group, meanwhile, the higher percentages were associated with periodontitis severity (mild: 5.43 %, moderate: 5.61 %, severe: 6.59 % vs. normal: 3.73 %; $P < 0.05$).

Prevalence of anemia among periodontitis groups

In the total sample, 49.57 % met the diagnostic criteria for periodontitis according to the CDC/AAP, and 9.09 % had anemia. Mild, moderate, severe periodontitis accounted for 3.03 %, 35.43 %, and 11.10 % of the sample, respectively. The prevalence of anemia in the mild, moderate, and severe periodontitis groups was 8.12 %, 10.79 %, and 11.19 %, respectively. The prevalence of anemia significantly differed among the different periodontitis severity groups (Table 2).

Associations between periodontitis and anemia

We explored the associations between periodontitis groups and anemia by using logistic regression models adjusted for different confounding factors (Table 3). In Model 1, without adjusting any covariates, participants with moderate and severe periodontitis were associated with increased odds of anemia, while persons with mild periodontitis did not show a significant association with anemia. In Model 2, after adjusting for socioeconomic and lifestyle factors, participants with moderate periodontitis and severe periodontitis were associated with increased odds of anemia (adjusted odds ratio (AOR): 1.33, 95 % CI: 1.09—1.62; AOR: 1.48, 95 % CI: 1.03—2.10, respectively). In Model 3, after adjusting for chronic diseases, participants with moderate and severe periodontitis were associated with increased odds of anemia (AOR: 1.29, 95 % CI: 1.05—1.57; AOR: 1.45, 95 % CI: 1.02—2.06, respectively). In Model 4, after adjusting for other comorbidities, participants with moderate and severe periodontitis remained associated with increased odds of anemia, and AORs for anemia in the moderate periodontitis group and severe periodontitis group were 1.27 (95 % CI: 1.04—1.55) and 1.46 (95 % CI: 1.02—2.10), respectively.

Additional subgroup analyses were conducted, with separate logistic regression models stratified by age and sex categories. In the age group of 30—49, moderate periodontitis was associated with increased odds of anemia, and the AOR was 1.40 (95 % CI: 1.02—1.93) (Table 4).

Discussion

To our knowledge, this is the first report examining the association between periodontal status and anemia based on a large population-based sample at the national level derived from the NHANES. Notably, our findings revealed a significant increase in the prevalence of anemia with the severity of periodontitis. Specifically, moderate periodontitis and severe periodontitis were associated with elevated odds of anemia, particularly among young adults aged 30—49 years. Overall, these findings suggest the risk of periodontitis-related anemia, and meanwhile, emphasize the importance of regular periodontal examination, early detection of periodontitis and effective periodontal therapies to prevent periodontitis progression; thus, reducing the risk of anemia and other systemic comorbidities. This preliminary study advances the understanding of periodontitis systemic implications, while meaningfully broadens the scope of recognized inflammatory conditions associated with anemia.

The NHANES 2009 to 2014 database applicate the standard periodontal assessment protocols with probing at six sites for both PD and CEJ for the first time, which established the most comprehensive global benchmark for periodontitis prevalence estimates based on a national population-level with high validity and reliability data.[23] This study included 10,321 participants from the NHANES database, and the results align with a recent meta-analysis which demonstrated a positive association between periodontitis and anemia[14] and other observational studies.[9—12,17,18] However, most previous studies did not compare the prevalence of anemia in periodontitis patients but only analyzed the reduce of anemia-related parameters (such as hemoglobin, hematocrit, red blood cells, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration). Using the large nationally representative sample, we could examine the prevalence of anemia among periodontitis participants, moreover, the higher prevalence in the moderate and severe periodontitis groups suggests a need for increased awareness of the systemic health implications of periodontitis among these patients. Nevertheless, this prevalence is lower than the prevalence of anemia in other diseases, such as the prevalence in chronic kidney disease (15.4 %),[24] asthma (15 %),[25] and rheumatoid arthritis (33 %).[26,27] This difference might be explained by periodontitis typically being a more chronic and milder inflammatory condition than other systemic infections or conditions.

Several previous researches have detected the association between periodontitis severity and anemia. Nibali divided patients into chronic periodontitis and aggressive periodontitis, and observed a correlation between periodontitis severity (measured as the number of PDs ≥5 mm) and reduced hematocrit levels.[9] Yamamoto reported that the progression of periodontal disease (defined by either radiographic evidence of ≥3 mm longitudinal attachment loss at least one tooth, or tooth loss attributable to periodontal disease) was associated with decreased erythrocyte counts.[17] However, retrieved studies did not conducted detailed analyses of the severity of periodontitis with anemia possibly because of the lack of consistent

Table 1 Characteristics of the study sample, stratified by the periodontitis group: NHANES 2009–2014.

Characteristics	Total n = 10,321	Normal n = 3657	Mild periodontitis n = 313	Moderate periodontitis n = 5205	Severe periodontitis n = 1146	
	%(SE)	% (95%CI)	% (95%CI)	% (95%CI)	%(95%CI)	*P*-value
Age group						<0.001
30–49	49.57 (1.92)	58.01 (52.30–63.72)	63.37 (51.48–75.26)	35.42 (31.73–39.11)	34.4 (28.71–40.09)	
50–64	33.02 (1.66)	29.79 (25.87–33.72)	25.28 (16.34–34.21)	36.92 (32.56–41.29)	45.55 (37.89–53.20)	
Above 65	17.41 (0.95)	12.20 (10.55–13.84)	11.35 (7.10–15.61)	27.66 (23.73–31.59)	20.05 (15.05–25.06)	
Sex						<0.001
Male	48.75 (1.94)	42.42 (37.97–46.88)	54.25 (43.38–65.12)	54.8 (49.66–59.94)	71.94 (61.22.82.68)	
Female	51.25 (2.07)	57.58 (51.70–63.45)	45.75 (33.39–58.11)	45.2 (40.21–50.18)	28.06 (22.92–33.19)	
Race/Ethnicity						<0.001
Non-Hispanic white	69.13 (4.35)	75.05 (65.05–85.06)	61.03 (44.66–77.40)	62.32 (52,48–72.15)	52.85 (39.75–65.95)	
Hispanic	13.38 (1.27)	10.56 (8.83–12.30)	20.47 (13.53–27.42)	16.87 (13.08–20.65)	18.93 (13.53–24.34)	
Non-Hispanic black	10.29 (0.70)	7.75 (6.75–8.74)	13.93 (10.46–17.40)	12.64 (10.47–14.80)	19.42 (15.06–23.78)	
Others	7.21 (0.55)	6.63 (5.55–7.71)	4.57 (1.91,7.23)	8.18 (6.46–9.90)	8.79 (5.72–11.87)	
Education						<0.001
Under 11th grade	15.08 (0.84)	9.1 (7.85–10.34)	18.54 (13.26–23.81)	22.38 (19.43–25.34)	31.61 (26.07–37.14)	
High school/AA degree	20.76 (1.20)	17.34 (14.88–19.80)	26.99 (18.90.35.09)	24.72 (21.23–28.20)	29.47 (24.38–34.57)	
College or above	64.16 (2.97)	73.57 (65.30–81.83)	54.47 (42.77–66.17)	52.9 (47.57–58.23)	38.92 (31.21–46.62)	
Marital status						<0.001
Unmarried	36.28 (1.18)	31.53 (29.14–33.92)	39.56 (30.55–48.57)	42.66 (37.92–47.40)	46.94 (39.53–54.35)	
Married	63.72 (3.05)	68.47 (60.40–76.55)	60.44 (48.64–72.24)	57.34 (51.15–63.53)	53.06 (43.42–62.69)	
Annual household income						<0.001
<$25,000	23.88 (1.00)	18.01 (16.21–19.82)	27.18 (19.77–34.59)	31.65 (27.84–35.47)	37.67 (32.45–42.88)	
$25,000 - $75,000	39.37 (1.90)	35.44 (31.44–39.45)	44.14 (21.84–56.43)	44.67 (39.23–50.12)	47.38 (37.87–56.88)	
Above $75,000	36.75 (2.23)	46.54 (40.37–52.72)	28.68 (18.36–39.01)	23.67 (20.62–26.72)	14.96 (9.86–20.05)	
Alcohol abuse						<0.001
No	86.50 (3.54)	89.55 (80.17–98.92)	88.85 (73.32,100.0)	83.27 (75.28–91.25)	74.8 (63.63–85.96)	
Yes	13.50 (0.68)	10.45 (8.92–11.98)	11.15 (6.50–15.80)	16.73 (14.37–19.10)	25.2 (21.28–29.22)	
Smoking status						<0.001
No	82.67 (3.40)	88.71 (79.77–97.65)	81.35 (66.41–96.29)	76.04 (68.38–83.70)	62.44 (52.69–72.19)	
Yes	17.23 (0.69)	11.29 (9.90–12.68)	18.65 (12.58–24.71)	23.96 (21.13–26.79)	37.56 (31.82–43.29)	
BMI						<0.001
<25	26.19 (1.31)	28.5 (24.87–32.12)	16.56 (10.56–22.55)	26.2 (23.07–29.33)	26.28 (22.39–30.17)	
25–30	35.73 (1.62)	35.61 (31.67–39.55)	39.49 (29.62–49.37)	34.53 (30.64–38.43)	36.31 (30.03–42.60)	
≥30	37.08 (1.47)	35.89 (32.28–39.50)	43.95 (34.42–53.47)	39.27 (34.86–43.68)	37.41 (29.99–44.82)	
White blood cell count						<0.001
Lower (<4 cells/μL)	3.23 (0.27)	3.77 (2.96,4.58)	1.11 (0.06,2.16)	2.78 (2.02,3.53)	1.57 (0.84,2.30)	
Normal (4–11 cells/μL)	92.22 (3.70)	92.51 (83.08,100.0)	93.46 (77.42,100.0)	91.61 (82.59,100.0)	91.84 (78.65,100.0)	
Higher (>11 cells/μL)	4.55 (0.30)	3.72 (3.17,4.28)	5.43 (2.00,8.86)	5.61 (4.44,6.78)	6.59 (4.10,9.08)	

(*continued on next page*)

Table 1 *(continued)*

Characteristics	Total n = 10,321	Normal n = 3657	Mild periodontitis n = 313	Moderate periodontitis n = 5205	Severe periodontitis n = 1146	*P*-value
	%(SE)	% (95%CI)	% (95%CI)	% (95%CI)	%(95%CI)	
Health conditions						
Hypertension	34.30 (1.58)	30.05 (27.04–33.07)	31.42 (21.05–41.79)	41.15 (35.73–46.57)	41.57 (33.48–49.66)	<0.001
High cholesterol	37.22 (1.80)	35.76 (31.57–39.96)	31.17 (19.94–42.40)	41.89 (37.12–46.65)	32.65 (26.23–39.08)	0.003
Diabetes	9.61 (0.47)	6.7 (5.72–7.68)	10.29 (5.24–15.33)	14.35 (12.31–16.39)	13.45 (10.25–16.65)	<0.001
Cardiovascular diseases	16.33 (0.75)	14.31 (12.21–16.42)	9.78 (5.25–14.31)	20.03 (17.64–22.41)	19.92 (16.69–23.16)	<0.001
Stomach or intestinal illness	5.99 (0.46)	5.95 (4.71–7.19)	4.78 (2.27–7.29)	5.95 (4.86–7.05)	6.98 (4.48–9.48)	<0.001
Rheumatoid arthritis	3.61 (0.23)	3.13 (2.60,3.66)	1.38 (0.31,2.66)	4.68 (3.79,5.57)	3.96 (2.62,5.29)	<0.001
Chronic kidney disease	2.08 (0.19)	1.57 (1.09,2.05)	0.52 (0.00,1.53)	3.25 (2.45,4.05)	2.03 (1.20,2.88)	<0.001
Chronic bronchitis	4.97 (0.42)	4.46 (3.61,5.31)	2.92 (0.35,5.49)	6.24 (4.78,7.70)	4.71 (2.24,7.17)	<0.001
Liver illness	3.28 (0.26)	3.08 (2.43,3.72)	2.36 (0.53,4.19)	3.67 (2.99,4.34)	3.65 (2.18,5.11)	<0.001
Cancer or malignancy	10.61 (0.66)	9.99 (8.44,11.55)	6.57 (2.91,10.23)	13.08 (10.69,15.47)	7.28 (4.94,9.63)	<0.001
Congestive heart failure	1.77 (0.17)	0.85 (0.58,1.13)	0.86 (0.00,1.99)	3.17 (2.27,4.07)	3.71 (1.98,5.44)	<0.001

SE: Standard error; CI: Confidence interval; BMI: Body mass index.

definitions. In our current study, participants could be distinctly classified into no, mild, moderate, or severe periodontitis groups according to the definition of periodontitis from the CDC/AAP definitions, which were designed specifically for population-based research and population surveillance[21] and commonly used for studies about periodontitis based on NHANES.[28–30] The specific classification enabled a thorough exploration and illustration of the association between periodontitis severity and anemia.

Various comorbidities, including socioeconomic factors, lifestyle factors, and chronic and inflammatory diseases, have been found associated with periodontitis or anemia,[7,19,20] which may complicate the analyses of association between periodontitis or anemia. Traditional observational studies could not avoid bias due to insufficient information on these factors. One advantage of our study is that the NHANES provides sufficient demographics, examination and questionnaire data, which reduces susceptibility to bias and confounding variables. We conducted multiple logistic regression models after adjusting for socioeconomic and lifestyle factors, chronic disease and other comorbidities with the purpose of minimizing bias as much as possible. In summary, our study, based on the NHANES database, which could provide a presentative nationally sample, clear classification of periodontitis severity, and sufficient information with fewer bias, further provides strong evidence that periodontitis and its severity were associated with anemia.

Our study highlights the clinical significance of the systemic implications of periodontitis on overall health status for both the public and dentist. In particular, more attention should be given to moderate and severe periodontitis patients to mitigate the risk of periodontitis-related anemia. Moreover, routine hematological parameter assessments might be necessary in clinical periodontal practice. Although the AORs for anemia in the moderate and severe periodontitis group were 1.27 and 1.46, respectively, these changes should not be ignored because the risk of anemia could contribute to the inflammatory burden and disorders associated with other systemic inflammatory comorbidities, particularly in patients with severe periodontitis.[31] Additionally, the logistic regression analyses stratified by age or sex subgroups interestingly found that younger patients (30-49-year-old group) with moderate periodontitis and severe periodontitis were more susceptible to anemia. Therefore, individuals with risk factors including more severe periodontitis and younger age, should engage in healthy oral habits and undergo regular periodontal examination to maintain periodontal health. Meanwhile, dentists should play a crucial role in conducting regular periodontal assessments to diligently monitor the oral health status of their patients. Additionally, this study recommend that physicians could include periodontal examinations as part of examination for patients with unexplained anemia.

The type of periodontitis-related anemia is so called anemia of inflammation. Anemia of inflammation ranked as the world's second most common type of anemia and is a mild-to-moderate type of anemia associated with inflammatory disorders.[7] Periodontitis is classified as an immune-inflammatory disorder characterized by dysregulated host responses to pathogenic microbial biofilms. Our previous

Table 2 Prevalence of anemia among periodontitis groups: NHANES 2009–2014.

Classification	Anemia		No anemia		
	%	95 % CI	%	95 % CI	*P*-value
Total	9.09	(8.04–10.14)	90.91	(83.66–98.17)	<0.001
No periodontitis	8.00	(6.79–9.21)	92.00	(82.80–100.00)	
Mild periodontitis	8.12	(3.83–12.42)	91.88	(81.58,100.00)	
Moderate periodontitis	10.79	(9.09–12.50)	89.21	(80.58–97.83)	
Severe periodontitis	11.19	(8.36–14.01)	88.81	(77.98–99.65)	

CI: Confidence interval.

studies have explored the pathological mechanisms of periodontitis-related anemia.[15,16] Hepcidin serves as the central regulator in anemia of inflammation, and inflammation-induced hepcidin overexpression drives the pathogenesis through iron metabolism dysregulation, leading to iron-restricted erythropoiesis, and finally leading to anemia of inflammation.[32] Our previous study revealed a significant elevation in serum hepcidin levels among periodontitis patients compared to controls (35.85 ± 32.23 vs. 17.15 ± 16.58 ng/ml, $P < 0.01$) and 4.4-fold higher hepcidin concentrations in mice with ligature-induced periodontitis (73.21 ± 13.54 vs. 16.65 ± 7.48 ng/ml).[16] Periodontitis could result in increased white blood cell counts, C-reactive protein levels and other various inflammatory cytokines levels. We further detected that among these inflammatory mediators, increased levels of pro-inflammatory cytokine interleukin-6 (IL-6) induces hepcidin synthesis via the JAK-STAT signaling pathway.[16] Periodontal inflammation induced hepcidin impairs the release of iron and causes iron retention, eventually leading to decreased hemoglobin and red blood cell counts and the development of anemia. Additionally, recent evidence suggests that periodontitis-associated low-grade systemic inflammation may explain its independent link with

Table 3 Logistic regression analyses of associations between anemia and the periodontitis groups: NHANES 2009–2014.

Classification	Model 1		Model 2		Model 3		Model 4	
	Normal (95%CI)	*P*-value	AOR (95%CI)	*P*-value	AOR (95%CI)	*P*-value	AOR (95%CI)	*P*-value
Mild periodontitis	1.04 (0.49, 2.20)	0.922	1.01 (0.48, 2.11)	0.985	0.97 (0.47, 2.03)	0.945	0.97 (0.47, 1.98)	0.931
Moderate periodontitis	1.47 (1.21, 1.79)	<0.001	1.33 (1.09, 1.62)	0.009	1.29 (1.05, 1.57)	0.021	1.27 (1.04, 1.55)	0.026
Severe periodontitis	1.55 (1.20, 2.01)	0.002	1.48 (1.03, 2.10)	0.042	1.45 (1.02, 2.06)	0.046	1.46 (1.02, 2.10)	0.048

Model 1: Unadjusted.
Model 2: Adjusted for age, sex, race, education, marital status, annual household income, alcohol abuse, smoking status, BMI.
Model 3: Model 2 + chronic diseases (hypertension, high cholesterol, cardiovascular disease, diabetes).
Model 4: Model 3 + other comorbidities (rheumatoid arthritis, chronic kidney disease, stomach or intestinal illness, asthma, chronic bronchitis, liver illness, cancer or malignancy, congestive heart failure).
AOR: Adjusted odds Ratio; CI: Confidence interval.

Table 4 Logistic regression analyses of associations between anemia and the periodontitis group stratified by age or sex group: NHANES 2009–2014.

		Mild periodontitis		Moderate periodontitis		Severe periodontitis	
Classification	Normal	AOR (95%CI)	*P*-value	AOR (95%CI)	*P*-value	AOR (95%CI)	*P*-value
Age group							
30–49	Reference	0.89 (0.32, 2.49)	0.775	1.40 (1.02, 1.93)	0.043	1.46 (0.79, 2.68)	0.238
50–64	Reference	1.17 (0.34, 4.04)	0.804	1.09 (0.73, 1.62)	0.629	1.40 (0.76, 2.60)	0.291
Above 65	Reference	1.11 (0.27, 5.37)	0.814	1.33 (0.88, 2.02)	0.181	1.14 (0.64, 2.03)	0.670
Sex group							
Male	Reference	1.18 (0.42, 3.27)	0.754	1.29 (0.89, 1.87)	0.190	1.41 (0.82, 2.42)	0.230
Female	Reference	0.94 (0.40, 2.18)	0.881	1.29 (1.00, 1.70)	0.054	1.45 (0.92, 2.28)	0.116

AOR: Adjusted odds ratio; CI: Confidence interval.

inflammatory comorbidities, as this mechanism underlies many chronic diseases.[33] Meanwhile, the results of NHANES database showed higher white blood cell count in participants with more severe periodontitis, which indicated systemic inflammation of periodontitis. These findings make sense for periodontitis-related anemia.

The following limitations of the current investigation should be noted. First, the NHANES lacked information about sufficient systemic inflammatory markers, such as IL-6, and systemic iron metabolism parameters, such as serum hepcidin, iron, and ferritin, which are helpful for defining the anemia type as anemia of inflammation. Second, the study was unable to adjust for all potential residual confounding factors, including conditions not available in the NHANES database or those not yet reported to be associated with periodontitis or anemia. Third, the NHANES protocol employed a periodontal probe with 2-mm increments rather than the standard 1-mm probe, potentially introducing measurement bias in clinical periodontal indices and periodontitis classification. Finally, the 2017 classification scheme was not utilized due to insufficient information, such as tooth loss reason, radiographic images, or local periodontitis complexity factors in the NHANES database.[34] Further researches are necessary to investigate the relationship between periodontal disease and anemia based on the latest 2017 classification scheme in the future to obtain a more comprehensive perspective.

In summary, with a large nationally representative sample, our findings provided preliminary evidence supporting the association between periodontitis and its severity were associated with anemia. This study advances the understanding of periodontitis systemic implications, highlights the importance of preventing periodontitis progression, while meaningfully broadens the scope of recognized inflammatory conditions associated with anemia.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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References

1. Frencken JE, Sharma P, Stenhouse L, et al. Global epidemiology of dental caries and severe periodontitis - a comprehensive review. *J Clin Periodontol* 2017;44:S94—105.
2. Li Y, Yuan X, Zheng Q, et al. The association of periodontal disease and oral health with hypertension, NHANES 2009-2018. *BMC Public Health* 2023;23:1122.
3. Potempa J, Mydel P, Koziel J. The case for periodontitis in the pathogenesis of rheumatoid arthritis. *Nat Rev Rheumatol* 2017;13:606—20.
4. Acharya C, Sahingur SE, Bajaj JS. Microbiota, cirrhosis, and the emerging oral-gut-liver axis. *JCI Insight* 2017;2:e94416.
5. Genco RJ, Sanz M. Clinical and public health implications of periodontal and systemic diseases: an overview. *Periodontol 2000* 2020;83:7—13.
6. Linden GJ, Lyons A, Scannapieco FA. Periodontal systemic associations: review of the evidence. *J Periodontol* 2013;84:S8—19.
7. Ganz T. Anemia of inflammation. *N Engl J Med* 2019;381:1148—57.
8. Amano A. Host—parasite interactions in periodontitis: microbial pathogenicity and innate immunity. *Periodontol 2000* 2010;54:9—14.
9. Hutter JW, Velden UVD, Varoufaki A, et al. Lower numbers of erythrocytes and lower levels of hemoglobin in periodontitis patients compared to control subjects. *J Clin Periodontol* 2001;28:930—6.
10. Gokhale SR, Sumanth S, Padhye AM. Evaluation of blood parameters in patients with chronic periodontitis for signs of anemia. *J Periodontol* 2010;81:1202—6.
11. Anand PS, Sagar DK, Ashok S, et al. Association of aggressive periodontitis with reduced erythrocyte counts and reduced hemoglobin levels. *J Periodontal Res* 2014;49:719—28.
12. Nibali L, Darbar U, Rakmanee T, et al. Anemia of inflammation associated with periodontitis: analysis of two clinical studies. *J Periodontol* 2019;90:1252—9.
13. Franca LFC, da Silva FRP, di Lenardo D, et al. Comparative analysis of blood parameters of the erythrocyte lineage between patients with chronic periodontitis and healthy patients: results obtained from a meta-analysis. *Arch Oral Biol* 2019;97:144—9.
14. Wu D, Lin Z, Zhang S, et al. Decreased hemoglobin concentration and iron metabolism disorder in periodontitis: systematic review and meta-analysis. *Front Physiol* 2019;10:1620.
15. Han Y, Luo Z, Yue ZG, et al. The tendency of anemia of inflammation in periodontal diseases. *Clin Sci (Lond)* 2023;137:251—64.
16. Han Y, Huang W, Meng H, et al. Pro-inflammatory cytokine interleukin-6-induced hepcidin, a key mediator of periodontitis-related anemia of inflammation. *J Periodontal Res* 2021;56:690—701.
17. Yamamoto T, Tsuneishi M, Furuta M, et al. Relationship between decrease of erythrocyte count and progression of periodontal disease in a rural Japanese population. *J Periodontol* 2011;82:106—13.
18. Pradeep AR, Anuj S. Anemia of chronic disease and chronic periodontitis: does periodontal therapy have an effect on anemic status? *J Periodontol* 2011;82:388—94.
19. Buchwald S, Kocher T, Biffar R, et al. Tooth loss and periodontitis by socio-economic status and inflammation in a longitudinal population-based study. *J Clin Periodontol* 2013;40:203—11.
20. Wang C, Wang Y. Trends in prevalence and treatment rate of anemia in the U.S. population: cross-sectional study using data from NHANES 2005-2018. *Hematology* 2022;27:881—8.
21. Eke PI, Page RC, Wei L, et al. Update of the case definitions for population-based surveillance of periodontitis. *J Periodontol* 2012;83:1449—54.
22. R Core Team. *R: a language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing; 2022. URL, https://www.R-project.org.
23. Eke PI, Borgnakke WS, Genco RJ. Recent epidemiologic trends in periodontitis in the USA. *Periodontol 2000* 2020;82:257—67.

24. Stauffer ME, Fan T. Prevalence of anemia in chronic kidney disease in the United States. *PLoS One* 2014;9:e84943.
25. Rhew K, Choi J, Kim K, et al. Increased risk of anemia in patients with asthma. *Clin Epidemiol* 2023;15:31—8.
26. Weiss G, Schett G. Anaemia in inflammatory rheumatic diseases. *Nat Rev Rheumatol* 2013;9:205—15.
27. Goodnough LT, Nissenson AR. Anemia and its clinical consequences in patients with chronic diseases. *Am J Med* 2004;116: 1S—2S.
28. Cao R, Li C, Geng F, Pan Y. J-shaped association between systemic immune-inflammation index and periodontitis: results from NHANES 2009-2014. *J Periodontol* 2024;95:397—406.
29. Pu R, Fu M, Yang G, Jiang Z. The association of work physical activity and recreational physical activity with periodontitis in the NHANES (2009-2014). *J Periodontol* 2023;94:1220—30.
30. Ren Z, Xue Y, Zhang H, et al. Association between probiotic consumption and periodontitis: evidence from NHANES 2009-2014. *J Clin Periodontol* 2023;50:1476—86.
31. Falcao A, Bullon P. A review of the influence of periodontal treatment in systemic diseases. *Periodontol 2000* 2019;79: 117—28.
32. Ganz T, Nemeth E. Hepcidin and iron homeostasis. *Biochim Biophys Acta* 2012;1823:1434—43.
33. Hajishengallis G. Interconnection of periodontal disease and comorbidities: evidence, mechanisms, and implications. *Periodontol 2000* 2022;89:9—18.
34. Ghassib IH, Batarseh FA, Wang HL, et al. Clustering by periodontitis-associated factors: a novel application to NHANES data. *J Periodontol* 2021;92:1136—50.