The Associations of Bedtime, Sleep Duration, Inflammation, and Insulin Resistance Among Adults in the United States: Cross-sectional NHANES 2021-2023

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Abstract

Using national data, this study aims to explore the direct associations of bedtime, sleep duration, inflammation, and insulin resistance, as well as the mediation effect of inflammation on the relationship between sleep and insulin resistance among adults in the U.S. Adults aged 18 and older from the National Health and Nutrition Examination Survey (NHANES) 2021–2023 were included. The analytic sample consisted of 2,843 participants. Structural Equation Modeling and the Monte Carlo method were employed for data analysis. Sleep duration and bedtime were self-reported. Inflammation was assessed using C-reactive protein (CRP) and insulin resistance using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) formula. The structural Equation Model (SEM) path model and the Monte Carlo method were used for testing the direct and indirect (mediation) effects. The results revealed that long sleep duration was associated with a higher HOMA-IR level, compared to recommended sleep duration (β=2.40, $p<.001$). Bedtime was positively associated with HOMA-IR (β=.49, $p<.01$) and CRP (β=.28, $p<.05$). CRP was significantly associated with HOMA-IR; for every 1mg/L increase in CRP, there was a .10 increase in HOMA-IR (β=.10, $p<.001$). CRP mediated the impact of bedtime on HOMA-IR by 3% (RID=.03, $p<.05$). Overall, the later one sleeps, the higher insulin resistance and inflammation levels. Inflammation mediated the relationship between bedtime and insulin resistance. Long sleep duration was associated with increased inflammation levels, compared to the recommended sleep duration. To prevent the development of insulin resistance and inflammation, it is recommended to sleep early with a proper sleep duration (7-9 hours).

Keywords: Sleep duration; Bedtime; Inflammation; Insulin resistance; Structural Equation Modeling (SEM)

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Introduction

Insulin resistance is defined as a decreased effectiveness of insulin, resulting in elevated insulin levels required for normal glucose uptake and utilization compared to the general population (Lebovitz, 2001). It is a significant risk factor for type 2 diabetes mellitus (T2DM) (Lillioja et al., 1993) and affects approximately 47% of adults globally (Fahed et al., 2020).

Evidence suggests that both short (<5 hours) and long (>9 hours) sleep durations are associated with an increased risk of insulin resistance (Buxton et al., 2010; Cedernaes et al., 2015; Javaheri et al., 2011; Shan et al., 2015; Spiegel et al., 1999). However, these findings are not consistent across all studies. Several meta-analyses have found no significant associations between long sleep duration and metabolic health outcomes, including insulin resistance, particularly in longitudinal studies (Iftikhar et al., 2015; Xi et al., 2014; Xie et al., 2021).

Circadian rhythms also regulate metabolism. The human body's internal clock,

regulated by the suprachiasmatic nucleus (SCN) in the brain, is influenced by environmental cues such as light exposure (Saini et al., 2016) and modulated by molecular mechanisms involving period and cryptochrome genes. These are activated by the transcription factors CLOCK and BMAL1 and various nuclear receptors (Partch et al., 2014; Dibner & Schibler, 2015). Misalignment between the internal circadian clock and external cues has been shown to impair metabolic health and contribute to insulin resistance (Stenvers et al., 2016).

A 2015 meta-analysis found that shift workers had a higher risk of developing insulin resistance compared to non-shift workers (Gan et al., 2015). Further, the risk was positively associated with the frequency of monthly night shifts (Vetter et al., 2018). Acute circadian misalignment has been shown to increase insulin resistance in both shift and non-shift workers (Leproult et al., 2014; Morris et al., 2016; Qian et al., 2018). Additionally, later bedtimes have been linked to higher Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) scores, a common marker of insulin resistance (Chen et al., 2021). Nonetheless, the extent to which circadian misalignment affects metabolic health remains debated (Shamsi et al., 2014; Stenvers et al., 2016).

Inflammation may serve as a potential mediator in the relationship between sleep (both duration and timing) and insulin resistance. Short sleep has been associated with elevated inflammatory markers, including interleukins (ILs) and C-reactive protein (CRP) (Ferrie et al., 2013; Smiley et al., 2019). Similarly, circadian disruption caused by misaligned sleep timing may also contribute to systemic inflammation (Bae et al., 2019; Leproult et al., 2014). In turn, chronic inflammation has been linked to insulin resistance (Wu & Ballantyne, 2020). Despite this, inflammation as a mediating mechanism in the relationship between sleep patterns and insulin resistance remains underexplored. Therefore, this study aims to explore the associations of insulin resistance, sleep (duration and bedtime), and inflammation; in addition, inflammation, as a mediator in the relationship between insulin resistance and sleep, is also tested.

Methods

Study population

The National Health and Nutrition Examination Survey (NHANES), conducted by the National Center for Health Statistics (NCHS), employs a multistage probability sampling design to assess the health and nutritional status of the civilian, non-institutionalized U.S. population (CDC, 2022). This study utilized data from the 2021–2023 NHANES cycle, including a total of 8,128 adults aged 18 years and older. Following the approach of Cheng et al. (2024), this study excluded participants with missing or irrelevant data, including sleep (n = 113) and bedtime (n = 89). Most of the missing data were from outcome biomarkers, such as glucose (n = 4,799) and insulin (n = 4,950), which affected the calculation of HOMA-IR (n = 4,970) and CRP (n = 2,307). A total of 2,843 participants were included in the analysis.

Measures

Exogenous variable: Sleep

Sleep duration was collected by asking “the number of hours usually sleep on weekdays” in the NHANES dataset. Following the guidance of the American Academy of Sleep Medicine (Watson et al., 2015) and the Centers for Disease Control and Prevention (CDC) (CDC, 2019), sleep duration was categorized into four sleep duration levels: 1. Sleep deprivation (<5 hours); 2. Short sleep (5-7 hours); 3. Recommended sleep (7-9 hours); and 4. Long sleep (>9 hours).

The circadian rhythm is primarily synchronized to the 24-hour day by sunlight, which serves as the strongest external cue. Exposure to morning light advances the circadian rhythm, promoting earlier sleep–wake timing and increased morning alertness, whereas evening light exposure delays the rhythm, leading to later sleep onset. Therefore, bedtime was used in this study as a behavioral indicator of circadian alignment. Bedtime was collected by asking participants, "What time usually fall asleep on weekdays?" In this study, we included bedtime from 9 pm to 5 am; participants with bedtime between 6 am and 9 pm were removed (n=89). Bedtime was treated as a continuous variable, for each one hour later than the previous one, one unit is added for coding; bedtime: 22:00-23:00 = 2; 23:00-24:00 = 3; 24:00-1:00 = 4; 1:00-2:00 = 5; 2:00-3:00 = 6; 3:00-4:00 = 7; and 4:00-5:00 = 8.

Endogenous variable: Insulin resistance (HOMA-IR)

Following previous studies (Chen et al., 2021) insulin resistance was treated as a continuous variable, measured by HOMA-IR, calculated by insulin(μU/mL) x glucose(mmol/L)/22.5. HOMA-IR is used as a continuous variable in the main analysis to test its associations with sleep (duration and bedtime) and inflammation.

Mediator: Inflammation (C-reactive protein, mg/L)

Following the previous study, this study assessed inflammation by measuring CRP, a synthesized protein engaged in the complement activation, phagocytosis enhancement, and detoxification of damaged tissue, and considered one of the most sensitive measurements of inflammation. In NHANES, CRP was treated as a continuous variable in the unit of mg/L.

NHANES collected glucose, insulin, and CRP data through blood samples taken in the Mobile Examination Centers (MECs) and analyzed in certified laboratories. Participants were asked to fast for at least 8–9 hours before the MEC exam. Fasting insulin was collected by a two-site immunoenzymometric assay, AIA-PACK IRI, to measure the quantity of insulin in human serum and reported in the unit of μU/mL. Fasting glucose was collected by an enzymatic method to measure the glucose-specific metabolites and was reported in the unit of mmol/L. CRP was measured by a two-reagent immunoturbidimetric system, which provides sensitive detection of low-grade inflammation relevant for cardiovascular risk.

Covariates

Age, sex, and race/ethnicity were included as covariates. In addition, dietary intakes, including total fat intake, protein intake, carbohydrate intake, and fiber intake, were also included as covariates in the analysis. In the NHANES 2021–2023 dataset, dietary intake data were collected through 24-hour dietary recall interviews to estimate the types and amounts of foods and beverages (including all types of water) consumed during the previous 24-hour period (midnight to midnight). These data were used to estimate intakes of energy, nutrients, and other dietary components. Each participant completed two 24-hour dietary recalls: the first was conducted in person at the Mobile Examination Center (MEC), and the second was conducted by telephone 3 to 10 days later. For this study, the average of the two rounds of dietary intake was included.

Statistical analysis

Sample weights were applied for statistical analysis (CDC, 2024). Due to the high rate of missing data, we conducted chi-square analyses to compare sex and race distributions between included and excluded participants to assess potential selection bias. In addition, the mean ages of the two groups

were visually compared. For descriptive statistics, demographic characteristics of sleep duration levels and bedtime intervals are presented with frequency and percentage within each demographic feature. Demographic characteristics of HOMA-IR and CRP were shown in mean (m) and standard deviation (SD). For testing the associations of HOMA-IR, sleep (duration and bedtime), and CRP, this study used the Structural Equation Model (SEM) path model. Comparative Fit Index (CFI), Root Mean Squared Error of Approximation (RMSEA), and Standardized Root Mean Square Residual (SRMR) were used for model fitness reference (See Figure 1 for the path diagram). The Monte Carlo method in the Stata "medsem" package was used for testing indirect (mediation) effects. The ratio of the mediation effect to the direct effect (RID) was calculated and reported (Zhao et al., 2010). Additionally, a sensitivity analysis was conducted, excluding individuals who reported bedtimes later than 24:00 (n = 702). Such late sleep timing is considered atypical, a nocturnal sleep behavior, which affects approximately 14% of the population, as reported in a previous population-based study (Tse et al., 2021). A p-value <.05 was used for statistical significance inference. All statistical analyses in this study were conducted in the Stata/SE 18.0 version (College Station, Texas).

Results

Demographic characteristics

The chi-square analyses indicated no significant distributional differences in sex, Mexican Americans, other Hispanics, or individuals of other races between included and excluded participants. However, significant differences were observed in the proportions of White and Black Americans (ps < .01), with a higher percentage of White Americans and a lower percentage of Black Americans among included participants compared with those excluded. Additionally, the mean ages of the two groups were identical.

Demographic characteristics among included participants across various sleep durations and bedtimes are shown in Tables 2 and 3. Overall, the mean age of the participants was 53; 71% of participants have recommended sleep durations (7-9 hours/day), and most of the participants (65%) sleep between 21:00 and 24:00.

Descriptive statistics

As shown in Table 4, the average HOMA-IR and CRP levels among participants were 4.28 and 3.77 mg/L, respectively. Participants with sleep deprivation had the highest average CRP level of 4.64 mg/L; participants with long sleep duration had the highest average HOMA-IR level of 5.45. As for bedtime, the average levels of CRP and HOMA-IR are seemingly low among participants of bedtime between 21:00 and 23:00, compared to those between 23:00 and 5:00.

Direct paths among sleep (duration and bedtime), CRP, and HOMA-IR

The relationships between sleep duration, bedtime, CRP, and HOMA-IR were investigated in an SEM path analysis, controlling for demographics (age, sex, and race/ethnicity). The results showed that those with long sleep duration demonstrated higher HOMA-IR by 2.40, compared to those with recommended sleep duration (β=2.40, p<.001). Bedtime was positively associated with HOMA-IR (β=.49, p<.01) and CRP (β=.28, p<.001), indicating for every one hour late in bedtime after 9 pm, there is a .49 increase in the HOMA-IR level and .28 mg/L increase in the CRP level. CRP was significantly associated with HOMA-IR; for every 1mg/L increase in CRP, there was a .10

Table 1. *Comparison of demographics between included participants and excluded participants*

	Included participants	Excluded participants
Age (M, SD)[a]	52.69 (18.04)	51.85 (18.82)
Sex		
Female (n,%)[b]	1,592 (56.00%)	2,396 (45.33%)
Male (n, %)	1,251 (44.00%)	2,889 (54.67%)
		Chi2(1)=1.41, p=.24
Race		
Mexican American (n, %)	212 (7.46%)	384 (7.26%)
		Chi2(1)=10.49, p=.75
Other Hispanic (n, %)	307 (10.80%)	509 (9.63%)
		Chi2(1)=2.85, p=.09
White American (n, %)	1,712 (60.19%)	2,979 (56.37%)
		Chi2(1)=10.88, p<.01
Black American (n, %)	286 (10.06%)	754 (14.27%)
		Chi2(1)=28.24, p<.001
Other (n, %)	326 (11.47%)	659 (12.47%)
		Chi2 (1)=.02, p=.88
Total	2843	5,285

Note. [a]M, SD refers to the mean and standard deviation.
[b]n,% refers to the number of participants and percentage within each associated demographic feature.

Table 2. *Demographic characteristics of sleep durations*

	Sleep deprivation	Short sleep	Recommended sleep	Long sleep	Total
Age (M, SD)[a]	53.55 (16.02)	52.18 (16.74)	52.68 (18.06)	54.12 (21.07)	52.78 (18.02)
Sex					
Female (n,%)[b]	98 (6.16%)	216 (13.57%)	1,131 (71.09%)	147 (9.23%)	1,592 (100%)
Male (n,%)	79 (6.32%)	202 (16.14%)	879 (70.26%)	91 (7.27%)	1,251 (100%)
Race					
Mexican (n,%)	12 (5.66%)	30 (14.15%)	150 (70.75%)	20 (9.43%)	212 (100%)
Other Hispanics (n,%)	27 (8.79%)	51 (16.61%)	198 (64.56%)	31 (10.10%)	307 (100%)
White (n,%)	74 (4.32%)	225 (13.14%)	1,276 (74.59%)	137 (8.00%)	1,712 (100%)
Black (n,%)	32 (11.19%)	59 (20.63%)	168 (58.74%)	27 (9.44%)	286 (100%)
Other (n,%)	32 (9.82%)	53 (16.26%)	218 (66.81%)	23 (7.06%)	326 (100%)
Total (n,%)	177 (6.22%)	418 (14.70%)	2,010 (70.72%)	238 (8.38%)	2,843 (100%)

Note. [a]M, SD refers to the mean and standard deviation.
[b]n,% refers to the number of participants and percentage within each associated demographic feature.

Table 3. *Demographic characteristics of bedtime*

	21:00	22:00	23:00	24:00	1:00	2:00	3:00	4:00	Total
Age (M, SD)[a]	55 (16)	54 (17)	53 (19)	50 (19)	51 (19)	44 (18)	46 (20)	41 (15)	53 (18)
Sex									
Female (n,%)[b]	226 (14%)	550 (35%)	413 (26%)	243 (15%)	74 (5%)	58 (4%)	23 (1%)	5 (.3%)	1,592 (100%)
Male (n,%)	203 (16%)	402 (32%)	347 (28%)	172 (14%)	67 (5%)	37 (3%)	16 (1%)	7 (.6%)	1,251 (100%)
Race									
Mexican (n,%)	26 (12%)	80 (38%)	49 (23%)	34 (16%)	12 (6%)	4 (2%)	5 (2%)	2 (1%)	212 (100%)
Other Hispanics(n,%)	36 (12%)	90 (29%)	98 (32%)	52 (17%)	17 (6%)	12 (4%)	0	2 (.7%)	307 (100%)
White (n,%)	280 (16%)	623 (36%)	461 (27%)	204 (12%)	66 (4%)	56 (3%)	18 (1%)	4 (.2%)	1,712 (100%)
Black (n,%)	43 (15%)	69 (24%)	74 (26%)	51 (18%)	28 (10%)	11 (4%)	10 (4%)	0	286 (100%)
Other (n,%)	44 (13%)	90 (28%)	78 (24%)	74 (23%)	18 (5%)	12 (4%)	6 (2%)	4 (1%)	326 (100%)
Total	429 (15%)	952 (33%)	760 (27%)	415 (15%)	141 (5%)	95 (3%)	39 (1%)	12 (.4%)	2,843 (100%)

Note. [a]M, SD refers to the mean and standard deviation.
[b]n,% refers to the number of participants and percentage within each associated demographic feature.

Table 4. *Descriptive statistics of insulin resistance, inflammation, sleep (duration and bedtime), and demographics*

	n[b]	C-reactive protein, mg/L (M, SD)[a]	HOMA-IR (M, SD)[a]
Sleep duration			
Sleep deprivation (<5 hrs)	177	4.64 (7.34)	4.61 (8.02)
Short sleep (5-7 hrs)	418	3.82 (7.63)	3.83 (4.65)
Recommended sleep (7-9 hrs)	2,010	3.59 (7.03)	4.21 (11.34)
Long sleep (>9 hrs)	238	4.53 (10.63)	5.45 (8.25)
Bedtime			
21:00-22:00	429	3.57 (5.30)	3.48 (4.26)
22:00-23:00	952	3.36 (6.13)	3.84 (6.17)
23:00-24:00	760	4.04 (8.25)	4.69 (12.67)
24:00-1:00	415	3.46 (6.05)	5.18 (16.46)
1:00-2:00	141	5.11 (13.90)	4.66 (9.76)
2:00-3:00	95	5.38 (12.58)	4.43 (4.43)
3:00-4:00	39	4.64 (7.86)	3.88 (4.08)
4:00-5:00	12	4.57 (6.52)	6.38 (5.56)
Sex			
Female	1,592	4.14 (7.03)	3.77 (8.56)
Male	1,251	3.27 (8.05)	4.93 (11.92)
Race			
Mexican American	212	3.72 (5.40)	5.35 (14.86)
Other Hispanics	307	3.65 (4.60)	5.26 (8.96)
White	1,712	3.76 (8.48)	4.03 (10.69)
Black	286	5.17 (7.92)	4.32 (6.61)
Other	326	2.67 (4.17)	3.93 (6.81)
Total	2,843	3.77 (7.51)	4.28 (10.19)

Note. [a]M, SD refers to the mean and standard deviation.
[b]n refers to the number of participants

Table 5. *Path model of insulin resistance, inflammation, sleep (duration and bedtime), and covariates*

		Coefficient b	Linearized S.E.	t	p-value
HOMA-IR					
	Bedtime	.49	.13	3.66	<.01
	C-reactive protein	.10	.02	5.33	<.001
	Sleep duration		(Recommended sleep as ref.)		
	Sleep deprivation	.03	1.54	.02	.99
	Short sleep	-.57	.42	-1.38	.19
	Long sleep	2.40	.53	4.50	<.001
	Sex		(Male as ref.)		
	Female	-1.02	.26	-3.95	<.01
	Age	.04	.01	2..75	<.05
	Race		(White as ref.)		
	Mexican American	2.44	1.55	1.57	.14
	Other Hispanics	2.24	.73	3.07	<.01
	Black	1.16	.72	1.61	.13
	Other	-.04	.35	-.12	.91
	Fat intake	.01	.01	1.04	.32
	Fiber intake	-.01	.02	-.55	.59
	Protein intake	.001	.004	.03	.98
	Carb intake	-.003	.004	-.84	.41
C-Reactive Protein					
	Bedtime	.28	.11	2.56	<.05
	Sleep duration		(Recommended sleep as ref.)		
	Sleep deprivation	.65	1.16	.56	.58
	Short sleep	-.74	.60	-1.24	.25
	Long sleep	-.04	.52	-.07	.94
	Sex		(Male as ref.)		
	Female	1.06	.23	4.43	<.001
	Age	-.002	.01	-.20	.84
	Race		(White as ref.)		
	Mexican American	.98	1.08	.91	.38
	Other Hispanics	.76	.58	1.30	.21
	Black	1.41	1.24	1.13	.27
	Other	-.88	.42	-2.11	.06
	Fat intake	-.005	.008	-.64	.53
	Fiber intake	-.10	.03	-3.78	<.01
	Protein intake	.005	.007	.63	.54
	Carb intake	.004	.004	.98	.34

Note. Nationally representative of the US adult population 18 years or older by use of National Health and Nutrition Examination Survey (NHANES) survey weights. N=2,843; Number of strata=15; Number of PSUs=30; Population size=89,236,940

Table 6. *Sensitivity analysis of the associations between HOMA-IR, C-reactive protein, and sleep, and covariates*

		Coefficient b	Linearized S.E.	t	p-value
HOMA-IR					
	Bedtime	.66	.30	2.16	<.05
	C-reactive protein	.12	.05	2.40	<.05
	Sleep duration		(Recommended sleep as ref.)		
	Sleep deprivation	1.28	2.61	.49	.63
	Short sleep	-.54	.54	-1.00	.33
	Long sleep	2.32	.56	4.14	<.01
	Sex		(Male as ref.)		
	Female	-.86	.32	-2.69	<.05
	Age	.04	.01	2..50	<.05
	Race		(White as ref.)		
	Mexican American	2.90	1.91	1.52	.15
	Other Hispanics	2.40	.71	3.40	<.01
	Black	1.23	.80	1.54	.14
	Other	-.13	.36	-.36	.72
	Fat intake	.01	.01	1.04	.32
	Fiber intake	-.02	.02	-.78	.45
	Protein intake	-.001	.004	-.15	.88
	Carb intake	-.001	.004	-.33	.75
C-Reactive Protein					
	Bedtime	.10	.14	.74	.47
	Sleep duration		(Recommended sleep as ref.)		
	Sleep deprivation	-.12	.69	-.17	.87
	Short sleep	-.21	.90	-.24	.82
	Long sleep	-.14	.49	-.29	.78
	Sex		(Male as ref.)		
	Female	1.19	.26	4.45	<.001
	Age	-.002	.01	-.25	.81
	Race		(White as ref.)		
	Mexican American	.07	.63	.11	.91
	Other Hispanics	1.16	.63	1.85	.08
	Black	1.64	1.25	1.32	.21
	Other	-1.14	.30	-3.76	<.01
	Fat intake	-.005	.007	-.68	.51
	Fiber intake	-.09	.02	-3.56	<.01
	Protein intake	.001	.006	.17	.87
	Carb intake	.004	.003	1.44	.17

Note. Nationally representative of the US adult population 18 years or older by use of National Health and Nutrition Examination Survey (NHANES) survey weights. N=1,843; Number of strata=15; Number of PSUs=30; Population size=55,410,442

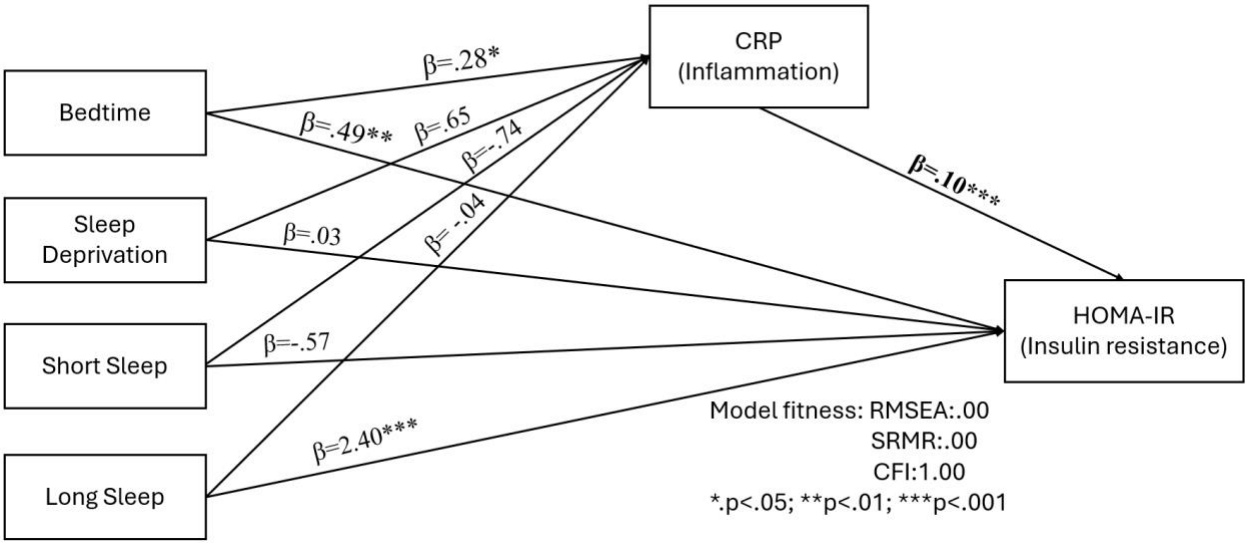

Figure 1. SEM path diagram

increase in HOMA-IR (β=.10, p<.001) (Table 5).

Among covariates, age was positively associated with HOMA-IR (β = 0.04, p < .05). Females, compared to males, had significantly lower HOMA-IR (β=-1.02, p<.01) and higher CRP (β=1.06, p<.001). Compared to White Americans, other Hispanics had higher values of HOMA-IR (β=2.24, p<.01). Fiber intake was negatively associated with CRP (β=-.10, p<.01) (Table 5).

Indirect path (mediation) of CRP to the path between sleep and HOMA-IR

The result showed that CRP mediated the impact of bedtime on HOMA-IR by 5%, meaning that about 5 % of the effect of bedtime on HOMA-IR is mediated by CRP (RIT=.05, p<.01).

Sensitivity analysis

The sensitivity analysis excluding individuals with bedtimes later than 24:00 confirmed most of the findings from the primary analyses. However, the association between bedtime and CRP was no longer significant in this restricted sample. Consequently, CRP did not mediate the relationship between bedtime and HOMA-IR in the sensitivity analysis (Table 6).

Discussion

Using the newly released NHANES 2021–2023 dataset, this study identified significant associations between sleep patterns and insulin resistance. Specifically, later bedtime was positively associated with both HOMA-IR and C-reactive protein (CRP) levels, with CRP significantly mediating the relationship between bedtime and insulin resistance. Regarding sleep duration, participants with long sleep (>9 hours) exhibited significantly higher HOMA-IR compared to those with recommended sleep duration (7–9 hours).

Bedtime, inflammation, and insulin resistance

Similar associations between circadian misalignment and insulin resistance have been reported in prior studies (Morris et al., 2016; Stenvers et al., 2016; Vetter et al., 2018). For instance, a study conducted among adolescent girls in Mexico City found

that each hour delay in midpoint bedtime was associated with a 0.09 increase in HOMA-IR (Chen et al., 2021). Consistent with these findings, the current study demonstrates that, among U.S. adults, each one-hour delay in bedtime after 9:00 PM was associated with a 0.49 increase in HOMA-IR.

Several biological mechanisms may underlie these associations. The circadian clock is known to regulate insulin secretion and sensitivity via endocrine control of organ function (la Fleur et al., 2001; Marcheva et al., 2013). Disruptions in the β-cell clock of the pancreas can impair insulin secretion (Marcheva et al., 2010; Sadacca et al., 2010), contributing to diurnal variations in whole-body insulin sensitivity (Gibson & Jarrett, 1972) and the development of insulin resistance. Additionally, irregular sleep schedules may misalign eating patterns and disrupt the gut microbiome, further promoting inflammation and insulin resistance (Bae et al., 2019).

This study also corroborates earlier findings linking circadian misalignment to systemic inflammation (Leproult et al., 2014; Morris et al., 2016; Morris et al., 2017). In the sensitivity analysis, excluding individuals who slept later than 24:00 rendered the association nonsignificant. This may suggest that later bedtimes are associated with more pronounced adverse effects on CRP. Descriptive statistics also indicated higher CRP levels among those with bedtimes after 24:00. Disrupted sleep timing impairs the 24-hour rhythm of neural and hormonal activity, including elevations in cortisol (Morris et al., 2017), which may drive inflammatory responses through altered gene expression in central and peripheral circadian clocks (Castanon-Cervantes et al., 2010).

Moreover, consistent with previous research (Rehman & Akash, 2016), this study found that elevated inflammatory markers, such as CRP, were significantly associated with insulin resistance. Mechanistically, inflammatory cytokines interfere with insulin signaling by inducing serine phosphorylation and degradation of insulin receptor substrate-1 (IRS-1), ultimately impairing insulin activity (Haruta et al., 2000; Hotamisligil, 1999).

A mediation effect of CRP was observed in this study, with approximately 5% of the association between bedtime and HOMA-IR mediated by CRP. However, the effect size was relatively small, and the sensitivity analysis revealed no evidence of mediation. Therefore, caution is warranted when interpreting the mediation effect identified in the primary analysis. These findings highlight the need for further studies to explore the relationships between sleep, inflammation, and metabolic health, particularly their potential interactions.

Sleep duration, inflammation, and insulin resistance

Consistent with previous studies (Javaheri et al., 2011; Shan et al., 2015), this study found that long sleep duration was significantly associated with higher levels of insulin resistance, as measured by HOMA-IR, compared to recommended sleep duration. However, in contrast to several earlier studies (Buxton et al., 2010; Cedernaes et al., 2015; Ferrie et al., 2013; Smiley et al., 2019; Spiegel et al., 1999; St-Onge et al., 2012), short sleep duration was not significantly associated with insulin resistance in this analysis. Additionally, no significant association was found between sleep duration and CRP levels.

These discrepancies may be explained by the inclusion of bedtime as a covariate in the statistical model. Bedtime may independently influence both insulin resistance and inflammation, potentially attenuating the observed effects of sleep duration when included in the model. Supporting this hypothesis, an animal study by Castanon-Cervantes et al. (2010)

demonstrated that circadian disruption—rather than sleep deprivation per se—was responsible for dysregulation of the innate immune system and elevated inflammation. This suggests that circadian misalignment, as reflected by later bedtimes, may play a more critical role in metabolic and inflammatory processes than sleep duration alone.

Strengths and Limitations

This study has several strengths. It utilized the most recent, population-representative NHANES 2021–2023 dataset, which reflects the civilian noninstitutionalized U.S. population, enhancing the generalizability of the findings. Moreover, NHANES provides biomarker data for insulin resistance and inflammation, offering objective outcome measures that are less susceptible to biases inherent in self-reported data, such as those influenced by stress (Tavenier et al., 2022). However, there are some limitations. Missing data represents a major limitation of this analysis and may offset the advantages of using a large, nationally representative sample. The cross-sectional nature of NHANES could only generate associations, rather than causations. Data is missing in the biomarker variables. People who provided biomarkers in laboratories might be more likely to care about their health and consider more health than those who did not provide biomarkers. To evaluate potential selection bias, we compared demographic distributions between included and excluded participants. While no significant differences were observed for most demographic characteristics, significant differences were found in the distributions of White and Black Americans. These racial differences may affect the accuracy and generalizability of the results. In addition, NHANES collects sleep duration and bedtime for both weekdays and weekends. T-tests revealed significant differences between weekdays and weekends, with participants tending to sleep longer but later on weekends. This study focused exclusively on weekday sleep patterns, as they represent a more regular behavior, encompassing five of the seven days, compared with only two weekend days. This approach better aligns with the study's objective of examining the association between sleep patterns and insulin resistance. Although related to circadian health, given the primary objective of our study was to examine the direct associations of bedtime and sleep duration with inflammation (CRP) and insulin resistance (HOMA-IR), social jetlag was not included as a factor in the analysis. This study focused on habitual bedtime and sleep duration as core behavioral sleep parameters. Social jetlag represents a distinct circadian misalignment construct, and future analyses should investigate its potential contribution to inflammation and insulin resistance. Lastly, sleep duration was self-reported, which is subject to recall bias and a tendency to overestimate actual sleep time.

Conclusions

This study used NHANES 2021–2023 data to examine the relationships among sleep patterns, inflammation, insulin resistance, and various metabolic health indicators. Findings revealed that later bedtimes were positively associated with both insulin resistance and inflammation, with inflammation partially mediating the effect of bedtime on insulin resistance. Compared to recommended sleep duration, long sleep duration was linked to increased inflammation levels. To prevent the development of insulin resistance and inflammation, it is recommended to sleep early with a proper sleep duration (7-9 hours).

Implications for Health Behavior Research

The results revealed that, besides sleep duration, bedtime is also significantly

associated with metabolic health. The later one sleeps, the higher the inflammation levels and insulin resistance. This study implies that the importance of educating the public on keeping a healthy circadian rhythm by sleeping early, and future studies shall explore the risk factors for late sleep.

Discussion Questions

What are the driving factors for sleeping late and not having the recommended sleep duration? And what can the health professionals do about it?

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