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ORIGINAL ARTICLE

The relationship between high-density lipoprotein cholesterol and overall sleep quality in the adult population with asthma

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Abstract

Previous basic studies have shown that high-density lipoprotein cholesterol (HDL-C) has anti-inflammatory effects that protect against asthma. Our study was aimed at examining the association between blood lipid levels and sleep quality in the adult population with asthma. We evaluated the blood lipid levels and sleep scores of 1013 adult participants in the Midlife in the United States (MIDUS) study to investigate the association of lipid levels with overall sleep quality using linear regression models in subjects with asthma and without asthma, respectively. In a total of 1013 participants (with asthma = 127 and without asthma = 886) included in our study, participants with asthma had poor sleep quality, compared with participants without asthma. Moreover, our smooth curves suggested that blood HDL-C and triglyceride levels, rather than total cholesterol and low-density lipoprotein cholesterol (LDL-C), were significantly associated with global sleep score. Multivariate correction models were used to further evaluate blood lipid profiles and the overall sleep quality. We observed that only blood HDL-C levels were still negatively and independently associated with global sleep score in participants with asthma ($S\beta = -0.224$, 95% CI -0.448, -0.001, $P = 0.049$) but not in participants without asthma ($S\beta = -0.016$, 95% CI -0.087, 0.055, $P = 0.656$) in Model 3 after adjusting for age, gender, ever smoker, number of drinking years, exercise and body mass index (BMI). Obviously, asthma had a modification effect on the independent association (P interaction = 0.022). Our study suggested that elevated blood HDL-C levels are associated with a reduced risk for poor sleep quality in the adult population with asthma but not in those without asthma.

Keywords Blood lipid · Sleep quality · Asthma · Linear regression

Introduction

Sleep deprivation has been increasingly considered an important risk factor for cardiovascular diseases (CVDs) [1–4]. Sleep studies have reported that abnormal changes in neuroendocrine and autonomic pathways, including alterations in insulin sensitivity, inflammatory markers and cortisol levels, appetite hormones and sympathetic activation, may contribute to increased cardiometabolic risk in individuals with poor sleep [5–7]. However, sleep has not been considered a satisfactory target to improve CVD risk, because many cardiometabolic risk, such as dyslipidemia, eating and drinking too much and different concomitant diseases, may mediate the interaction between sleep and CVDs [8–10]. Interestingly, cardiometabolic risk factors, such as dyslipidemia, have been also shown to be associated with asthma in developed countries. Recently, numerous clinical studies have demonstrated the association between blood lipid levels and asthma [11–15]. However, they observed inconsistently negative [11], positive [12, 13], or irrelevant results [14, 15] between high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) or total cholesterol and the risk of asthma [16–19].

In view of the above research, we hypothesized that asthma might modify the association between changes in blood lipid levels and sleep quality. It is interesting to determine whether blood lipid levels are independently associated with sleep quality and further evaluate whether asthma mediates the association. As a component of the Midlife in the United States (MIDUS) study, a biomarker project

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included sufficient sleep-related variables to be analyzed. Our analysis aimed to explore whether blood lipid levels contribute to an increased risk of poor sleep quality and whether asthma has a modification effect on the association of blood lipid levels with sleep quality.

Materials and methods

Study samples

The MIDUS study is based on a national sample of adult Americans [20]. Our study data are from MIDUS II performed from 2004 to 2006. A biomarker project and data collection were conducted in clinical research centers of the MIDUS study during a 2-day visit [21]. Clinicians or trained staff evaluated the behavioral, psychological, social factors and disease history including asthma. In summary, a total of 1013 participants were included in our study after 242 participants had missing complete variables. Blood samples from all included participants were measured to determine blood levels of HDL-C, LDL-C, triglycerides and total cholesterol. Consistent with the Declaration of Helsinki guidelines, IRB approval was obtained for data collection at the three sites of the MIDUS study and written consent was collected from all included participants.

Assessment of Pittsburgh Sleep Quality Index (PSQI)

Overall sleep quality was evaluated using the PSQI [22]. The PSQI was compiled by Dr. Buysse, a psychiatrist at the University of Pittsburgh, in 1989 [22]. The scale is applicable to the evaluation of sleep quality in patients with sleep disorders and mental disorders, as well as the evaluation of sleep quality in the general population. The global sleep score ranged from 0 to 21. The higher the score, the worse the sleep quality [22, 23].

Confounding factors

Several confounding factors may affect the independent variables (blood lipid profiles) and dependent variables (sleep scores). Sociodemographic characteristics and lifestyle, including age, sex (male), smoking status (ever smoker), number of drinking years, body mass index (BMI) and exercise (frequency of exercise ≥ 3/week), were also included in our study. Smoking status was defined as "ever smoker" or "not ever smoker". Exercise was also classified as "frequency of exercise ≥ 3/week" or "not frequency of exercise ≥ 3/week".

Statistical analyses

Comparisons between continuous variables were performed using the *T* test or Mann–Whitney *U* test. The distribution of categorical variables was studied using the chi-square test.

Statistical analysis was performed using EmpowerStats 3.0. $P \leq 0.05$ was defined as statistically significant. First, we analyzed the associations between the blood lipid profiles (total cholesterol, triglycerides, HDL-C, LDL-C and total/HDL-C ratio) and seven component scores that reflect the severity of various sleep problems (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleep medication and daytime dysfunction) using Pearson correlation analysis in participants with asthma and without asthma, respectively. Then, we used a smooth curve to analyze the relationship between blood lipids and global sleep score. Furthermore, multivariate linear regression models were applied to analyze the associations between blood lipid profiles and global sleep score. In these corrected models, the crude model was adjusted for no confounding factors; Model 1 was adjusted for age and gender; Model 2 was adjusted for age, gender, ever smoker, number of drinking years and exercise; and Model 3 was adjusted for age, gender, ever smoker, number of drinking years, exercise and BMI. Additionally, interaction analysis assessed whether asthma significantly modified the relationship.

Results

Characteristics of participants

In a total of 1013 participants (with asthma = 127 and without asthma = 886) included in our study (Table 1), the blood median values of total cholesterol, triglycerides, HDL-C, LDL-C and ratio total/HDL-C in participants with asthma were 184.00 mg/dL, 114.00 mg/dL, 53.00 mg/dL, 104.00 mg/dL and 3.56, respectively. The median values of blood lipid profiles of participants without asthma were 185.00 mg/dL, 105.00 mg/dL, 53.00 mg/dL, 102.00 mg/dL and 3.42, respectively. There were no significant differences on blood lipid profiles between the two groups (all $P > 0.05$). However, participants with asthma tended to be younger and female, have a higher rate of exercise ≥ 3/week and have a higher BMI. More importantly, participants with asthma had poor sleep quality, based on global sleep score, compared with participants without asthma.

Table 1 Characteristics of participants ($N = 1013$)

Variables	With asthma ($N = 127$)	Without asthma ($N = 886$)	P value
Age (years)	51.00 (43.50–60.50)	54.00 (45.00–62.00)	0.049
Gender (male, *n* (%)	44 (34.65)	411 (46.39)	0.013
BMI (kg/m^2)	29.89 (25.66–34.84)	28.41 (25.06–32.58)	0.015
Ever smoker, *n* (%)	67 (52.76)	449 (50.68)	0.661
Number of drinking years	4.00 (2.00–13.25)	5.00 (2.00–15.00)	0.250
Frequency of exercises ≥ 3/ week, *n* (%)	89 (70.08)	692 (78.10)	0.044
Sleep status			
SLEEP: Global Score	6.00 (4.00–10.00)	5.00 (4.00–8.00)	0.028
SLEEP Component 1—Subjective sleep quality	1.00 (1.00–1.00)	1.00 (1.00–1.00)	0.006
SLEEP Component 2—Sleep latency	1.00 (0.00–2.00)	1.00 (0.00–1.00)	0.100
SLEEP Component 3—Sleep duration	1.00 (0.00–1.00)	1.00 (0.00–1.00)	0.435
SLEEP Component 4—Habitual sleep efficiency	0.00 (0.00–2.00)	0.00 (0.00–1.00)	0.279
SLEEP Component 5—Sleep disturbances range	2.00 (1.00–2.00)	1.00 (1.00–2.00)	< 0.001
SLEEP Component 6—Use of sleeping medication	0.00 (0.00–1.00)	0.00 (0.00–1.00)	0.188
SLEEP Component 7—Daytime dysfunction	1.00 (0.00–1.00)	1.00 (0.00–1.00)	0.249
Blood analysis			
Blood triglycerides (mg/dL)	114.00 (82.50–156.00)	105.00 (75.00–155.75)	0.329
Blood total cholesterol (mg/dL)	184.00 (164.00–215.00)	185.00 (160.00–211.00)	0.506
Blood HDL-C (mg/dL)	53.00 (44.00–66.50)	53.00 (42.00–65.75)	0.362
Blood LDL-C (mg/dL)	104.00 (80.50–132.00)	102.00 (82.00–128.00)	0.863
Blood ratio total / HDL-C	3.56 (2.61–4.49)	3.42 (2.74–4.42)	0.618

BMI body mass index, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol

Pearson correlation analysis of blood lipid profiles and sleep score

The Pearson correlation analysis was performed to evaluate blood lipid profiles and overall sleep quality (Table 2). In participants with asthma, we found that blood triglyceride levels were associated with daytime dysfunction ($r = 0.181$, $P < 0.05$) and blood total cholesterol levels were associated with subjective sleep quality ($r = 0.187$, $P < 0.05$). Blood HDL-C levels were only associated with the use of sleeping medication ($r = -0.269$, $P < 0.01$) and global sleep score ($r = -0.199$, $P < 0.05$). Ratio total/HDL-C levels were only associated with sleep disturbance range ($r = 0.180$, $P < 0.05$), use of sleeping medication ($r = 0.251$, $P < 0.01$) and daytime dysfunction ($r = 0.187$, $P < 0.05$). These results only suggested a significant association between blood lipid profiles and overall sleep quality evaluated using sleep score in participants with asthma. The results of correlation analysis in participants without asthma are also shown in Table 2.

Multivariate correction analysis for blood lipid profiles and global sleep score

Furthermore, as shown in Fig. 1A–D, our smooth curves suggested that only blood HDL-C (Fig. 1A) and triglyceride (Fig. 1D) levels, rather than total cholesterol (Fig. 1C) and LDL-C (Fig. 1B), were associated with global sleep score. Therefore, multivariate correction models were used to further evaluate the relationships between blood lipid profiles and overall sleep quality. As shown in Table 3, we observed that blood HDL-C levels were negatively and independently associated with global sleep score in participants with asthma ($S\beta = -0.224$, 95% CI − 0.448, − 0.001, $P = 0.049$) but not in participants without asthma ($S\beta = -0.016$, 95% CI − 0.087, 0.055, $P = 0.656$) in Model 3 after adjusting for age, gender, ever smoker, number of drinking years, exercise and BMI. Asthma had a modification effect on the independent association (P interaction = 0.022) between HDL-C and global sleep score. Furthermore, blood triglyceride levels were positively and independently associated with global sleep score only in participants without asthma ($S\beta = 0.082$, 95% CI 0.017, 0.147, $P = 0.014$) but not in participants with asthma ($S\beta = 0.146$ 95%CI − 0.096, 0.387, $P = 0.240$) in Model 3. However, asthma did not have a modification effect on the association (P interaction = 0.434). Moreover, we did not find that blood total cholesterol and LDL-C levels were associated with global sleep score in participants with asthma or without asthma in Model 3.

Table 2 Bivariate correlations using standardized variables in participants

Variables	Sleep global score	Subjective sleep quality	Sleep latency	Sleep duration	Habitual sleep Efficiency	Sleep disturbances range	Use of sleeping medication	Daytime dysfunction
With asthma								
Triglycerides	0.136	0.068	0.051	0.152	– 0.053	0.162	0.144	0.181*
Total cholesterol	– 0.062	– 0.187*	– 0.007	– 0.018	– 0.147	0.072	– 0.022	0.056
HDL-C	– 0.199*	– 0.167	– 0.092	– 0.117	– 0.034	– 0.145	– 0.269#	– 0.100
LDL-C	– 0.018	– 0.150	0.022	– 0.019	– 0.126	0.094	0.059	0.048
Ratio total/HDL-C	0.154	0.007	0.070	0.110	– 0.066	0.180*	0.251#	0.187*
Without asthma								
Triglycerides	0.083*	0.084*	0.065	0.026	0.001	0.076*	0.051	0.093#
Total cholesterol	0.036	– 0.013	0.062	– 0.014	0.029	0.074*	0.019	0.002
HDL-C	– 0.005	– 0.032	0.036	– 0.012	– 0.002	0.043	0.014	– 0.085*
LDL-C	0.004	– 0.035	0.020	– 0.023	0.028	0.024	– 0.008	0.009
Ratio total/HDL-C	0.030	0.037	0.001	0.015	0.008	0.011	– 0.003	0.084*

HDL-C high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol

*$P < 0.05$, #$P < 0.01$. Pearson correlation analysis was used

Discussion

Blood lipids, including LDL-C, are a well-known risk factor for CVDs [24, 25]. Whether blood lipid levels are related to sleep quality remains to be confirmed. In a large sample of adults from the MIDUS study, we observed that elevated blood HDL-C levels are related to a reduced risk for poor sleep quality in individuals with asthma but not in those without asthma. Interestingly, asthma has a modification effect on the independent association, suggesting a potential causal pathway for poor sleep quality that is independently associated with asthma. This study is the first to provide evidence on the association of elevated HDL-C levels with poor sleep in individuals with asthma after adjusting for demographic characteristics and lifestyle.

Existing evidence has reported that approximately 1/3 of individuals with high cardiometabolic risk, such as low HDL and high LDL levels, have short sleep times and/or poor sleep quality [26]. Observational studies have demonstrated an inconsistency in the relationship between lipid profiles and sleep quality due to different exposures or outcomes and different study types [27, 28]. In the last several years, new prospective studies on the association between lipid profiles and sleep quality have been explored. For example, in one meta-analysis including 64 observational studies of approximately 20,000 patients, they found that dyslipidemia (low HDL-C and high total cholesterol, triglyceride and LDL-C) was related to an elevated risk of obstructive sleep apnea (OSA) [29]. In contrast, our study found that total cholesterol, triglycerides and LDL-C did not contribute to an increased risk of poor quality of sleep. This difference may come from different age groups and different methods of analysis. However, there is a consistent conclusion that reduced blood HDL-C levels are associated with a higher risk of poor sleep. In the present study, we also compared the blood levels of total cholesterol, triglycerides, LDL-C and HDL-C with sleep between individuals with asthma and those without asthma. We only observed that low blood HDL-C levels are significantly associated with poor sleep in individuals with asthma but not in individuals without asthma. Consistently, another previous meta-analysis including 10 cohort studies suggested significant associations of serum levels of HDL-C with asthma in adults and children, respectively [30, 31].

Existing basic experiments have demonstrated that apoA-I and apoA-II, as well as HDL, have anti-inflammatory effects and exert antioxidant activity by inhibiting the expression of adhesion factors in different organs and tissues [32–36]. A clinical epidemiological investigation has shown that serum apolipoprotein A levels have a positive relationship with asthma outcomes among children, which is consistent with our findings that reduced blood HDL-C levels contributed to poor sleep quality in individuals with asthma but not in those without asthma [37]. Many recent studies have also confirmed that apolipoprotein A-I can reduce asthma occurrence and alleviate oxidative stress, inflammation and airway hyperresponsiveness in animal models [38, 39], which may partly account for why asthma has a significant modifying

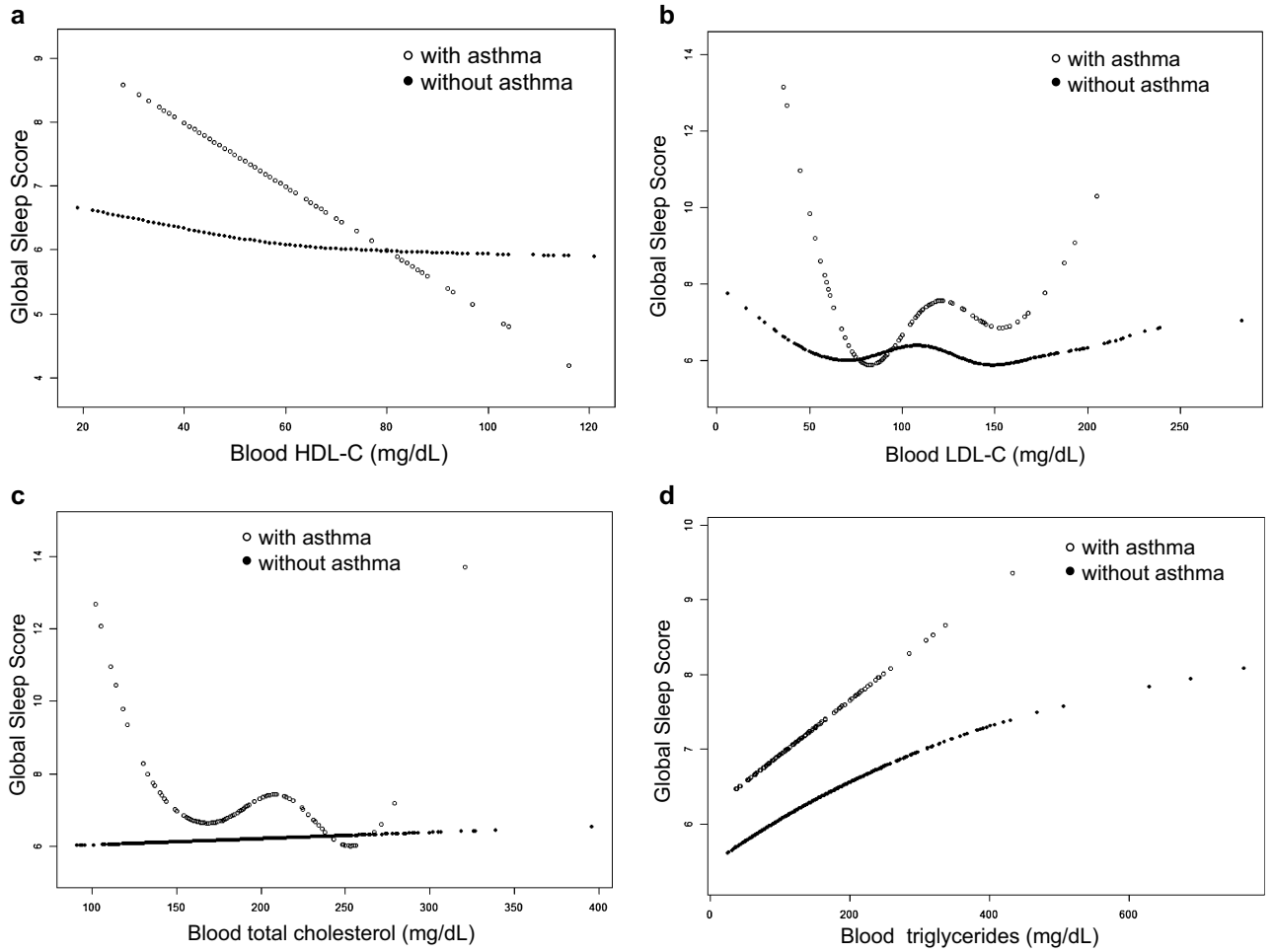

Fig. 1 **A-D**. Smooth curves of the association between lipid profiles and global sleep score

effect on the relationship between HDL-C and sleep quality. Another explanation for the association between low blood HDL-C and poor sleep in individuals with asthma is the sharing of a common proinflammatory response, as suggested in the current perspective that poor sleep quality is significantly related to a high inflammatory response. In our results, the increased risk for poor sleep conferred by low HDL-C levels was mainly observed in individuals with asthma, suggesting that asthma might mediate the interaction between HDL-C and sleep quality. Further causality studies and clinical trials are needed to prove our conclusions.

One of the main strengths of the present study includes the sleep parameters (global sleep score, subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance range, use of sleeping medication and daytime dysfunction) and objectively measured cardiometabolic markers (total cholesterol, triglyceride, HDL-C and LDL-C) that were used to evaluate the correlation between blood lipids and overall sleep quality, which contributes to the limited previous studies on the subject. Our results not only provide characteristics that affect sleep at night (sleep latency and sleep duration) but also those of sleep during the day (daytime dysfunction). Furthermore, we adjusted for many critical confounders, including demographic characteristics (including age and gender), lifestyle (including smoking history and years of alcohol consumption), exercise and BMI in the adult population simultaneously, which makes our conclusion more accurate and reliable. Above all, our study is the first to be performed by stratifying for asthma and found that asthma has a modification effect on the independent association between blood HDL-C levels and overall sleep quality.

This study has several limitations. First, although we have data on asthma, the cross-sectional analysis does not allow us to evaluate causality between HDL-C and sleep scores. However, this limitation does not affect the validity of the relationship of low HDL-C with poor sleep in individuals with asthma. Another limitation is the relatively low number of subjects with asthma ($N = 127$) compared with those without asthma ($N = 886$), which may

Table 3 Multiple linear regression analysis for relationship between blood lipid and sleep global score by adding "with/without asthma" as covariates in participants

Variables	With asthma			Without asthma			*P*#
	Sβ	95% CI	*P* value	*Sβ*	95% CI	*P* value	
Triglycerides							
Crude model	0.183	– 0.050, 0.415	0.126	0.080	0.017, 0.143	0.013	0.352
Model 1	0.181	– 0.053, 0.416	0.132	0.100	0.037, 0.163	0.002	0.462
Model 2	0.170	– 0.070, 0.409	0.168	0.097	0.034, 0.160	0.003	0.458
Model 3	0.146	– 0.096, 0.387	0.240	0.082	0.017, 0.147	0.014	0.434
Total cholesterol							
Crude model	– 0.069	– 0.267, 0.128	0.492	0.035	– 0.029, 0.100	0.284	0.273
Model 1	– 0.075	– 0.274, 0.124	0.463	0.008	– 0.057, 0.072	0.814	0.382
Model 2	– 0.056	– 0.260, 0.148	0.592	0.019	– 0.045, 0.083	0.560	0.377
Model 3	– 0.064	– 0.267, 0.140	0.540	0.017	– 0.047, 0.081	0.596	0.351
HDL-C							
Crude model	– 0.226	– 0.421, – 0.030	0.025	– 0.005	– 0.069, 0.059	0.882	0.021
Model 1	– 0.255	– 0.464, – 0.046	0.018	– 0.053	– 0.122, 0.015	0.126	0.050
Model 2	– 0.251	– 0.462, – 0.041	0.021	– 0.039	– 0.107, 0.029	0.263	0.021
Model 3	– 0.224	– 0.448, – 0.001	0.049	– 0.016	– 0.087, 0.055	0.656	0.022
LDL-C							
Crude model	– 0.020	– 0.217, 0.177	0.844	0.004	– 0.060, 0.069	0.897	0.800
Model 1	– 0.025	– 0.224, 0.173	0.802	– 0.013	– 0.077, 0.051	0.683	0.890
Model 2	0.001	– 0.203, 0.204	0.993	– 0.006	– 0.070, 0.058	0.849	0.939
Model 3	– 0.023	– 0.228, 0.182	0.826	– 0.010	– 0.073, 0.054	0.767	0.978
Ratio total/HDL-C							
Crude model	0.190	– 0.024, 0.405	0.084	0.029	– 0.035, 0.092	0.377	0.118
Model 1	0.200	– 0.024, 0.424	0.083	0.052	– 0.013, 0.118	0.118	0.174
Model 2	0.208	– 0.018, 0.435	0.074	0.049	– 0.017, 0.114	0.143	0.090
Model 3	0.172	– 0.068, 0.412	0.162	0.031	– 0.036, 0.098	0.366	0.107

Crude Model: No adjustment

Model 1: Adjusted for age and gender

Model 2: Adjusted for age, gender, ever smoker, number of drinking years and exercise

Model 3: Adjusted for age, gender, ever smoker, number of drinking years, exercise and BMI

P#: *P i*nteraction

BMI body mass index, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol

lead to bias in real-world analysis results. In addition, although we adjusted the HDL-C-sleep relationship for many covariates, we did not exclude residual covariates, including known and unknown confounding factors. For instance, important factors we did not control for diet and depression, which are associated with HDL-C levels and sleep quality. Finally, self-reported sleep data were used in our study, which may lead to misclassification because of reporting error. Thus, the measurement of objective sleep (actigraphy or polysomnography) should be used.

Conclusion

This study reports for the first time that increased blood HDL-C levels, rather than the other three blood lipid profiles, are associated with reduced risk of poor sleep quality in individuals with asthma but not in those without asthma.

Declarations

Ethical statement IRB approval was obtained for data collection at the three sites of the MIDUS study, and written consent was obtained from all study participants.

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