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Periodontal disease, sleep duration, and white blood cell markers in the 2009 to 2014 National Health and Nutrition Examination Surveys

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Abstract

Background: Elevated levels of inflammatory biomarkers are consistently associated with chronic conditions, for which periodontitis and sleep are established risk factors. We examined the relationships between periodontitis, hours of sleep and white blood cell (WBC) markers among a nationally representative sample of US adults.

Methods: Cross-sectional study using existing demographic, examination, laboratory and questionnaire data on 11,813 participants (5,814 men and 5,999 women, mean age ± SE; range: 52.74 ± 0.24; 30 to 80 years) from the 2009 to 2014 National Health and Nutrition Examination Surveys. Unadjusted, sex- and age-adjusted, as well as fully adjusted linear and logistic regression models were conducted in addition to generalized structural equations models, while considering sampling design complexity. β, odds ratios with their 95% confidence intervals, indirect effects and mediation proportions were estimated.

Results: The weighted mean WBC count was 7,130 cells/μL, with the WBC 5-part differential estimated in terms of percentages of lymphocytes (29.50%), monocytes (7.99%), neutrophils (59.03%), eosinophils (2.84%), and basophils (71.88%). Furthermore, 36.2% of participants reported <7 hours of sleep and 49.8% had periodontitis. In fully adjusted models controlling for sociodemographic, lifestyle, and health characteristics, neither WBC markers nor periodontitis were related to hours of sleep. By contrast, periodontitis was directly related to WBC count and %neutrophils and inversely related to %lymphocytes, especially among men. However, the

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AUTHOR CONTRIBUTIONS

Conceptualization, HAB; Methodology, HAB, MAB; Software, HAB, MAB, ABZ; Validation, MAB, SH, JW; Formal Analysis, HAB, MAB; Investigation, HAB, SH; Resources, ABZ, SE; Data Curation, HAB; Writing – Original Draft Preparation, HAB, MAB; Writing – Review & Editing, MAB, SH, JW, ABZ, SE; Visualization, HAB; Supervision, ABZ, SE; Project Administration, MAB, ABZ, SE; Funding Acquisition, ABZ.

relationship of periodontitis with %neutrophils and %lymphocytes may be modified by hours of sleep, as it was specific to individuals reporting ≥7 hours of sleep.

Conclusion: Periodontitis may be directly related to WBC count and %neutrophils and inversely related to %lymphocytes, especially among men and individuals reporting ≥7 hours of sleep, with implications for primary and secondary prevention.

Keywords

inflammation; leukocytes; periodontitis; sleep; surveys and questionnaires

1 | INTRODUCTION

Elevated levels of inflammatory biomarkers (e.g., C-reactive protein [CRP], interleukin-6 [IL-6], interleukin-8 [IL-8], interleukin-10 [IL-10], tumor necrosis factor-alpha [TNF-α], and white blood cells [WBCs]) are associated with risk and prognosis of chronic conditions, including cardiovascular disease[1–3] and cancer.[4–9] Recent studies have also suggested that periodontal disease[10–12] and sleep behavior[13,14] may increase the risk of chronic disease onset and progression through inflammatory mechanisms, and may be linked to each other.[15–17] Current evidence linking periodontal disease[18,19] and sleep behavior[20–22] to systemic inflammation focused primarily on CRP with limited evidence for WBCs or their products as inflammatory biomarkers.

Periodontal disease, or periodontitis, is a highly prevalent condition that predominantly affects men, older individuals, smokers, those with diabetes, as well as individuals of lower socioeconomic status, and specific ethnic groups.[23,24] Although genetic factors may play a role in the etiology of periodontitis, environmental factors are key to its onset and progression.[23,25] Characterized by gingival tissue inflammation, clinical loss of attachment of the periodontal ligament, pocket formation, and alveolar bone support loss, periodontal disease is often the result of overwhelming or inadequate host inflammatory response to microbial (bacterial) pathogens.[23,24,26] In the context of the host's immune dysbiosis, these microorganisms can trigger an inflammatory response, leading to destruction of supporting tissues and tooth loss.[24,25] Although equivocal, current evidence suggests that periodontal disease may be associated with numerous chronic conditions including rheumatoid arthritis, osteoporosis, insulin resistance, diabetes, cardiovascular disease, and Alzheimer disease,[25,27] with proposed biological mechanisms involving a direct effect of microbial pathogens, common risk factors among chronic conditions and systemic inflammation.[24] Similar to other inflammation-related chronic conditions, periodontal disease could be associated with a "sickness behavior" characterized by pain, fatigue, and sleep disturbance, depressed mood, loss of appetite, and cognitive dysfunction.[28]

Recent studies have estimated that, since the mid-1970s, an increasing proportion of the worldwide population is reporting <7 hours of sleep.[23] Short sleep duration can have a negative impact on physical and mental health outcomes potentially through an immune-inflammatory mechanism, also pertaining to periodontitis.[23–26,29] Moreover, short sleep duration has been linked to several chronic conditions, including diabetes mellitus, metabolic syndrome, hypertension, coronary artery disease and cerebrovascular disease.[26]

Recent epidemiologic studies identified a relationship between sleep disorders (insomnia, sleep apnea, restless leg syndrome) associated with short sleep duration and cardiovascular disease-specific morbidity and mortality risks.[30] On the other hand, short sleep duration may be a symptom of depression, an established risk factor for coronary artery disease and cerebrovascular disease, which in turn are associated with elevated inflammatory biomarkers such as CRP.[27] Finally, short sleep duration may increase susceptibility to periodontal disease by acting as an environmental stressor that predisposes the host to microbial infections as well as through increased inflammatory host response.[24,26]

As such, it is plausible that periodontal disease may be linked to inflammatory markers, either directly or indirectly, through sleep duration. The purpose of this cross-sectional study was to examine the relationships among periodontal disease, hours of sleep and WBC markers in a nationally representative sample of US adults. We hypothesized that periodontal disease and short sleep duration would be directly associated with WBC count as well as to altered percentages of distinct types of WBCs. We also hypothesized that periodontal disease would be directly and indirectly associated with WBC markers, through hours of sleep. Finally, we tested the hypotheses that these relationships differ by sex.

2 | MATERIALS AND METHODS

2.1 | Data source

Secondary analyses were performed using publicly available data from three recent waves (2009 to 2010, 2011 to 2012, and 2013 to 2014) of the National Health and Nutrition Examination Survey (NHANES). Led by the Centers for Disease Control and Prevention (CDC) National Center for Health Statistics (NCHS), the NHANES consists of a series of nationally representative stratified multistage sample surveys that are conducted every 2 years to assess the health and nutritional status of civilian non-institutionalized adults and children in the United States. Further details of the CDC/NCHS/NHANES design, methodology and procedures are provided on the NHANES. Briefly, ≈5,000 NHANES participants are selected each year on the basis of counties, blocks, households and individuals within households, with over-sampling of specific groups, including Non-Hispanic blacks and Mexican Americans, to ensure stable estimation. Demographic, dietary, examination, laboratory and questionnaire data are collected for all, or in some cases, subgroups of NHANES participants by trained personnel during in-home visits or at a mobile examination center (MEC). The original NHANES protocol was approved by the NCHS Institutional Review Board, with written informed consent obtained from all study participants, whereas the current study was determined as not being research involving human subjects. The study was conducted in accordance with the Helsinki Declaration as revised in 2013.

2.2 | Study design and population

In this cross-sectional study, we restricted 2009 to 2014 NHANES participants to a sub-sample of individuals, aged ≥30 years, who had non-missing data on all relevant variables. It is worth noting that periodontal data collected by NHANES was limited to participants who were at least 30 years of age. A total of 30,468 individuals were selected to participate in the

2009 to 2014 NHANES (2009 to 2010: 10,537; 2011 to 2012: 9,756; 2013 to 2014: 10,175) waves. Of those, 14,556 (2009 to 2010: 5,177; 2011 to 2012: 4,566; 2013 to 2014: 4,813) participants were at least 30 years of age and therefore eligible for periodontal disease assessment. Finally, we excluded individuals with missing data on any of periodontal disease, hours of sleep, WBC markers as well as socio-demographic, lifestyle and health characteristics, thereby limiting the study sample to 11,813 (2009 to 2010: 4,176; 2011 to 2012: 3,597; 2013 to 2014: 4,040) 2009 to 2014 NHANES participants. As expected, there were significant differences in distribution by sex, age group, and race/ethnicity between individuals, aged ≥30 years, with (n = 2,737) and without (n = 11,813) missing data on key variables.

2.3 | Measures

2.3.1 | Periodontal disease—

Periodontitis was defined as a dichotomous "yes" or "no" variable among study-eligible 2009 to 2014 NHANES MEC participants, aged ≥30 years, who received an oral health examination by licensed dentists and dental hygienists. This oral health examination involved multiple measurements pertaining to loss of attachment on various aspects of multiple teeth, including FGM to CEJ measurement (mm), FGM to sulcus base (pocket depth) (mm) and a calculation (FGM to CEJ measurement) – (FGM to sulcus base measurement) (mm). The case definition for periodontitis was based on those previously reported by the CDC and the American Academy of Periodontology for use in research and surveillance of this condition. Specifically, individuals who exhibited at least two interproximal sites with an attachment loss of at least 3 mm and at least two interproximal sites with probing depths of at least 4 mm which are not on the same tooth or at least one site with a probing depth of at least 5 mm, were considered to have at least mild periodontitis.

2.3.2 | Hours of sleep—

Sleep habits and disorders questionnaire items were administered to 2009 to 2014 NHANES participants, aged ≥16 years, using computer-assisted personal interviews. Consistent with previously conducted NHANES waves, hours of sleep were defined on the basis of one questionnaire item ("How much sleep do you usually get at night on weekdays or workdays?"), whereby responses were recorded, in hours, if they ranged between 2 and 11 hours, with ≥12 hours being the maximum value. Taking into account the optimal number of sleep hours reported in the literature, we dichotomized hours of sleep as <7 hours versus ≥7 hours.[23] For sensitivity analysis and to evaluate consistency of study findings when comparing two distinct methodologies, both the continuous and categorical definitions for hours of sleep were applied in current analyses.

2.3.3 | White blood cell markers—

Blood specimens were collected, processed, and analyzed from all 2009 to 2014 NHANES MEC participants. The Beckman Coulter MAXM instrument in the MEC produced a complete blood count (CBC) on blood specimens and provided a distribution of blood cells for all MEC participants. CBC parameters were derived using the Beckman Coulter method of counting and sizing, along with an automatic diluting and mixing device for sample processing, and a single beam photometer for hemoglobinometry. Whereas the total white blood cell (WBC) count was measured in 1000

cells/μL, the WBC 5-part differential (lymphocyte %, monocyte %, segmented neutrophil %, eosinophil % and basophil %) used volume, conductivity, scatter technology.

2.3.4 | Covariates—*A priori* confounders for the hypothesized relationships were identified based on the existing literature[16,20,25,26,28,29,31–41] and classified as sociodemographic, lifestyle, and health-related characteristics. Sociodemographic characteristics included *age* (in years; 30 to 34, 35 to 39, 40 to 44, 45 to 49, 50 to 54, 55 to 59, 60 to 64, 65 to 96, and ≥70), *race* (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, and other), *education* (<high school, 9th to 11th grade, high school graduate/GED or equivalent, some college or AA degree, college graduate or higher), *marital status* (married/living with partner, other) and *poverty income ratio* (<100%, 100% to <200%, and ≥200%). Lifestyle characteristics were defined as *smoking status* (non-smoker, ex-smoker, current smoker) and *physical activity,* namely walking/bicycling, tasks around home/yard, moderate activity, or vigorous activity in the past 30 days (yes, no). Finally, health characteristics were defined as *weight status* based on body mass index (BMI) categories, *depressive symptoms* based on the 9-item Patient Health Questionnaire (PHQ-9) and *self-rated health* (SRH). The BMI was calculated as weight (kg) divided by height squared (m^2) and categorized using to the World Health Organization definition of weight status, namely underweight/normal-weight (BMI: <25 kg/m^2), overweight (BMI: 25 to 29.9 kg/m^2), and obese (BMI ≥30 kg/m^2). The PHQ-9 is a valid and reliable questionnaire that assesses the frequency of nine depressive symptoms (anhedonia, depressed mood, sleep disturbance, fatigue, appetite changes, low self-esteem, concentration problems, psychomotor retardation/agitation, and suicidal ideation) on a four-point scale (0 = not at all, 1 = several days, 2 = more than half the days, 3 = nearly every day) over the past 2 weeks, based on the Diagnostic and Statistical Manual of Mental Disorders-IV criteria for major depressive disorder.[20,27] Accordingly, the total PHQ-9 score can range between 0 and 27, and a score of 10 or higher is indicative of clinically significant depressive symptoms.[20,27] The SRH is based on a single general health questionnaire item, namely, “Would you say your health in general is excellent, very good, good, fair or poor?” and further categorized as “excellent/very good/good” versus “fair/poor.”

2.4 | Statistical analysis

All analyses were conducted by the lead author using STATA v. 15 (StataCorp, College Station, TX) and the 2009 to 2014 NHANES recommended 2-year MEC sample weights. First, we estimated means with standard error of the mean *(svy:mean* and *svy:reg)* and/or proportions with their 95% confidence intervals (CI) *(svy:prop* and *svy:tab)* for each of the variables of interest, before and after stratifying by sex and examined differences between males and females using and *F* tests or Chi-square tests, as appropriate. Second, we performed a series of unadjusted, sex- and age-adjusted as well as fully adjusted linear regression *(svy:reg)* and logistic regression *(svy:logit)* analyses to examine WBC markers as predictors of hours of sleep (continuous and dichotomous (<7 hours versus ≥7 hours)), overall and by sex. Third, we performed a series of unadjusted, sex- and age-adjusted as well as fully adjusted linear regression models *(svy:reg)* to examine periodontal disease as a predictor of WBC markers, overall and by sex. Fourth, we performed a series of unadjusted, sex- and age-adjusted as well as fully adjusted linear *(svy:reg)* and logistic *(svy:logit)*

regression models to examine periodontal disease as a predictor of hours of sleep (continuous and dichotomous (<7 hours versus ≥ 7 hours)), overall and by sex. Fifth, we performed a series of unadjusted, sex- and age-adjusted as well as fully adjusted linear regression models *(svy:reg)* to examine WBC markers as outcomes of an interaction variable defined on the basis of periodontal disease and hours of sleep (No periodontal disease and sleep ≥7; Periodontal disease and sleep ≥7; No periodontal disease and sleep < 7; Periodontal disease and sleep <7). Fully adjusted models examine the relationships between an exposure and an outcome after controlling for a priori confounders, namely sex, age group, race, education, marital status, poverty income ratio, smoking status, physical activity, weight status, depressive symptoms and self-rated health. Finally, we performed generalized structural equations modeling (*gsem* command) to examine mediation through direct and indirect effects corresponding to the paths (periodontal disease → hours of sleep → WBC marker) (see Supplementary Figure S1 in online *Journal of Periodontology*). Further, the mediation proportion (MP, %) was computed to quantify the proportion of the total effect of a variable that is explained by a particular pathway.[42,43] For instance, if interested in the pathway A→B→C, the mediation proportion using Equations (2) and (3) is MP = Indirect*100/Total = $(a_{12} \times a_{23})$*100/$(a_{12} \times a_{23} + a_{13})$. In this example, the direct effect a_{13} should be in the same direction as the indirect effect to obtain a meaningful positive MP.[44]

$$A = \sum_{j=1}^{k} \alpha_{Z_{j1}} Z_j + e_1 \quad (1)$$

$$B = \alpha_{12} A + \sum_{j=1}^{k} \alpha_{Z_{j2}} Z_j + e_2 \quad (2)$$

$$C = \alpha_{13} A + \alpha_{23} B + \sum_{j=1}^{k} \alpha_{Z_{j3}} Z_j + e_3 \quad (3)$$

Fully adjusted linear and logistic regression models included a priori sociodemographic, lifestyle, and health confounders. All statistics, including means, proportions, SEM, beta coefficients (β) and odds ratios (OR) with their 95% CI were estimated taking sampling weights into consideration. Two-sided statistical tests were performed at α-level of 0.05.

3 | RESULTS

3.1 | Sociodemographic, lifestyle, and health characteristics overall and by sex

The study sample consisted of 5,814 men and 5,999 women, with mean ± SEM age of 52.74 ± 0.24 years. Nearly 71% were non-Hispanic white, 32% were college graduates or higher, 68% were married or living with a partner, 69% were ≥200% of the poverty-income-ratio, 54% were never-smokers, 76% were physically active, 39% were obese, 8.2% exhibited a high level of depressive symptoms, and 18.4% self-reported their health as being fair or poor. On average, the WBC count was 7130 cells/μL, with the WBC 5-part differential

estimated in terms of percentages of lymphocytes (29.50%), monocytes (7.99%), neutrophils (59.03%), eosinophils (2.84%), and basophils (71.88%). Also, 36.2% of study participants reported <7 hours of sleep, with a mean ± SEM of 6.89 ± 0.02 hours of sleep, and 49.8% of study participants were classified as having periodontal disease. There were statistically significant differences between men and women in most sociodemographic, lifestyle, and health characteristics of interest, with the exception of self-rated health, WBC count, %neutrophils and %basophils. Of note, men were significantly younger, more likely to be married or living with a partner, to be physically active, to report <7 hours of sleep and to have periodontal disease and less likely to exhibit high levels of depressive symptoms than women. On average, men had lower BMI and %lymphocytes and higher %monocytes and %eosinophils than women (Table 1).

3.2 | White blood cell markers as predictors of hours of sleep overall and by sex

In linear regression models for each WBC marker as a predictor of hours of sleep, defined as a continuous variable, WBC count and %lymphocytes were significant predictors in unadjusted as well as sex- and age-adjusted models, but not in fully adjusted models, whereas %neutrophils was a significant predictor in the unadjusted model only. Among men, %lymphocytes and %neutrophils, and among women, %monocytes were significant predictors in the unadjusted model only. Of note, WBC count and %lymphocytes were inversely related to hours of sleep, whereas %neutrophils and %monocytes were positively related to hours of sleep. In logistic regression models for each WBC marker as a predictor of hours of sleep, defined as a categorical variable, WBC count was directly related to the odds of <7 hours of sleep, in the unadjusted and sex- and age-adjusted models for men, women, and both sexes combined. Furthermore, %lymphocytes were directly related to the odds of <7 hours of sleep in the unadjusted overall model and %monocytes were directly related to the odds of <7 hours of sleep in the unadjusted model for women. None of the WBC markers were significant predictors of hours of sleep in the fully adjusted model (Table 2).

3.3 | Periodontal disease as predictor of white blood cell markers overall and by sex

Periodontal disease was a significant predictor of several WBC markers in the unadjusted, sex- and age-adjusted and fully adjusted models. Specifically, periodontal disease was directly related to WBC count in the unadjusted, sex- and age-adjusted and fully adjusted models for the overall sample and among men; it was also predictive of WBC count in the age-adjusted model for women. Furthermore, periodontal disease was inversely related to %lymphocytes and directly related to %neutrophils in the unadjusted and fully adjusted models for the overall sample and among men. For sex- and age-adjusted models, periodontal disease was inversely related to %lymphocytes and directly related to %neutrophils among men and directly related to WBC count among women (Table 3).

3.4 | Periodontal disease as predictor of hours of sleep overall and by sex

Periodontal disease was directly related to the odds of <7 hours of sleep in the unadjusted model for the overall sample as well as the sex- and age-adjusted models corresponding to the overall sample, men and women. In the sex- and age-adjusted models of the overall sample and among women, periodontal disease predicted fewer hours of sleep. There were

no significant associations between periodontal disease and hours of sleep, overall and by sex, in the fully adjusted models (Table 4).

3.5 | Periodontal disease and hours of sleep interaction as predictor of white blood cell markers by sex

The interaction variable between periodontal disease and hours of sleep was not significantly related to %eosinophils or %basophils. Fully adjusted models indicated that periodontal disease was directly related to WBC count, irrespective of hours of sleep in the overall sample and among men. Similarly, fully adjusted models indicated an inverse relationship between periodontal disease and %lymphocytes among the overall sample of participants who reported ≥7 hours of sleep and among men who reported <7 hours of sleep. Finally, periodontal disease was directly associated with %neutrophils among study participants, and in particular among men who reported sleeping at least 7 hours (Table 5).

3.6 | Path analysis linking periodontal disease, hours of sleep, and WBC markers

Using structural equation models, we evaluated direct and indirect effects between the three variables of interest, namely periodontal disease, hours of sleep (continuous), and three WBC markers (WBC count, %lymphocytes and %neutrophils). Our results mirror previous findings which indicate no significant relationship between periodontal disease and hours of sleep, after controlling for socio-demographic, lifestyle, and health characteristics. However, when both periodontal disease and sleep (continuous) were included in fully adjusted models for predictors, periodontal disease, but not hours of sleep, was significantly related to WBC markers. Therefore, hours of sleep does not mediate the relationship between periodontal disease and WBC markers (Table 6).

4 | DISCUSSION

In this cross-sectional study of a nationally representative sample of US adults, we examined the relationships between periodontal disease, WBC markers, and hours of sleep. Study findings suggest that periodontal diseases are linked to specific WBC markers, namely WBC count, %neutrophils and %lymphocytes, especially among men. Although hours of sleep were found to be unrelated to either WBC markers or periodontal disease, it may act as an effect modifier for the relationship between periodontal disease and specific WBC markers. In the overall sample, whereas periodontal disease was directly associated with WBC count irrespective of hours of sleep, it was inversely related to %lymphocytes and directly related to %neutrophils only among individuals reporting ≥7 hours of sleep. Among men, the direct relationship between periodontal disease and WBC count and the inverse relationship between periodontal disease and %lymphocytes did not depend on hours of sleep, whereas the direct relationship between periodontal disease and %neutrophils was specific to those who slept ≥7 hours. Finally, no statistically significant relationships were observed between periodontal disease and WBC markers among women, irrespective of hours of sleep.

This study found no association between sleep behaviors and periodontal disease, consistent with a previously conducted study by Wiener et al.,[23] although other studies did observe an association between these two risk factors for chronic disease.[24,26,45,46] A recently

conducted clinical study correlated periodontitis with obstructive sleep apnea (OSA), a sleep disorder linked to cardiovascular disease through chronic intermittent hypoxia associated with sympathetic activation, oxidative stress, systemic inflammation, hypercoagulability, endothelial dysfunction, and metabolic dysregulation.[24] Previously conducted cross-sectional, case-control, prospective cohort studies as well as randomized controlled trials provided evidence for a positive association between sleep behaviors and inflammatory mediators such as CRP, IL-6, IL-8, TNF-α, and von Willebrand factor antigen.[20,32,35,37,40,41,47] However, these studies were heterogeneous with respect to target population as well as definition of sleep behavior, with the majority focused on OSA. We found that hours of sleep were not related to WBC markers, after controlling for sociodemographics, lifestyle, and health characteristics, including periodontitis. On the other hand, the finding that periodontal disease may be linked to systemic inflammation is corroborated by previous research.[10–12,48]

Although WBCs are often the source for inflammatory mediators, we could not identify studies that examined periodontitis or sleep behaviors in relationship to WBC markers. In this study, periodontitis was associated with increased WBC count and %neutrophils and with decreased %lymphocytes. This finding is consistent with the idea that neutrophils, or polymorphonuclear leukocytes, play a role in the innate immune response against invading bacteria, whereas lymphocytes (T cells, B cells, and natural killer cells) are key to adaptive immunity as they recognize antigens, produce antibodies, and destroy cells that could cause damage. The finding that periodontitis-WBC marker relationships were stronger among men, may be an artifact of a greater prevalence of periodontitis among men. By contrast, the effect modification of periodontal disease-WBC marker relationship by hours of sleep needs further examination; in fact, researchers have previously suggested that sleep behavior may be an environmental stressor that can influence immune response and that inflammation caused by pathogens in the context of periodontal disease may be linked to “sickness behavior” which includes sleep disturbance.

To our knowledge, this is the first study to examine mediation of the relationship between periodontal disease and WBC markers by hours of sleep using generalized structural equations modeling. Our study findings should be interpreted with caution and in light of several limitations. First, the cross-sectional nature of the study design precludes our ability to establish a temporal or causal relationship between variables of interest. Although we examined direct- and indirect-effects whereby mediation was hypothesized, longitudinal data whereby a temporal sequence of events and potentially causal relationships can be established are needed to validate our study findings. Furthermore, secondary analyses were performed using existing data; thus, limiting our ability to establish clear case definitions and to control for key confounders. For instance, hours of sleep does not reflect sleep quality or a diagnosis of sleep disorders such as OSA, which have been previously linked to systemic inflammation and periodontitis; also, the selected waves of NHANES did not have data on CRP for all its participants, precluding adjustment for this potential confounder in multivariate analyses. Second, sub-samples of the 2009 to 2014 NHANES participants had valid data on all variables of interest, potentially leading to selection bias. Third, although a large study sample was used with nearly equal number of male and female participants, sex-specific results may be due to sample size limitations or multiple testing. Similarly, the

limited sample size precluded us from evaluating hypothesized relationships while examining mild, moderate, and severe types of periodontitis. Fourth, study findings can only be generalized to US adults, aged ≥30 years, and future research is needed to confirm study findings in a wider population that includes children, adolescents, and young adults.

5 | CONCLUSION

Periodontal disease may be directly related to WBC count and %neutrophils and inversely related to %lymphocytes, especially among men as well as individuals who reported at least 7 hours of sleep. Although cause-and-effect relationships cannot be established through cross-sectional studies, these findings may have implications for primary and secondary prevention of periodontitis, sleep disorders, and related chronic conditions. Better understanding of inter-relationships among these characteristics can inform guide-lines for health education and screening activities. Prospective cohort studies are needed to further elucidate these inter-relationships.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Socio-demographic, lifestyle and health characteristics overall and by sex – 2009–2014 National Health and Nutrition Examination Surveys (n=11,813)

	Total (n = 11,813)		Males (n = 5,814)		Females (n = 5,999)		P value
	%	95% CI	%	95% CI	%	95% CI	
Age (years):							
Mean ± SEM	*52.74 ± 0.24*		*51.99 ± 0.26*		*53.45 ± 0.27*		<0.0001
30–34	10.7	9.9, 11.5	11.5	10.5, 12.6	10.0	9.1, 11.0	0.0001
35–39	10.4	9.5, 11.3	10.8	9.7, 12.0	9.9	9.1, 11.1	
40–49	23.2	22.1, 24.4	23.7	22.3, 25.1	22.8	21.4, 24.3	
50–59	23.3	22.3, 24.4	23.9	22.5, 25.4	22.8	21.4, 24.3	
60–69	17.6	16.7, 18.5	17.2	15.9, 18.6	17.9	16.7, 19.1	
70+	14.7	13.7, 15.7	12.9	11.9, 13.9	16.4	15.3, 17.7	
Race/Ethnicity:							0.0010
Mexican American	7.5	5.6, 9.8	7.9	6.1, 10.5	6.9	5.2, 9.3	
Other Hispanic	5.1	3.9, 6.7	5.1	3.9, 6.7	5.1	3.8, 6.8	
Non-Hispanic White	70.9	66.9, 74.6	71.2	67.4, 74.8	70.6	66.4, 74.5	
Non-Hispanic Black	10.2	8.5, 12.1	9.2	7.8, 11.1	11.0	9.2, 13.2	
Other	6.4	5.5, 7.4	6.4	5.4, 7.6	6.3	5.3, 7.5	
Education:							0.0002
< Less Than 9th Grade	5.4	4.7, 6.3	5.7	4.9, 6.7	5.2	4.4, 6.1	
9–11th Grade	11.1	9.8, 12.7	11.2	9.7, 12.9	11.1	9.7, 12.7	
High School Grad/GED or Equivalent	21.6	20.0, 23.3	22.6	20.7, 24.6	20.7	18.9, 22.6	
Some College or AA degree	30.1	28.8, 31.5	27.8	26.4, 29.3	32.2	30.6, 34.0	
College Graduate or above	31.6	29.1, 34.3	32.6	29.8, 35.5	30.7	28.1, 33.4	
Marital status:							<0.0001
Married/Living with partner	68.1	66.6, 69.6	73.8	71.4, 75.9	62.8	61.3, 64.3	
Other	31.9	30.3, 33.4	26.2	24.0, 28.6	37.2	35.7, 38.7	
Poverty-income ratio:							<0.0001
< 100%	11.5	10.2, 13.1	10.3	8.9, 11.9	12.7	11.1, 14.3	
100%-<200%	18.9	17.4, 20.6	17.8	16.3, 19.5	19.9	18.3, 21.8	
≥ 200%	69.5	66.8, 72.1	71.8	69.1, 74.4	67.4	64.4, 70.1	
Smoking status:							<0.0001
Never smoker	53.8	52.1, 55.4	47.6	45.2, 49.9	59.7	57.8, 61.5	
Ex-smoker	27.7	26.2, 29.3	31.9	29.9, 34.0	23.7	21.7, 25.8	
Current smoker	18.5	17.3, 19.8	20.5	19.1, 21.9	16.6	14.9, 18.5	
Physical activity:							<0.0001
Yes	75.9	74.7, 77.2	80.6	79.1, 82.0	71.6	70.0, 73.1	
No	24.0	22.8, 25.3	19.4	17.9, 20.9	28.4	26.8, 29.9	
Body mass index (kg/m^2):							

	Total (n = 11,813)		Males (n = 5,814)		Females (n = 5,999)		P value
	%	95% CI	%	95% CI	%	95% CI	
Mean ± SEM	*29.35 ± 0.11*		*29.16 ± 0.12*		*29.50 ± 0.14*		0.025
< 25.0	26.2	24.9, 27.4	21.8	20.2, 23.4	30.3	28.8, 31.9	<0.0001
25.0–29.9	35.1	33.8, 36.5	40.9	39.3, 42.7	29.6	27.9, 31.5	
≥ 30.0	38.7	37.3, 40.1	37.3	35.5, 39.0	40.0	38.1, 41.9	
Depressive symptoms:							
Mean ± SEM	*3.03 ± 0.08*		*2.51 ± 0.09*		*3.53 ± 0.09*		<0.0001
High (≥ 10)	8.2	7.4, 9.1	5.8	4.9, 6.8	10.5	9.3, 11.7	<0.0001
Low (<10)	91.8	90.9, 92.6	94.2	93.2, 95.0	89.5	88.3, 90.7	
Self-rated health:							0.11
Excellent/Very good/Good	81.6	80.0, 82.9	82.2	80.8, 83.5	80.9	78.8, 82.8	
Fair/Poor	18.4	17.0, 19.9	17.8	16.5, 19.1	19.1	17.2, 21.1	
WBC count:							
Mean ± SEM	*7.13 ± 0.04*		*7.10 ± 0.05*		*7.15 ± 0.05*		0.33
% Lymphocytes:							
Mean ± SEM	*29.50 ± 0.15*		*28.78 ± 0.17*		*30.17 ± 0.17*		<0.0001
% Monocytes:							
Mean ± SEM	*7.99 ± 0.05*		*8.39 ± 0.07*		*7.54 ± 0.04*		<0.0001
% Neutrophils:							
Mean ± SEM	*59.03 ± 0.16*		*59.09 ± 0.19*		*58.96 ± 0.18*		0.46
% Eosinophils:							
Mean ± SEM	*2.84 ± 0.03*		*3.05 ± 0.04*		*2.64 ± 0.03*		<0.0001
% Basophils:							
Mean ± SEM	*71.88 ± 0.01*		*71.39 ± 0.01*		*72.36 ± 0.01*		0.39
Hours of sleep:							
Mean ± SEM	*6.89 ± 0.02*		*6.82 ± 0.02*		*6.94 ± 0.02*		0.001
< 7	36.2	35.0, 37.4	38.1	36.6, 39.7	34.4	32.6, 36.3	0.004
≥ 7	63.8	62.6, 64.9	61.8	60.3, 63.4	65.6	63.7, 67.4	
Periodontitis:							<0.0001
Yes	49.8	47.6, 52.1	55.6	53.1, 58.1	44.3	42.0, 46.7	
No	50.2	47.9, 52.4	44.4	41.9, 46.9	55.6	53.3, 57.9	

Table 2.

White blood cell markers as predictors of hours of sleep overall and by sex – 2009–2014 National Health and Nutrition Examination Surveys (n=11,813)

	Hours of sleep					
	Unadjusted*		Gender & Age-Adjusted †		Fully-Adjusted‡	
Continuous (hours)	β	95% CI	β	95% CI	β	95% CI
Overall:						
WBC count:	−.016	−.029, −.0034	−.014	−.026, −.00057	.0029	−.010, .016
% Lymphocytes:	−.006	−.010, −.002	−.0040	−.0077, −.00025	−.0022	−.0061, .0016
% Monocytes:	.0078	−.0047, .020	.0026	−.010, .015	−.0038	−.015, .0069
% Neutrophils:	.0043	.00092, .0077	.0029	−.00024, .0062	.0020	−.0014, .0055
% Eosinophils:	.0011	−.014, .016	−.00091	−.016, .014	−.0013	−.017, .015
% Basophils:	−.0057	−.058, .046	−.0088	−.061, .044	.011	−.041, .064
Males:						
WBC count:	−.017	−.035, .0016	−.016	−.034, .0022	−.0073	−.027, .013
% Lymphocytes:	−.0085	−.014, −.0030	−.0029	−.0082, .0024	−.0011	−.0066, .0044
% Monocytes:	.0064	−.0145, .027	−.0012	−.019, .018	−.0036	−.021, .014
% Neutrophils:	.0062	.0015, .011	.0028	−.0017, .0073	.0017	−.0032, .0065
% Eosinophils:	−.0042	−.027, .018	−.011	−.033, .012	−.011	−.034, .012
% Basophils:	.0097	−.076, .095	.021	−.065, .11	.044	−.044, .13
Females:						
WBC count:	−.016	−.038, .0049	−.013	−.035, .0094	.013	−.0085, .033
% Lymphocytes:	−.0055	−.011, .00027	−.0041	−.0097, .0015	−.0024	−.0077, .0029
% Monocytes:	.020	.00011, .041	.0094	−.012, .031	−.0029	−.023, .018
% Neutrophils:	.0026	−.0022, .0073	.0024	−.0022, .0069	.0017	−.0027, .0061
% Eosinophils:	.015	−.0060, .036	.011	−.011, .033	.0093	−.013, .032
% Basophils:	−.025	−.11, .062	−.036	−.12, .049	−.017	−.096, .062
Categorical (< 7 vs. ≥ 7)	cOR (95% CI)		aOR (95% CI)		aOR (95% CI)	
Overall:						
WBC count:	1.045 (1.019, 1.072)		1.041 (1.016, 1.067)		1.009 (.987, 1.033)	
% Lymphocytes:	1.007 (1.000, 1.014)		1.004 (.998, 1.012)		1.002 (.994, 1.009)	
% Monocytes:	.988 (.959, 1.019)		.994 (.965, 1.026)		1.008 (.984, 1.033)	
% Neutrophils:	.995 (.989, 1.00)		.996 (.99, 1.00)		.998 (.991, 1.00)	
% Eosinophils:	.997 (.974, 1.020)		.999 (.976, 1.024)		1.000 (.974, 1.027)	
% Basophils:	.995 (.903, 1.096)		1.00 (.907, 1.105)		.964 (.874, 1.065)	
Males:						
WBC count:	1.047 (1.008, 1.087)		1.046 (1.009, 1.085)		1.019 (.987, 1.053)	
% Lymphocytes:	1.007 (.998, 1.0159)		1.000 (.991, 1.008)		.997 (.987, 1.007)	
% Monocytes:	1.002 (.962, 1.043)		1.011 (.974, 1.049)		1.020 (.987, 1.054)	

	Hours of sleep					
	Unadjusted*		Gender & Age-Adjusted †		Fully-Adjusted‡	
Continuous (hours)	**β**	**95% CI**	**β**	**95% CI**	**β**	**95% CI**
% Neutrophils:	.994 (.985, 1.003)		.998 (.989, 1.007)		.999 (.989, 1.009)	
% Eosinophils:	1.009 (.973, 1.048)		1.018 (.980, 1.057)		1.018 (.978, 1.060)	
% Basophils:	.961 (.823, 1.123)		.950 (.812, 1.112)		.905 (.771, 1.062)	
Females:						
WBC count:	1.045 (1.009, 1.083)		1.038 (1.000, 1.077)		.997 (.958, 1.037)	
% Lymphocytes:	1.009 (.999, 1.018)		1.008 (.998, 1.018)		1.005 (.995, 1.015)	
% Monocytes:	.955 (.920, .992)		.968 (.931, 1.006)		.989 (.951, 1.029)	
% Neutrophils:	.996 (.988, 1.004)		.995 (.987, 1.004)		.997 (.988, 1.006)	
% Eosinophils:	.969 (.937, 1.004)		.977 (.942, 1.013)		.978 (.940, 1.018)	
% Basophils:	1.038 (.892, 1.207)		1.052 (.904, 1.224)		1.020 (.881, 1.182)	

*No significant interaction effects by gender;

†No significant interaction effects by gender;

‡No significant interaction effects by gender.

Table 3.

Periodontal disease as predictor of white blood cell markers overall and by sex – 2009–2014 National Health and Nutrition Examination Surveys (n=11,813)

	Unadjusted*	Gender & Age-Adjusted†	Fully-Adjusted‡
	β (95% CI)	β (95% CI)	β (95% CI)
Overall:			
WBC count:	.277 (.162, .393)	.353 (.236, .471)	.199 (.088, .310)
% Lymphocytes:	−.774 (−1.234, −.314)	−.340 (−.773, .092)	−.606 (−1.023, −.188)
% Monocytes:	.0836 (−.078, .245)	−.120 (−.273, .033)	−.0174 (−.162, .128)
% Neutrophils:	.628 (.103, 1.154)	.487 (−.0088, .985)	.659 (.180, 1.138)
% Eosinophils:	.063 (−.044, .170)	−.0225 (−.130, .0849)	−.0247 (−.134, .0848)
% Basophils:	−.0011 (−.029, .026)	−.00385 (−.0326, .0249)	−.0105 (−.0406, .0197)
Males:			
WBC count:	.463 (.301, .627)	.482 (.315, .651)	.295 (.144, .447)
% Lymphocytes:	−1.089 (−1.687, −.491)	−.588 (−1.161, −.0157)	−.840 (−1.408, −.272)
% Monocytes:	−.0171 (−.256, .222)	−.0877 (−.320, .145)	.0340 (−.1901, .259)
% Neutrophils:	1.148 (.368, 1.928)	.755 (.0191, 1.492)	.927 (.207, 1.646)
% Eosinophils:	−.031 (−.188, .125)	.0627 (−.214, .0881)	−.0899 (−.243, .0632)
% Basophils:	−.0109 (−.047, .0255)	−.0158 (−.0538, .0222)	−.0291 (−.0677, .00944)
Females:			
WBC count:	.120 (−.0186, .259)	.231 (.0941, .368)	.105 (−.0427, .253)
% Lymphocytes:	−.187 (−.804, .429)	−.1218 (−.713, .469)	−.378 (−.935, .178)
% Monocytes:	−.00869 (−.177, .160)	−.157 (−.316, .00282)	−.0761 (−.234, .0818)
% Neutrophils:	.125 (−.530, .781)	.256 (−.374, .885)	.422 (−.178, 1.023)
% Eosinophils:	.0616 (−.0868, .210)	.0181 (−.129, .166)	.0311 (−.112, .175)
% Basophils:	.0102 (−.0217, .0421)	.00528 (−.0286, .0392)	.00134 (−.0354, .0380)

*Statistically significant (P<0.05) gender-by-periodontitis interaction effects for WBC count, %lymphocytes and %neutrophils

†Statistically significant (P<0.05) gender-by-periodontitis interaction effects for WBC count, %lymphocytes and %neutrophils

‡Statistically significant (P<0.05) gender-by-periodontitis interaction effects for WBC count, %lymphocytes and %neutrophils.

Table 4.

Periodontal disease as predictor of hours of sleep overall and by sex – 2009–2014 National Health and Nutrition Examination Surveys (n=11,813)

	Unadjusted *		Gender & Age-adjusted †		Fully-adjusted ‡	
	β or OR	95% CI	β or OR	95% CI	β or OR	95% CI
Overall:						
Sleep (hours)	−.0511	−.116, .0141	−.0694	−.138, −.000170	−.00394	−.0727, .0648
***Sleep* < 7**	1.141	1.033, 1.260	1.178	1.063, 1.305	1.020	.917, 1.135
Males:						
Sleep (hours)	−.0045	−.0948, .0856	−.0338	−.127, .0600	.0111	−.0839, .106
***Sleep* < 7**	1.104	.963, 1.267	1.157	1.001, 1.337	1.013	.870, 1.179
Females:						
Sleep (hours)	−.0694	−.152, .0133	−.099	−.188, −.012	−.0138	−.102, .0745
***Sleep* < 7**	1.139	1.001, 1.298	1.191	1.039, 1.366	1.015	.878, 1.173

*No significant interaction effects by gender;

†No significant interaction effects by gender;

‡No significant interaction effects by gender.

Table 5.

Interaction between hours of sleep (categorical) and periodontal disease as predictors of white blood cell markers – 2009–2014 National Health and Nutrition Examination Surveys (n=11,813)

	Unadjusted *	Gender & Age-adjusted †	Fully-adjusted ‡
	β (95% CI)	β (95% CI)	β (95% CI)
WBC count:			
OVERALL:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	.258 (.112, .404)	.334 (.185, .484)	.185 (.038, .331)
No periodontal disease & Sleep < 7	.193 (.050, .337)	.171 (.023, .318)	.022 (−.118, .162)
Periodontal disease & Sleep < 7	.486 (.318, .655)	.537 (.370, .704)	.247 (.106, .388)
MALE:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	.480 (.294, .665)	.495 (.304, .686)	.320 (.148, .493)
No periodontal disease & Sleep < 7	.255 (.059, .451)	.247 (.0507, .444)	.129 (−.060, .319)
Periodontal disease & Sleep < 7	.678 (.400, .955)	.690 (.414, .966)	.382 (.151, .612)
FEMALE:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	.0815 (−.0979, .261)	.199 (.024, .375)	.0690 (−.130, .268)
No periodontal disease & Sleep < 7	.165 (−.0342, .363)	.133 (−.0714, .338)	−.0587 (−.262, .145)
Periodontal disease & Sleep < 7	.341 (.118, .563)	.404 (.184, .624)	.113 (−.095, .323)
% Lymphocytes:			
OVERALL:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	−.861 (−1.421, −.301)	−.366 (−.899, .166)	−.625 (−1.143, −.106)
No periodontal disease & Sleep < 7	.403 (−.231, 1.037)	.312 (−.315, .939)	.0812 (−.529, .692)
Periodontal disease & Sleep < 7	−.260 (−.926, .406)	−.017 (−.681, .646)	−.493 (−1.141, .156)
MALE:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	−1.101 (−1.776, −.427)	−.549 (−1.178, .079)	−.804 (−1.443, −.165)
No periodontal disease & Sleep < 7	.488 (−.233, 1.211)	.0831 (−.581, .747)	−.107 (−.733, .518)
Periodontal disease & Sleep < 7	−.610 (−1.437, .216)	−.572 (−1.408, .265)	−1.003 (−1.847, −.1602)
FEMALE:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	−.368 (−1.184, .447)	−.279 (−1.085, .526)	−.495 (1.281, .291)
No periodontal disease & Sleep < 7	.399 (−.496, 1.294)	.391 (−.519, 1.302)	.194 (−.718, 1.107)
Periodontal disease & Sleep < 7	.499 (−.469, 1.467)	.500 (−.451, 1.452)	.0274 (−.843, .898)
% Monocytes:			
OVERALL:			

	Unadjusted *	Gender & Age-adjusted †	Fully-adjusted ‡
	β (95% CI)	β (95% CI)	β (95% CI)
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	.0106 (−.130, .151)	−.211 (−.351, −.073)	−.102 (−.235, .029)
No periodontal disease & Sleep < 7	−.177 (−.356, .00107)	−.154 (−.337, .027)	−.0697 (−.244, .104)
Periodontal disease & Sleep < 7	.0409 (−.255, .337)	−.110 (−.403, .181)	.0615 (−.222, .345)
MALE:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	−.122 (−.335, .0919)	−.203 (−.420, .015)	−.0807 (−.299, .138)
No periodontal disease & Sleep < 7	−.143 (−.343, .0578)	−.0821 (−.293, .128)	−.0271 (−.228, .174)
Periodontal disease & Sleep < 7	.0111 (−.486, .509)	.0123 (−.481, .506)	.194 (−.297, .686)
FEMALE:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	−.0403 (−.264, .183)	−.210 (−.421, .00111)	−.120 (−.319, .078)
No periodontal disease & Sleep < 7	−.268 (−.509, −.0274)	−.218 (−.459, .0218)	−.106 (−.358, .145)
Periodontal disease & Sleep < 7	−.198 (−.431, .0341)	−.260 (−.477, −.0432)	−.100 (−.329, .129)
% Neutrophils:			
OVERALL:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	.769 (.138, 1.399)	.593 (−.016, 1.204)	.753 (.163, 1.342)
No periodontal disease & Sleep < 7	−.235 (−.870, .398)	−.174 (−.806, .457)	−.019 (−.653, .613)
Periodontal disease & Sleep < 7	.179 (−.646, 1.005)	.158 (−.648, .968)	.478 (−.348, 1.304)
MALE:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	1.304 (.460, 2.147)	.874 (.0688, 1.679)	1.047 (.246, 1.848)
No periodontal disease & Sleep < 7	−.326 (−1.043, .391)	−.0125 (−.668, .643)	.135 (−.507, .778)
Periodontal disease & Sleep < 7	.602 (−.577, 1.781)	.564 (−.590, 1.717)	.864 (−.303, 2.032)
FEMALE:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	.260 (−.599, 1.121)	.396 (−.461, 1.254)	.515 (−.332, 1.362)
No periodontal disease & Sleep < 7	−.132 (−1.063, .799)	−.192 (−1.126, .742)	−.110 (−1.067, .846)
Periodontal disease & Sleep < 7	−.235 (−1.308, .837)	−.159 (−1.207, .888)	.143 (−.839, 1.125)
% Eosinophils:			
OVERALL:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	.083 (−.061, .227)	−.0100 (−.157, .137)	−.014 (.165, .136)
No periodontal disease & Sleep < 7	.012 (−.110, .135)	.017 (−.108, .142)	.0167 (−.120, .153)
Periodontal disease & Sleep < 7	.0418 (−.072, .156)	−.027 (−.138, .084)	−.026 (−.148, .095)
MALE:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.

	Unadjusted *	Gender & Age-adjusted †	Fully-adjusted ‡
	β (95% CI)	β (95% CI)	β (95% CI)
Periodontal disease & Sleep ≥ 7	−.068 (−.270, .133)	−.107 (−.306, .0914)	−.134 (−.334, .065)
No periodontal disease & Sleep < 7	−.0094 (−.250, .231)	.0217 (−.221, .264)	.0201 (−.237, .277)
Periodontal disease & Sleep < 7	.0172 (−.196, .231)	.0248 (−.186, .235)	.00185 (−.228, .232)
FEMALE:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	.141 (−.0538, .336)	.0921 (−.105, .289)	.102 (−.0928, .297)
No periodontal disease & Sleep < 7	−.0039 (−.173, .165)	.0121 (−.166, .189)	.0219 (−.164, .208)
Periodontal disease & Sleep < 7	−.083 (−.254, .0879)	−.0985 (−.266, .0694)	−.0781 (−.246, .0906)
% Basophils:			
OVERALL:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	−.0036 (−.0371, .0298)	−.0066 (−.0409, .0275)	−.012 (−.048, .024)
No periodontal disease & Sleep < 7	−.0047 (−.0374, .0278)	−.0034 (−.0364, .0294)	−.011 (−.045, .022)
Periodontal disease & Sleep < 7	−.0013 (−.0371, .0345)	−.0023 (−.0384, .0336)	−.019 (−.056, .018)
MALE:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	−.0123 (−.0608, .0362)	−.0151 (−.0649, .0347)	−.0268 (.0770, .0234)
No periodontal disease & Sleep < 7	−.0126 (−.0665, .0413)	−.0128 (−.0659, .0403)	−.0229 (−.0770, .0311)
Periodontal disease & Sleep < 7	−.0206 (−.0776, .0364)	−.0285 (−.0869, .0297)	−.0558 (−.115, .00323)
FEMALE:			
No periodontal disease & Sleep ≥ 7	Ref.	Ref.	Ref.
Periodontal disease & Sleep ≥ 7	.00455 (−.0342, .0433)	−.00202 (−.0416, .0376)	−.00539 (−.0474, .0366)
No periodontal disease & Sleep < 7	.00136 (−.0478, .0505)	.00301 (−.0463, .0523)	−.00369 (−.0516, .0442)
Periodontal disease & Sleep < 7	.0216 (−.0209, .0639)	.0205 (−.0244, 0655)	.0100 (−.0343, .0544)

*Statistically significant (P<0.05) gender-by-periodontitis interaction effects for WBC count

†Statistically significant (P<0.05) gender-by-periodontitis interaction effects for WBC count and %lymphocytes

‡Statistically significant (P<0.05) gender-by-periodontitis interaction effects for WBC count, %lymphocytes and %neutrophils.

Table 6.

Path analysis linking periodontal disease, hours of sleep and white blood cell markers in fully-adjusted models – 2009–2014 National Health and Nutrition Examination Surveys (n=11,813)

Model:	β	95% CI	P
1: PD → HS → WBC count			
PD → HS	−.0039	−.066, .058	0.90
HS → WBC count	.0078	−.028, .043	0.67
PD → WBC count	.19	.10, .29	< 0.0001
Indirect effect	−.000031	−.00053, .00047	0.90
Mediation proportion	−.015	−.26, .23	0.90
2: PD → HS → %LYMPH			
PD → HS	−.0039	−.066, .058	0.90
HS → %LYMPH	−.080	−.22, .058	0.26
PD →` %LYMPH	−.60	−.98, −.24	0.001
Indirect effect	.00032	−.0047, .0053	0.90
Mediation proportion	−.052	−.88, .78	0.90
3: PD → HS → %NEUTR			
PD → HS	−.0039	−.066, .058	0.90
HS → %LYMPH	.095	−.061, .25	0.23
PD → %LYMPH	.66	.24, 1.08	0.002
Indirect effect	−.00038	−.0063, .0055	0.90
Mediation proportion	−.057	−.96, .84	0.90

Abbreviations: PD=Periodontal disease; HS=Hours of Sleep; %LYMPH = % lymphocytes; %NEUTR = % neutrophils.