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Association between three thyroid disruptors and sleep quality with the interacting role of vitamins and cholesterol

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Abstract:

Sleep quality is one critical indicator of human health and sleep-associated diseases are threatening the health condition of a significant proportion of the population. To resolve sleep disorder, many studies have explored on the effect of nutrient intake but few concentrated on the role of biochemical components within human's body. Consequently, this study aims to explore the association of multiple biochemical components with sleep quality and therefore, contribute to future medications on sleep disorders. Data was extracted from NHANES 2017-2018 dataset and multiple models are constructed respectively to investigate the associations between perchlorate, nitrate, and thiocyanate exposures, and the risk of sleep disorder. Thiocyanate was observed to be significantly associated with sleep disturbance in both unadjusted (p=0.0278) and adjusted model (p=0.0421) while perchlorate (p=0.0257) and nitrate (p=0.0103) are merely significantly correlated with sleep disturbance in the adjusted model. Since causal relationships cannot be established, future studies are expected to explore underlying causal association and therefore, apply on medications targeting sleep disorders.

Keywords: Perchlorate, nitrate, thiocyanate, vitamin C, vitamin D3, cholesterol, HDL cholesterol, snore frequency, trouble sleeping/sleep too much, sleep duration

1 Introduction

Sleep quality plays a critical role in human health, influencing several physiological and psychological processes including sleepiness, cognition and mood (1). However, a significant proportion of the population suffers from sleep disorders, resulting in insufficient rest that can affect their daily routines. Poor sleep quality has been associated with a range of adverse health outcomes, including cardiovascular disease, diabetes, and mental health disorders (2). According to the American Sleep Association, up to 70 million people in the United States suffer from sleep disorders, with insomnia being the most common (3). In 2021, the National Sleep Foundation (NSF) suggested that 10-30% of adults suffer from insomnia and 2-9% suffer from obstructive sleep apnea (OSA) (4). Moreover, women may be more susceptible to sleep disorders due to hormonal changes that can lead to poor sleep quality, sleep deprivation, and an increased risk of developing OSA and insomnia (5).

Emerging evidence suggests a growing concern about the impact of perchlorate, nitrate, and thiocyanate on sleep health. These three biochemical components are considered as pollutants disrupting thyroid function essential for regulating sleep patterns by inhibiting enzyme thyroperoxidase and altering hormone synthesis, transport, metabolism, and action (6)(7)(8)(9), leading to sleep disturbances when thyroid hormones are disrupted (10). However, despite the potential significance of this association, few studies have explored the link between these thyroid disruptors and sleep disorders (11), and the results are not universally supported, with the underlying mechanisms remaining obscure.

While the impact of these thyroid disruptors on sleep is an emerging area of concern, various interacting factors, such as specific vitamins, and cholesterol, have also been investigated for their influence on sleep quality, albeit with some controversial results (14)(15). For example, vitamin B6 enhances sleep quality, while high concentrations of minerals like manganese (zinc) and aluminum are significantly associated with a higher risk of low sleep quality (12)(13). Additionally, weight gain and obesity, which can be indicated by the overload of cholesterol content at specific part of body, have been identified as independent risk factors for developing sleep problems, and obstructive sleep apnea syndrome (OSAS) severely disrupting sleep patterns (14). However, despite the substantial body of literature exploring the relationship between nutrition, weight, and sleep, the specific effects of cholesterol, vitamin C, and vitamin D3 on sleep quality have been understudied. Notably, their potential interaction with the three thyroid disruptors – perchlorate, nitrate, and thiocyanate – in influencing sleep quality requires further investigation.

The National Health and Nutrition Examination Survey (NHANES) is a national survey and research program conducted by the National Center for Health Statistics (NCHS) that collects demographic, dietary, and sleep quality data to assess the health and nutritional status of the population (16)(17). Our study aims to investigate the association between the three thyroid disruptors, as well as interacting factors including cholesterol, vitamin C, and vitamin D3, and sleep quality in different populations through NHANES data from 2017 to 2018. To assess sleep disorder, we select various factors from NHANES data as index of sleep quality. By examining these factors together, we aim to gain a more nuanced understanding of how the three thyroid disruptors, along with specific nutrients like cholesterol and vitamin interact to influence sleep quality, and potentially shed light on the underlying mechanisms involved in these associations.

2 Method

2.1 Study population

In this study, data from the 2017-2018 NHANES cycle were utilized. After excluding individuals with missing data on urinary perchlorate (n = 235), nitrate (n = 18), and thiocyanate (n = 67) levels, as well as those who did not fully respond to sleep quality questionnaires (n = 2083), and whose percentage of the missing variables lower than 25% (n = 57), the remained analytical sample consisted of 1,105 participants. As the potential outliers for the predictor and covariate variables were identified and removed (n = 60) subsequently, 1,045 participants are retained in the final analytical sample.

2.2 Factors and outcomes

This analysis utilized data from the continuous NHANES 2017-2018 database collected through CDC laboratories (urine specimens) and questionnaires. The main predictors analyzed included measurements of three potential thyroid disruptors levels (urine)- perchlorate, nitrate, and thiocyanate- with serum vitamin, urinal total cholesterol levels and high lipid lipoprotein (HDL) as interacting factors. While multiple fatty acids and other vitamin intake data were initially considered from the dietary interviews, vitamin C and D3 from laboratories database were retained as predictors after statistical testing and literature review. From the NHANES questionnaire data, several variables related to sleep quality were extracted to serve as the outcomes of interest and in this paper, weekly frequency of trouble sleeping or sleeping too much was elaborated as an illustrative example.

2.3 Covariates

To understand the independent associations between the different vitamins, cholesterol, as well as the 3 thyroid disruptors, and the sleep quality outcomes examined in this study, we adjusted for a number of covariates known to potentially affect sleep quality including gender, BMI, age, race and creatinine levels (3). Gender was categorized as male and female. BMI (measured in kg/m2) and age were categorized into diverse levels. Creatinine levels, a marker of kidney function, were also included as a continuous variable. By adjusting these covariates for factors that may affect sleep quality, we were able to examine more clearly the relationship between the predictors in

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this paper and sleep quality and sleep disturbance.

2.4 Statistical Methods

In this study, the analytical approach for the correlation between weekly frequency of trouble sleeping or sleeping too much and our predictors is described in detail as a representative case; analyses for additional outcomes followed analogous procedures. Between-group differences in categorical variables were evaluated via chi-square tests, whereas differences in continuous variables were assessed using one-way ANOVA or Kruskal-Wallis tests as appropriate. Urinary concentrations of perchlorate, nitrate, and thiocyanate were creatinine-standardized (unit: ng/mg creatinine), and these three disrupters with creatinine concentration were log-transformed to mitigate the influence of outliers and then analyzed by ANOVA test as well. Spearman's correlation coefficients examined bivariate associations among the predictors and sleep outcomes.

At stage 1, multivariate logistic regression models were employed to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the relationship between quartile levels of each anion biomarker and reports of trouble sleeping or oversleeping. Three models were constructed in which one includes no adjustments while the other two involved covariates and other factors. At Stage 2, a baseline multinomial logistic regression model examined the interaction between the anion biomarkers and vitamins/cholesterol levels in predicting categories of different levels of the sleep disorder, which treated the concentration of each predictor as continuous directly instead of grouping them into quartiles. Similar to stage one, three models were also built but all induced other covariates. All statistical analyses were performed using R version 4.3.2. and P-value < 0.05 was considered statistically significant.

3 Results

3.1 Characteristics of participants

A total of 1045 participants are involved in this research after removing the outliers, with 543 males (51.96%) and 502 females (48.04%). Race were divided into Mexican American for 160(15.31%), other Hispanic for 94(9.00%), non-Hispanic white for 358(34.26%), non-Hispanic black for 234(22.39%), non-Hispanic Asian for 140(39.40%) and other races including multiracial for 59(5.64%). Also, an average age of 48.75, weight of 81.84 as well as BMI of 29.12 were concluded from participants groups.

3.2 Association with sleep disturbance (trouble sleeping/too much)

Thiocyanate levels showed notable differences across sleep disturbance groups (p = 0.0278 in ANOVA; p = 0.0199 in Kruskal-Wallis), suggesting a potential impact on sleep. In addition, strong correlations were revealed between sleep disorders and gender (p = 9.842e-05) by the chi-square test. Conversely, perchlorate, nitrate, and creatinine levels did not present significant differences between sleep disturbance groups in the Kruskal-Wallis test. These findings suggest that while thiocyanate levels, gender and BMI are important factors in sleep disturbances, other demographic and biochemical variables do not show significant associations.

3.3 Association between exposure levels of perchlorate, nitrate, and thiocyanate and sleep disturbance

The results summarizing the association between chemical exposures and risks of sleep disturbances are shown in Table 2. Across all three models, individuals in the highest quartile of all of three anion exposure demonstrated substantially altered odds of trouble sleeping/oversleeping risk compared to the lowest quartile. In Model 1, one unit increase in the 4th quartile of the perchlorate had a OR of 1.59 (95% CI 1.08-2.34, p = 0.0203), and a OR of 1.60 (95% CI 1.02-2.51, p = 0.0421) was observed after adjustment for the total cholesterol, HDL cholesterol, vitamin C, vitamin D3, and creatinine levels in Model 2. In Model 3 which was adjusted for the additional five covariates, a marginal positive correlation between the 4th quartile of the perchlorate and the risk of trouble sleeping or oversleeping in a week was discovered with OR 2.21 (95% CI 1.76-2.78, p = 0.0257) as well. However, The risks were also pronounced for sleep disturbance issues in the highest thiocyanate quartile, as for Model 1, the 4th quartile of thiocyanate was significant associated with the risk of sleep disturbance, with a OR of 1.59 (95% CI 1.09-2.32, p = 0.0162). Notably, the P for trend in this case was 0.0466, which indicated the significance of the generalized positive correlation between the chemical disruptor and our outcome. When compared with the lowest thiocyanate concentration level quartile in Model 3, the highest quartile for thiocyanate had a OR of 1.59 (95% CI 1.01-2.50, p-value = 0.0446), with one unit increase in overall thiocyanate level were found to be considerably associated with increased risk of sleep disturbance by 0.0485 of P for trend value. For perchlorate, whereas the highest exposure level showed strikingly increased odds of sleep disturbances risk in all of the three models, the overall P for trend and P value for the Ln-transformed OR didn't provide the same robust evidence for that. Nitrate displayed an inverse correlation in the highest exposure quartile. While lower quartiles did not show any notable associations, the 4th quartile of nitrate emerged as potentially beneficial in Model 2 adjusting for cholesterol, vitamins and creatinine - with an OR of 0.59 (95% CI 0.39-0.88, p= 0.0103) for risk of trouble sleeping/oversleeping compared to the lowest quartile. This protective trend persisted in the fully adjusted Model 3, with an OR of 0.53 (95% CI 0.33-0.86, p= 0.0103) for the top nitrate quartile, though it did not reach statistical significance. However, across the models, the p-trends for nitrate quartiles were non-significant (p>0.05), suggesting no clear overall dose-response relationship.

Table 1 Characteristics of participants with Trouble sleeping/ sleep too much

variables	Overall	Weekly Frequency of Trouble sleeping/ sleep too much				p-value
		0 days	1~3 days	4~6 days	nearly 7 days	
Gender(n=1045)						
Male	543 (51.96%)	337 (69.43%)	88 (16.21%)	45 (8.29%)	33 (6.08%)	<0.001
Female	502 (48.04%)	283 (56.37%)	129 (25.70%)	46 (9.16%)	44 (8.76%)	
Age	48.75 (18.32)	49.02 (18.49)	47.97 (17.54)	48.63 (19.01)	48.78 (18.40)	0.909
BMI, kg/m^2	29.12 (6.30)	28.87 (6.29)	29.14 (6.12)	30.63 (6.56)	29.40 (6.39)	0.0923
weight, kg	81.84 (19.85)	81.66 (19.93)	80.44 (19.11)	86.22 (20.76)	82.09 (19.77)	0.135
Race(n=1045)						
Mexican American	160 (15.31%)	103 (64.38%)	37 (23.13%)	13 (8.13%)	7 (4.38%)	0.05703
other Hispanic	94 (9.00%)	55 (58.51%)	23 (24.47%)	7 (7.45%)	9 (9.57%)	
non-Hispanic white	358 (34.26%)	225 (62.85%)	79 (22.07%)	29 (8.10%)	25 (6.98%)	
non-Hispanic black	234 (22.39%)	151 (64.53%)	41 (17.52%)	24 (10.26%)	18 (7.69%)	
non-Hispanic Asian	140 (39.40%)	98 (70.00%)	26 (18.57%)	7 (5.00%)	9 (6.43%)	
other races	59 (5.64%)	28 (47.46%)	11 (18.64%)	11 (18.64%)	9 (15.25%)	
Total Cholesterol, mg/dL	184.04 (38.23)	183.02 (38.10)	186.01 (37.08)	188.15 (41.87)	182.31 (38.30)	0.522
High Density Lipoprotein, mg/dL	52.75 (13.59)	52.45 (13.44)	53.56 (13.43)	54.02 (13.96)	51.53 (14.88)	0.476
Vitamin C, mg/dL	0.88 (0.43)	0.90 (0.43)	0.87 (0.46)	0.78 (0.43)	0.83 (0.43)	0.122
25OHD3 (Vitamin D), nmol/L	64.35 (27.07)	66.01 (26.56)	62.45 (26.15)	61.31 (32.64)	59.56 (25.68)	0.139
Perchlorate, ng/mg	2.04 (1.29,3.39)	1.98 (1.25,3.27)	2.01 (1.32,3.50)	2.30 (1.52,3.78)	2.11 (1.16,3.66)	0.339
Nitrate, ng/mg	38820.22 (27407.41,56718.75)	39500.00 (28514.46,57460.28)	38969.07 (27292.11,56190.48)	36933.33 (26773.49,52056.48)	34000.00 (25247.52,58899.08)	0.307
Thiocyanate, ng/mg	979.4 (501.79,2145.45)	945.22 (469.98,2032.26)	885.85(479.23,2096.77)	1285.71(677.09,3237.19)	1289.16(625.00,3404.26)	0.0199
Creatinine, mg/dL	110.00 (66.00,163.00)	108.50 (65.00,165.25)	115.00 (69.00,154.00)	105.00 (70.00,172.00)	116.00 (62.00,178.00)	0.973
log Perchlorate	0.75(0.80)	0.72(0.78)	0.80(0.83)	0.88(0.82)	0.72(0.87)	0.268
log_Nitrate	10.58(0.68)	10.58(0.70)	10.61(0.61)	10.56(0.69)	10.45(0.74)	0.403
log Thiocyannate	6.98(1.13)	6.96(1.13)	6.89(1.11)	7.19(1.05)	7.25(1.23)	0.0278
log Creatinine	4.61(0.70)	4.60(0.72)	4.61(0.67)	4.66(0.74)	4.63(0.67)	0.87

Data are presented as n (%), mean (standard deviation, SD), or median (lower quartile, upper quartile).
Chi-square test: Race and Gender.
ANOVA test: Age, BMI, Weight, Total Cholesterol, High Density Lipoprotein, Vitamin C, 25OHD3, log Perchlorate, log Nitrate, log Thiocyannate, and log Creatinine.
Kruskal-Wallis test: Perchlorate, Nitrate, Thiocyanate, and Creatinine

3.4 Effect of exposure levels of perchlorate, nitrate, and thiocyanate on sleep disturbance with the interaction of vitamins and cholesterol

Table 3 delineates the effects of perchlorate, nitrate, and thiocyanate exposures on sleep disturbance severities, factoring in interactions with vitamins. Level 0, denoting no sleep issues in a week, serves as the reference level. In Model 1, evaluating independent correlations, a dose-response relationship emerged between thiocyanate and augmented sleep disturbance. At level 3 (near-daily issues), the correlation estimate was 0.239 (p=0.0643) relative to the referent. Perchlorate level 2 (4-6 days/week) also exhibited a significant positive estimate of 0.461 (p=0.00636). Contrastingly, nitrate demonstrated insignificant associations across all severities. Vitamin C level 2 showed a marginally significant inverse correlation (estimate: -0.647, p=0.0419).

Crucially, Model 2 elucidated a statistically robust interaction between nitrate and vitamin D3 (p=0.0213) in predicting sleep disturbance severity, after adjusting for vitamin effects. This interaction surpassed their individual impacts, implying a synergistic influence. Perchlorate level 1 (1-3 days/week) manifested a significant negative estimate of -0.849 (p=0.0218). Vitamin C interactions were insignificant. Regarding Model 3 with cholesterol interactions, thiocyanate level 3 recapitulated a robust positive association (estimate: 1.28, p=0.0353) with the highest

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disturbance severity versus the referent. Total cholesterol demonstrated insignificant effects across all severities.

While factors like nitrate, vitamin C, D3, and cholesterol exhibited insignificant independent correlations or interactions, their potential synergistic roles cannot be discounted. This analysis substantiates thiocyanate as the predominant risk factor for severe sleep dysregulation. Furthermore, the significant nitrate-vitamin D3 interaction effect, coupled with associations between perchlorate, HDL, and sleep disturbances, underscore prospective multi-modal interventions. These findings provide insights into targeting chemical exposures and nutritional status to ameliorate sleep outcomes.

Table 2

Association between exposure level of perchlorate, nitrate, thiocyanate and risk of trouble sleeping or oversleeping in a week

Chemicals, ng/mg creatinine		Ln-transformed OR (95% CI) P value	Q1 OR (95% CI)	Q2 OR (95% CI) P value	Q3 OR (95% CI) P value	Q4 OR (95% CI) P value	P for trend
Perchlorate	Range		<1.29	(1.29, 2.04)	(2.04, 3.39)	>3.39	
	Model 1	1.13 (0.97-1.33)	1.00 (reference)	1.22 (0.84-1.78)	1.35 (0.92-1.98)	**1.59 (1.08-2.34)**	0.126
		0.12		0.286	0.121	**0.0203 ***	
	Model 2	1.15 (0.94-1.40)	1.00 (reference)	1.20 (0.78-1.84)	1.41 (0.90-2.20)	**1.60 (1.02-2.51)**	0.132
		0.175		0.406	0.132	**0.0421 ***	
	Model 3	1.16 (0.95-1.42)	1.00 (reference)	1.27 (0.82-1.97)	1.47 (0.93-2.33)	**1.70 (1.07-2.71)**	0.108
		0.143		0.292	0.0985	**0.0257 ***	
Nitrate	Range		<27407.41	(27407.41 ,38820.22)	(38820.22, 56718.75)	>56718.75	
	Model 1	0.96 (0.80-1.16)	1.00 (reference)	0.79 (0.55-1.14)	0.70 (0.47-1.02)	**0.59 (0.39-0.88)**	0.239
		0.678		0.211	0.0629	**0.0103 ***	
	Model 2	0.93 (0.75-1.17)	1.00 (reference)	0.72 (0.47-1.08)	0.67 (0.43-1.04)	**0.53 (0.33-0.86)**	0.141
		0.54		0.113	0.0721	**0.0103 ***	
	Model 3	0.94 (0.75-1.18)	1.00 (reference)	0.72 (0.47-1.09)	0.66 (0.42-1.03)	0.49 (0.30-0.81)	0.0927
		0.584		0.12	0.0659	0.00518	
	Range		<501.79	(501.79, 979.41)	(979.41, 2145.45)	>2145.45	
Thiocyanate	Model 1	1.06 (0.95-1.19)	1.00 (reference)	1.31 (0.90-1.89)	1.19 (0.82-1.74)	**1.59 (1.09-2.32)**	**0.0466 ***
		0.304		0.155	0.354	**0.0162 ***	
	Model 2	1.03 (0.90-1.17)	1.00 (reference)	1.21 (0.80-1.84)	1.13 (0.73-1.74)	1.52 (0.99-2.36)	0.183
		0.674		0.376	0.587	0.0588	
	Model 3	1.03 (0.90-1.18)	1.00 (reference)	1.28 (0.84-1.98)	1.16 (0.75-1.82)	**1.59 (1.01-2.50)**	**0.0485 ***
		0.7		0.253	0.506	**0.0446 ***	

Model 1: crude model for NHANES 2017-2018 cycle without other factors
Model 2: adjusted for total cholesterol, HDL cholesterol, vitamin C, vitamin D3, and creatinine levels
Model 3: further adjusted for age, gender, weight, BMI, and race/ethnicity in addition to Model 2

Table 3

Effect of exposure levels of perchlorate, nitrate, and thiocyanate on sleep disturbance with the interaction of vitamins and cholesterol

Sleep disorder level	**Model 1**	Correlation estimate	P value	**Model 2**	Correlation estimate	P value	**Model 3**	Correlation estimate	P value
1	**Perchlorate**	0.0751	0.555	**Perchlorate**	**-0.849**	**0.0218 ***	**Perchlorate**	0.777	0.215
2		**0.461**	**0.00636 ****		-0.129	0.779		-0.0245	0.976
3		-0.0063	0.974		0.232	0.677		0.324	0.71
1	**Nitrate**	-0.00515	0.973	**Thiocyanate**	-0.263	0.278	**Thiocyanate**	0.0168	0.968
2		-0.207	0.276		0.434	0.163		-0.128	0.832
3		-0.341	/		0.247	0.501		**1.28**	**0.0353 ***
1	**Thiocyanate**	0.104	0.223	**Vitamin C**	7.64	0.0853	**HDL**	0.0812	0.441
2		0.197	0.0942		8.28	0.146		-0.0544	0.678
3		**0.239**	**0.0643 ***		1.16	0.843		0.154	0.285
1	**Vitamin C**	-0.124	0.574	**Nitrate +**	0.00706	0.25			
2		**-0.647**	**0.0419 ***	**X25OHD3**	**0.0181**	**0.0213 ***			
3		-0.0515	0.883	**(Vitamin D)**	0.00386	0.667			

Sleep disorder level: Weekly Frequency of Trouble sleeping/ sleep too much: 0 (0 days), 1 (1~3 days), 2 (4~6 days), 3 (nearly 7 days).
Model 1: Three disruptors, vitamins and cholesterol were tested generally for each independent correlation with the outcome.
Model 2: Interaction effect between disrupters and vitamins were investigated.
Model 3: Interaction effect between disrupters and cholesterols were investigated.
Remark: Results with ether insignificant or unavailable P values were not presented here for Model 1, 2 and 3.
Unit: Perchlorate, Nitrate, and Thiocyanate (ng/mg creatinine, log-tranformed); Vitamin C, Total Cholesterol, and HDL (mg/dL); Vitamin D (nmol/L)

4 Discussion

4.1 Perchlorate, nitrate, and thiocyanate and sleep quality

Based on Kruskal-Wallis test, a significant association was discovered between thiocyanate and the frequency of either trouble sleeping or oversleeping while perchlorate and nitrate did not show significant correlation. However, based on the results from multivariate logistic regression model, a significant correlation was observed between all three thyroid disrupters and sleep disturbance. This observation is partially consistent with another study, which indicates that thiocyanate is significantly associated with sleep complaints while perchlorate showed a moderate or null association (18). However, evidence on the direct association between perchlorate, nitrate, thiocyanate, and sleep quality is limited so it may be necessary to seek potential indirect association with sleep quality. For example, a US population-based study suggests an inverse relation between urinary thiocyanate and Parametric Thyroid Feedback Quantile-based index (PTFQI) (19). On the other hand, two critical hormones, thyroxine (T4) and triiodothyronine (T3), that regulate human physiological activity including body temperature maintenance, heart rate and respiration are produced by thyroid gland (20). Thyroid hormone may affect sleep quality by further activating mitochondria, enhancing ATP production (21). Some studies observed that thyroid dysfunction such as thyroid hormone deficiency and hyperthyroidism may be associated with Obstructive Sleep Apnea (OSA) (20) (22). Consequently, these studies may reflect that thiocyanate, perchlorate and nitrate may disturb sleeping by affecting the normal function of thyroid, which is not examined in our study. To seek a more accurate relationship, further direct studies on perchlorate, nitrate, and thiocyanate and sleep quality are necessary.

4.2 Cholesterol, vitamin and sleep quality

One interesting finding is that total cholesterol and HDL were observed to be insignificant related to frequency of either trouble sleeping or oversleeping. It is consistent with a study on the association between cholesterol and quality of sleep, which suggests that sleep quality has a null association with cholesterol-saturated fat index (CSI) (24). Nevertheless, some other studies result in opposite findings, which show that high fat or cholesterol intake is associated with sleep quality and multiple diseases related to sleeping (25)(26)(27). Vitamin C level from model 1 shows significant correlation with frequency of either trouble sleeping or oversleeping while vitamin D3 level represented by 25OHD3 level, is observed to be significantly correlated with sleep disturbance only when nitrate is added in model 2. Many studies show a consistent result that OSA is related to vitamin D deficiency since the lack of vitamin D may impair muscular function and pharyngeal patency, inducing sleep problems including shortened sleep duration and sleepness (28) (29) (30). In addition to vitamin D, many studies also reveal a potential role of vitamin C as supplementation to improve sleep quality. For example, one of them observes vitamin C is a cofactor of multiple neural-related enzymes including dopamine β-hydroxylase and tryptophan affecting mood and depression, which can become a critical cause of insomnia (31). Another interesting finding from this study is that vitamin C deficiency is significantly correlated with moderate to severe insomnia symptoms in the male subgroup while it shows a null association in the female subgroup (31). Gender was discovered to affect all of the outcomes in this study, which indicates that it may become a significant covariate. Referring to these studies, vitamin therapy can become a potential effective therapy for sleep disorder.

5 Conclusion

Association between sleep quality and diverse biochemical components was examined. This study suggests that thiocyanate is significantly related to trouble sleeping/oversleeping frequency. Both gender and race, rather than thiocyanate, show a significant relationship with snore frequency and vitamin D3 is significantly correlated with sleep duration. Considering the importance of sleep disorder prevention, further studies with adjustments are needed to explain the causal association and mechanism of how these biochemical components influence sleep performance and how they may be involved in medications of sleep diseases.

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Yanjun Jin and Weile Su contributed equally to this work and should be considered co-first authors.

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