Big Data Analysis of the Relationship between Sleep Duration, Hyperuricemia, and Hypertension

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Abstract

Previous studies have reported that sleep duration may increase the risk of hypertension and hyperuricemia. However, the results are contradictory. We investigated whether sleep duration was independently associated with hypertension and hyperuricemia. We aimed to assess the association between sleep duration, hypertension, and hyperuricemia in a population-based cross-sectional study. MJ Health Examination Center Database was used to obtain a large, representative sample of Taiwan population. This study revealed that short sleep duration is associated with an increased risk of hyperuricemia and hypertension. Patients who sleep ≤ 4 hours have a higher risk of hypertension than those who sleep 7 hours (Male: AOR = 1.131, 95% CI = 1.073-1.192; Female: AOR = 1.257, 95% CI = 1.190 -1.327). The risk of hyperuricemia in patients who sleep ≤ 4 hours is higher than those who sleep 7 hours (Male: AOR = 1.657, 95% CI = 1.213-5.768; Female: AOR = 1.583, 95% CI = 1.050-3.660). Besides, the risk of hyperuricemia in females who slept for more than 8 hours was 1.019 times that of those who slept for 7 hours.

Participants aged < 50 years who sleep less than 4 hours a day have a higher risk of hypertension and hyperuricemia than those of the ages of 50-75 and >75 years. There were excellent response rates to sleep duration associated with hypertension and hyperuricemia questions and measurements representative sample of Taiwan population.

Keywords: Big data, Hypertension, Hyperuricemia, Sleep duration

1 Introduction

Recent studies have reported that in terms of sleep duration or sleep quality, lack of sleep is associated with an increased risk of hypertension [1-2]. The results of the NHANES study demonstrated that there is an association between sleeping less than 5 hours a night and an increased risk of hypertension, but the results are conflicting [3]. Similarly, a study of non-insomnia elderly subjects also showed that sleep duration is not associated with the prevalence of hypertension. However, there are conflicting results. Therefore, the relationship between sleep duration and hypertension needs further research [4].

Hypertension is the main cause of death and disability from cardiovascular diseases, and 1.13 billion people worldwide suffer from this disease [5]. It is recommended that the diagnosis of hypertension is based on when a person's systolic blood pressure (SBP) in the office or clinic is ≥140 mm Hg and/or their diastolic blood pressure (DBP) is ≥90 mm Hg following repeated examination [6]. In the United States, 75 million adults (about one-third of the population) suffer from high blood pressure, and only about half of them have achieved the required therapeutic blood pressure control [7]. About 4.8 million adults in Taiwan suffer from hypertension, and about 1 in 4 people suffer from the disease. The prevalence rate has increased three times compared with 10 years ago [8].

Hyperuricemia is one of the most common metabolic diseases in modern society. Previous studies have shown that uric acid levels are related to certain medical conditions, such as chronic kidney disease, diabetes, non-alcoholic fatty liver, hypertension, and cardiovascular disease [9]. Most studies have found that sleep breathing disorders such as obstructive sleep apnea (OSA) are related to hyperuricemia and gout [10]. However, studies investigating the relationship between sleep duration and uric acid levels are limited [11].

Hyperuricemia is defined as men's serum urate concentration higher than 420μmol/L (7.0 mg/dL) and women's serum urate concentration higher than 360μmol/L (6.0 mg/dL) [10]. As many as 2.7 million people in Taiwan suffer from hyperuricemia, and about 5-20% of hyperuricemia patients will eventually develop gout [11].

More and more pieces of evidence show that uric acid is an independent risk factor for cardiovascular disease, and its pathological processes include insulin resistance, oxidative stress, and systemic inflammation, which are all considered to be important risk factors for the development or progression of hypertension [12-14]. Several studies have shown that there is an independent link between hyperuricemia and hypertension, although the issue of direct causality is still under debate [15]. As showed in Table 1, classified, and systematically reviewed the relationship between sleep duration, hyperuricemia, and hypertension [16-25].

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Table 1. Classified and systematically reviewed the relationship between sleep duration, hyperuricemia, and hypertension

Paradigm	Reference
Short sleep duration was associated with an increased risk of prevalent hypertension	Wang et al., (2012) [16] Faraut et al., 2012 [17] Li et al., 2018 [18]
Short sleep duration was associated with an increased risk of prevalent hyperuricemia	Chou et al., 2020 [19] Papandreou et al., 2019 [20] Cui et al., 2017 [21]
Hyperuricemia is an independent risk factor for incident hypertension	Stewart et al., 2019 [22] Cheng et al., 2017 [23] Lee et al., 2015 [24] Lin et al., 2012 [25]

In Table 2, summary of several studies has shown that sleep duration associated with/without hypertension or hyperuricemia [26-31].

Table 2. Summary of sleep duration associated with/without hypertension or hyperuricemia

First author/year	Conclusion
J. M. Bock et al., (2022) [26]	Long sleep may also be associated with hypertension and describe the parabolic relationship between total sleep time and blood pressure. The potential role of gut microbial health in the cross-communication of lifestyle patterns (exercise, diet, and sleep) with blood pressure regulation.
Li et al., (2021) [27]	Favorable sleep pattern was associated with a low risk of hypertension, regardless of genetic risk. These findings highlight the potential of sleep interventions to reduce risk of hypertension across entire populations.
Li et al., (2021) [28]	Poor sleep patterns were closely correlated with the risk of hypertension. Participants with poor sleep patterns were associated with an increased risk for hypertension. A short sleep duration, self-reported trouble sleeping, and sleep disorder were related to the risk of hypertension.
Yu et al., (2021) [29]	Short sleep duration is associated with higher risk of hyperuricemia independently of cardiometabolic risk factors, especially in individuals without traditional hyperuricemia risk factors.
Wang et al., (2021) [30]	We did not observe any relation between nocturnal sleep duration and risk of hyperuricemia in the study. Longer daytime napping duration (but not nocturnal sleep duration) was independently associated with risk of hyperuricemia in a Chinese population.
Chung et al., (2021) [31]	The sleep duration was not significantly associated with hyperuricemia in both males and females. Inadequate sleep duration was not significantly associated with the risk of hyperuricemia in Korean adults. In addition, the sleep duration was not significantly associated with serum uric acid levels in obese and non-obese participants.

However, sleep duration may be a key mediating factor linking hypertension, and hyperuricemia. Understanding this connection may contribute to effective therapeutic interventions for hypertension or hyperuricemia. At present, longitudinal observational studies evaluating the effect of sleep duration on hypertension or hyperuricemia are limited, and the results are inconsistent. Therefore, we hypothesize that short sleep duration is related to hypertension or hyperuricemia. We used MJ Health Examination Center database in Taiwan to investigate whether sleep duration increases the risk of subsequent hypertension or hyperuricemia in the population of 20 to 65 years old. Moreover, the role of age and sex in the relationship between sleep duration, hypertension or hyperuricemia was also evaluated.

2 Methods

2.1 Study Population

This population-based cross-sectional study enrolled 308,004 participants from MJ Health Examination Center Database, between 1 January 2016 and 31 December 2018 representative sample of Taiwan population. We included

patients aged above 18 years who were diagnosed with hyperuricemia and hypertension (n = 101,566). Patients diagnosed with hyperuricemia and hypertension before 1 January 2016 were excluded. In additional, participants aged <18 years, used drugs for hyperuricemia, hypertension, DM or dyslipidemia, and with incomplete data (n = 156,083) were excluded (n = 50,355). A total of 101,566 (49,040 males and 52,526 females) patients, whose ages ranged from 20 to 65 years old, who visited a Health Examination center for a general health assessment were selected in this study.

All subjects completed a structured questionnaire, which included demographic information, assessment of age, gender, marital status, education level, and current disease status. After an overnight fast (12 hours), all subjects were asked to draw blood. After the blood draw, the samples were taken from fasting plasma glucose (FPG), triglycerides (TG), and total cholesterol (TC) in the MJ Health Examination center in Taiwan. High-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), serum uric acid (SUA) analysis.

All subjects underwent a series of blood, urine, physical measurements, functional examinations, physical examinations, and medical examinations of medical history. The screening procedures of the same instrument model are used in all physical examination centers, and the results are managed and stored centrally. Secondary data without any personally identifiable information was used, and This study was approved by the Institutional Review Board of the Tri-Service General Hospital, and the requirement for individual written informed consent was waived (TSGHIRB No. B-109-39). All or part of the data used in the research were authorized by and received from MJ Health Research Foundation (Authorization Code: AP_A2020019). Any interpretation or conclusion de-scribed in the paper does not represent the views of MJ Health Research Foundation. This study was supported by Tri-Service General Hospital Research Foundation (TSGH-B-111018). The sponsor has no role in study design, data collection, and analysis, decision to publish, or preparation of the manuscript. The flowchart of participant selection from MJ Health Examination Center in Taiwan (Figure 1).

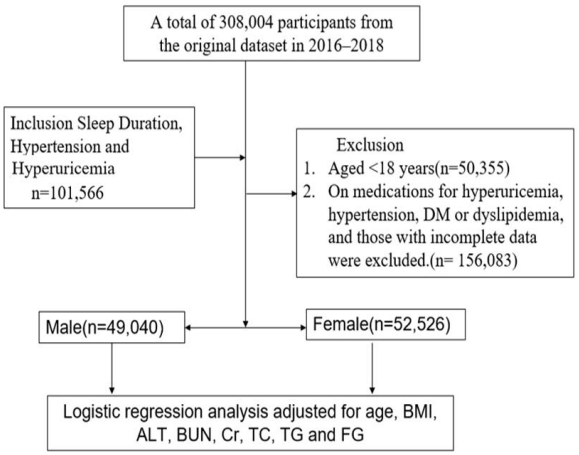

Figure 1. Flowchart of participant selection

Slightly different questionnaires were used to collect information about sleep duration, “How many hours do you usually sleep each night?” For both questions, the following four response options were provided: ≤ 4, 5, 6, 7, and ≥8 hours. As a result, all participants were divided into five groups for analysis: < 4 hours, 5, 6, 7, and ≥ 8 h/d [32]. We use the Pittsburgh Sleep Quality Index (PSQI) to assess sleep quality and define poor sleep quality as an overall PSQI score greater than 5 [33].

Hyperuricemia is defined as serum uric acid (SUA) >420 μmol/L (7.0 mg/dL) in men and >360 μmol/L (6.0 mg/dL) in women [10]. According to WHO criteria, BMI is divided into underweight (<18.5 kg/m2), normal (18.5-25 kg/m2), overweight (25-30 kg/m2) and obese (> 30 kg/m2) [34]. Hypertension is defined as systolic blood pressure (SBP) ≥140 mm Hg or/and diastolic blood pressure (DBP) ≥90 mm Hg [6]. Using the American Diabetes Association criteria, FBG was divided into normoglycemia (FBG < 5.6 mmol/L), impaired fasting glucose (IFG) (FBG ≥ 5.6 mmol/L ≤ FBG < 7.0 mmol/L), and diabetes (FBG ≥ 7.0 mmol/L) L)/B). Dyslipidemia is classified by ATP III, TG: normal <1.69 (mmol/L), critical value high 1.69-2.26 (mmol/L), highest 2.26-5.65 (mmol/L), very high ≥ 5.65 (mmol/L). TC: ideal value <5.17 (mmol/L), high critical value 5.16-6.24 (mmol/L), high value ≥6.24 (mmol/L). HDL-C: high 1.56 (mmol/L), best 1.03-1.56 (mmol/L), low <1.03 (mmol/L). LDL-C: optimal <2.59 (mmol/L), close to optimal 2.59-3.38 (mmol/L), critical height 3.38-4.16 (mmol/L), highest 4.16-4.94 (mmol/L), very high ≥ 4.94 (mmol/L) [35].

2.2 Statistical Analysis

The descriptive statistics were expressed in the form of percentages, averages, and standard deviations. Values are expressed as the mean and standard deviation (SD) of continuous variables and the sum (proportion) of categorical variables. Multivariate adjusted odds ratio (OR) and 95% confidence interval (CI) were used to analyze the effect of sleep duration on the development of hyperuricemia and hypertension. Conditional logistic regression analyses were performed to evaluate the relationship between sleep duration on the development of hyperuricemia and hypertension after adjusting for age, BMI, ALT, BUN, Cr, TC, TG, and FG. All analyses were performed using SPSS version 26 (IBM, Armonk, NY, USA). According to the central limit theorem, (a) if the sample data are approximately normal then the sampling distribution too will be normal; (b) in large samples (>30 or 40), the sampling distribution tends to be normal, regardless of the shape of the data; and (c) the means of the random samples from any distribution will themselves have normal distribution. A p-value < 0.05 is considered to be statistically significant.

3 Results

As presented in Table 3, we recruited 101 566 patients (49,040 Males and 52,526 Females), the average age of male patients was 38.96 ± 4.52 years, female patients were 38.98 ± 4.75 years. Of the 101,566 subjects, 21,602 (11,916 Males and 9,686 Females) met the diagnostic criteria for hypertension, 9,552 (6,326 Males and 3,226 Females) met the diagnostic criteria for hyperuricemia. Patients in the male group were a significantly higher prevalence of BMI, SBP, DBP, FBG, TG, SUA, hypertension, and hyperuricemia than did those in the female group (P<.05). In the female group, TC and HDL-C

levels were significant (TC: 5.24±0.89, HDL-C: 1.55±0.47, P <.01). Most subjects sleep for 7 hours (68.4% for Males, 65.1% for Females).

Table 3. Demographic and clinical characteristics of male and female subjects

Variables	Male (*n*=49,040)	Female (*n*=52,526)	*p*-value
Age (year)	38.96±4.52	38.98±4.75	0.942
20-39 (%)	15,200 (30.9%)	16,357 (31.1%)	
40-59 (%)	27,090 (55.2%)	28,521 (54.2%)	
≥ 60 (%)	6,750 (13.7%)	7,648 (14.5%)	
Marital Status			0.851
Single	11,965 (24.4%)	16,073 (30.6%)	
Married	37,075 (75.6%)	36,453 (69.4%)	
Education			0.251
High school	5,590 (11.4%)	10,873 (20.7%)	
College	20,547 (41.9%)	23,479 (44.7%)	
University	22,903 (46.7%)	18,174 (34.6%)	
Clinical characteristics			
BMI (kg/m2)	25.12±2.94	24.79±2.94	<0.001
SBP (mm Hg)	130.60±16.59	129.36±16.41	<0.05
DBP (mm Hg)	80.96±13.28	78.05±12.12	<0.001
FBG (mmol/L)	6.02±1.65	5.98±1.03	<0.01
TG (mmol/L)	1.62±2.03	1.35±1.02	<0.001
TC (mmol/L)	5.14±1.01	5.24±0.89	<0.01
HDL-C (mmol/L)	1.21±0.25	1.55±0.47	<0.01
LDL-C (mmol/L)	3.28±0.86	3.26±0.85	0.244
SUA (mmol/L)	356.53±78.42	275.31±56.85	<0.001
Hypertension (%)	11,916 (24.30)	9,686 (18.44)	<0.05
Hyperuricemia (%)	6,326 (12.96)	3,226 (6.14)	<0.001
Sleep Duration			<0.001
≤ 4 hours	343 (0.7%)	578 (1.1%)	
5 hours	9,808 (20.3%)	11,398 (21.7%)	
6 hours	4,855 (9.9%)	5,883 (11.2%)	
7 hours	33,691 (68.4%)	34,195 (65.1%)	
≥ 8 hours	343 (0.7%)	472 (0.9%)	

All values are mean±SD. BMI=body mass index, DBP=diastolic blood pressure, FBG=fasting blood glucose, HDL-C=high-density lipoprotein–cholesterol, LDLC=low-density lipoprotein–cholesterol, SBP=systolic blood pressure, SUA=serum uric acid, TC=total cholesterol, TG=triglycerides

Table 4 shows that patients in the hyperuricemia group had a higher prevalence of Weight, BMI, TG, and SUA than did those in the non-hyperuricemia group, while HDL-C is significantly lower. Male hyperuricemia subjects were significantly higher of TC level than that of non-hyperuricemia subjects.

Table 4. Clinical and biochemical variables of male and female hyperuricemia and non-hyperuricemia (mean ± SD)

Variables	Male (*n*=49,040)		Female (*n*=52,526)	
	Nonhyperuricemia	Hyperuricemia	Nonhyperuricemia	Hyperuricemia
Case count	42,714	6,326	49,300	3,226
Age (year)	40.23±4.66	40.50±4.07	40.15±4.86	40.38±4.05
Height (cm)	169.22±6.17	169.83±5.22	157.84±5.32	158.24±5.25
Weight (kg)	70.28±8.83*	73.51±7.71	59.44±7.85*	63.85±7.86
BMI (kg/m2)	24.58±3.08*	25.55±3.26	23.67±2.90*	25.53±3.23
SBP (mm Hg)	130.87±17.23	133.27±14.95	128.21±17.55	129.80±15.20
DBP (mm Hg)	81.85±13.31	84.88±13.19	77.72±12.26	80.30±12.13
FBG (mmol/L)	6.25±1.98*	5.84±0.65	5.81±1.08	5.86±0.75
TG (mmol/L)	1.62±1.32*	2.89±4.03	1.35±1.04*	1.90±1.07
TC (mmol/L)	4.97±0.85*	5.27±1.94	5.23±0.88	5.24±0.80
HDL-C (mmol/L)	1.24±0.27*	1.12±0.24	1.53±0.36*	1.36±0.30
LDL-C (mmol/L)	3.24±0.88	3.46±0.82	3.22±0.86	3.25±0.72
SUA (mmol/L)	331.31±53.45*	481.59±53.34	263.11±47.25*	398.41±41.0

BMI=body mass index, DBP=diastolic blood pressure, FBG=fasting blood glucose, HDL-C=high-density lipoprotein–cholesterol, LDL-C=lowdensity, TG=triglycerides lipoprotein–cholesterol, SBP=systolic blood pressure, SUA=serum uric acid, TC=total cholesterol (*P<0.05, variable means in male or female without hyperuricemia)

Table 5 summarizes the prevalence of SUA in the hypertensive group than in the non-hypertensive group (Male: 365.0±23.34 mmol/L vs 354.0±23.45 mmol/L, Female: 282.0±21.05 mmol/L vs 253.0±27.25mmol/ L). The age, BMI, and most other clinical parameters of hypertensive patients are much higher than those of normal blood pressure patients, except for the TBIL and Cr content of males and the TBIL content of females.

Table 5. Clinical and biochemical variables of hypertension and non-hypertension in men and women (mean ± SD)

Variables	Male (*n*=49,040)		Female (*n*=52,526)	
	Nonhypertension	Hypertension	Nonhypertension	Hypertension
Case count	37,124	11,916	42,840	9,686
Age (year)	42.23±2.66	45.50±2.07	42.15±2.86	48.38±2.05
BMI (kg/m2)	25.3±3.05*	26.8±3.18	23.1±2.85 *	26.0±3.15
SUA (mmol/L)	354.0±23.45*	365.0±23.34	253.0±27.25*	282.0±21.05
ALT (U/L)	22.0±7.65*	24.0±8.15	15.0±6.85	18.0±7.05
TBIL (μmol/L)	12.8±2.05	12.8±2.08	10.4±1.03	10.4±1.05
BUN (mmol/L)	4.8 ±1.06	5.0±2.05	4.2±2.08	4.7±2.03
Cr (μmol/L)	79.0 ±2.03	79.0±1.08	59.0±1.06	60.0±1.05
TC (mmol/L)	5.0 ±0.85*	5.22±1.94	5.0±0.88	5.59±0.88
TG (mmol/L)	1.4 ±1.32*	1.64±4.03	0.97±1.04*	1.44±1.07
FBG (mmol/L)	5.0 ±1.98*	5.3±0.65	4.8±1.08	5.2±0.75

BMI=body mass index, SUA=serum uric acid, ALT=alanine aminotransferase, TBIL= total bilirubin, BUN=blood urea nitrogen, Cr= creatinine, FBG=fasting blood glucose, TC=total cholesterol, TG=triglycerides lipoprotein–cholesterol, (*P<0.05, variable means in male or female without hypertension)

As presented in Table 6, patients who sleep ≤ 4 hours have a higher risk of hypertension than those who sleep 7 hours (Male: AOR = 1.131, 95% CI = 1.073-1.192; Female: AOR = 1.257, 95% CI = 1.190 -1.327). The risk of hyperuricemia in patients who sleep ≤ 4 hours is higher than those who sleep 7 hours (Male: AOR = 1.657, 95% CI = 1.213-5.768; Female: AOR = 1.583, 95% CI = 1.050-3.660). Besides, the risk of hyperuricemia in females who slept for more than 8 hours was 1.019 times than those who slept for 7 hours (Female: AOR = 1.019, 95% CI = 1.007-2.143).

Table 6. Regression analysis of the relationship between sleep duration in Gender with hypertension and hyperuricemia

	Male	Female
Variable	AOR (95% CI)	AOR (95% CI)
Hypertension		
7 hrs	1.000 Reference	1.000 Reference
≤ 4 hrs	1.131 (1.073-1.192) **	1.257 (1.190-1.327) **
5 hrs	0.914 (0.880-1.202)	0.827 (0.739-0.890)
6 hrs	0.878 (0.834–0.939)	0.952 (0.928–0.996)
≥ 8hrs	0.935 (0.772-1.132)	0.948 (0.684-1.314)
Hyperuricemia		
7hrs	1.00 Reference	1.000 Reference
≤ 4 hrs	1.657 (1.213–5.768) **	1.583(1.050–3.660) **
5hrs	0.944 (0.975-1.119)	0.867 (0.588-1.179)
6hrs	0.930 (0.769-1.125)	0.953 (0.688-1.320)
≥ 8hrs	0.947 (0.808-1.110)	1.019 (1.007-2.143) *

OR: odds ratio; CI: confidence interval; SBP: systolic blood pressure; DBP: diastolic blood pressure. *Adjusted for age, BMI, ALT, BUN, TC, TG, and FG. **Adjusted for age, BMI, ALT, BUN, Cr, TC, TG, and FG. *P < 0.05 and **P < 0.01

Table 7 shows the results of multiple logistic regressions performed to test the association between sleep duration with hypertension and hyperuricemia after adjusted for different potential confounders. The logistic regression analyses were repeated after stratifying by age (< 50, 50-75, >75 years). Subjects between the ages of < 50 years who slept less than 4 hours and 5 hours per day were associated with a higher probability of hypertension and hyperuricemia after considering different covariates (Hypertension: slept ≤ 4 hrs: OR=1.349, 95%CI: 1.110-1.640; slept 5 hrs: OR=1.197, 95%CI: 1.080-1.327; Hyperuricemia: slept ≤ 4 hrs: OR=1.135, 95%CI: 1.012-1.272; slept 5 hrs: OR=1.387, 95%CI: 1.311-1.468). However, subjects between the ages of 50-75 and >75 years failed to show any significant associations between sleep duration with hypertension and hyperuricemia.

Table 7. Logistic regression analysis of the relationship between sleep duration in age with hypertension and hyperuricemia

	< 50	50-75	>75
Variable		Adjusted OR (95% CI) **	
Hypertension			
7 hrs	1.000 Reference	1.000 Reference	1.000 Reference
≤ 4 hrs	1.349 (1.110-1.640) **	0.874 (0.717-1.065)	0.910 (0.9675-2.467)
5 hrs	1.197 (1.080-1.327) **	0.886 (0.758-1.035)	0.865 (0.617-1.839)
6 hrs	0.985 (0.910-1.110)	0.836 (0.716-0.976)	0.999 (0.577-1.731)
≥ 8hrs	0.954 (0.859-1.059)	0.898 (0.764-1.055)	0.834 (0.747-2.382)
Hyperuricemia			
7hrs	1.00 Reference	1.00 Reference	1.000 Reference
≤ 4 hrs	1.135 (1.012-1.272) **	0.760 (0.663-0.871)	0.852 (0.767-1.731)
5hrs	1.387 (1.311-1.468) **	0.809 (0.734-0.891)	0.825 (0.744-1.411)
6hrs	0.839 (0.668-1.414)	0.834 (0.758-0.916)	0.848 (0.761-1.443)
≥ 8hrs	0.908 (0.842-1.279)	0.911 (0.826-1.006)	0.930 (0.915-1.790)

OR: odds ratio; CI: confidence interval; SBP: systolic blood pressure; DBP: diastolic blood pressure. *Adjusted for age, BMI, ALT, BUN, TC, TG, and FG. **Adjusted for BMI, ALT, BUN, Cr, TC, TG, and FG. *P < 0.05 and **P < 0.01

4 Discussion

This study described an analysis of data, collected from the MJ Health Examination Center Database, which found that short sleep duration is associated with an increased risk of hyperuricemia and hypertension. After adjusting for potential confounding factors, it was found that males and females who slept for less than 4 hours had a significantly increased risk of hyperuricemia and hypertension. Females who sleep more than 8 hours have a significantly increased risk of hyperuricemia than males. Compared with the ages of < 50 years, an association between short sleep duration with hypertension and hyperuricemia was not found for the ages of 50-75 and >75 years.

To the best of our knowledge, MJ Health Examination Center Database was used to obtain a large, representative sample of Taiwan population to prove that short sleep duration is associated with an increased risk of hyperuricemia and hypertension; however, the underlying reasons have yet to be elucidated. MJ Health Examination Center Database was excellent response rates to sleep duration associated with hypertension and hyperuricemia questions and measurements representative sample of Taiwan population.

Compared with subjects who sleep 7-8 hours a day, participants aged 18-44 years who sleep less than 7 hours a day have a higher risk of hypertension (OR = 1.24, 95% CI: 1.05 - 1.46) is comparable to our research results [36]. Michael et al's studies have shown that in most people, short sleep duration and long sleep duration are related to increased risk of hypertension, and the relationship between long sleep duration affects covariates. Among young people and females, the relationship with shorter sleep duration is stronger, which is consistent with our research results [37]. The biological mechanism of short sleep duration and the risk of hypertension remains unclear. The relationship between hypertension and sleep duration may vary with age. In addition to short sleep duration, sleep disorders also include such as sleep insomnia, obstructive sleep apnea (OSA), etc. Sleep quality problems have also been proven to be risk factors of hypertension [38].

Papandreou et al. found that for every hour of sleep increase, the ratio of SUA to creatinine is inversely proportional (β = -0.15, P = 0.001). Studies have shown that longer sleep duration is associated with lower SUA concentration and lower SUA to creatinine ratio in elderly participants with higher cardiovascular risk [39]. Chou et al's studies have shown that poor sleep quality is related to decreased uric acid levels, while short sleep duration is related to increased uric acid levels, which is consistent with our study [40]. Other studies have shown that high levels of BMI, SBP, FPG, TG, LDL-C, ALT, BUN, and creatinine increase the risk of hyperuricemia. Subjects with elevated DBP, TG, BUN, creatinine, or reduced HDL-C are more likely to develop hyperuricemia, which is consistent with our study [41].

According to our research, we divide sleep duration into three parts (Short sleep duration：0-4 hours, Good sleep duration：4-7 hours, Long sleep duration：>8hours) to illustrate the relationship between sleep duration and hyperuricemia.

First (Short sleep duration：0-4 hours), our study showed that males and females who slept for less than 4 hours had a significantly increased risk of hyperuricemia. Our results are similar to other studies, suggesting an association between short sleep duration and hyperuricemia [42-44]. The mechanism related to short sleep duration and hyperuricemia may be due to reduced sleep duration, which cause overactive renal angiotensin-aldosterone system, endothelial dysfunction and systemic inflammation that may destroy kidney function and increase uric acid levels, which ultimately leads to hyperuricemia [45-46]. Other potential mechanisms include epigenetics and transcriptional profiles of core circadian clock genes [47]. Reduced sleep duration may further lead to obesity, diabetes, dyslipidemia, hypertension and metabolic syndrome through neuroendocrine and autonomic nervous system pathophysiological changes [48-49], increasing the burden on the kidneys.

Another possible mechanism between short sleep duration and hyperuricemia may be caused by cardiometabolic disorders, because studies have shown that short sleep duration increases the risks associated with obesity, metabolic syndrome, and hypertension [50-52], which are all common risk factors for hyperuricemia. After adjusting for potential confounding factors, our study found that sleep duration less than 4 hours increased the risk of hyperuricemia (Table 4).

Second (Good sleep duration：4-7 hours), the beneficial aspects of uric acid may play an important role in good sleep duration. Uric acid already has antioxidant and neuroprotective effects [53-57]. A study conducted by Bowman et al. showed that uric acid is an important

endogenous antioxidant in the central nervous system [58]. A Korean study showed that higher uric acid is associated with better antioxidant capacity [59]. After adjusting for potential confounding factors, our study found that compared with sleep duration between 7-8 hours, sleep duration between 4-7 hours reduced the risk of hyperuricemia (Table 4).

Third (Long sleep duration ： >8hours), the possible mechanism for the relationship between long sleep duration and hyperuricemia may associated with sleep disorders. Long sleep duration may be related to sleep disorders. Since sleep disorders are associated with increased systemic inflammation and oxidative stress [60], Verhulst et al. demonstrated that serum level of uric acid was positively associated with sleep disorders severity in an overweight and obese pediatric population (independently from waist circumference) [61]. Cantalejo Moreira et al. demonstrated that patients with gout have a trend towards severe sleep disorders compared to patients with osteoarthritis [62]. Another finding in the study performed by Cantalejo Moreira et al. was that there is a greater burden of cardiovascular risk factors among patients with gout [63]. Circulating UA levels in women are clearly lower than those in men, which is putatively the result of the sex hormone in action [64]. After adjusting for potential confounding factors, our study found that females who sleep more than 8 hours have a significantly increased risk of hyperuricemia (Table 4).

The association between serum uric acid levels and hypertension in humans has been well established [65]. A cross-sectional study showed that in the general population who did not receive hyperuricemia and hypertension treatment, each increase of 1 mg/dL of serum uric acid would increase the prevalence of hypertension by 20% [66]. Similarly, in longitudinal cohort studies, asymptomatic hyperuricemia without comorbidities predicted the development of hypertension [67]. Besides, hyperuricemia also contributes to the development of hypertension from prehypertension [68]. Therefore, it is still necessary to determine the underlying molecular and cellular mechanisms of hyperuricemia causing hypertension in basic and clinical research [65]. Research by Lin et al. showed that the most important risk factors for hyperuricemia are impaired renal function and the use of diuretics. The use of diuretics and renal function status have a great influence on the prevalence of hyperuricemia in patients with hypertension in Taiwan. However, whether diuretics cause renal failure by increasing serum uric acid levels is unclear [25].

This analysis has several strengths. This study is based on data from a large representative sample of Taiwan population, and this prospective study minimized selection and recall biases. There were excellent response rates to sleep-duration, hypertension and hyperuricemia questions, and measurements. Finally, a broad range of covariates were controlled in the analysis, including age, sex, education, marital status and BMI.

There are several potential limitations in this study. First, sleep duration is a subjective report, not objective data, such as objective data obtained from supervisory monitoring. Although the self-reported sleep duration is similar to the objective sleep duration, some studies have shown that it may be biased due to overestimation. Secondly, in most studies, hypertension is defined as SBP / DBP ≥140 / 90 mm Hg. There are also studies on blood pressure that have several small differences in the definition of hypertension. Furthermore, due to the limited information, various confounding factors, such as insomnia, cannot be considered. This is an important confounding factor.

Among the short sleepers, the prevalence and incidence of hypertension in insomniacs were significantly higher than those in normal sleepers. Therefore, patients with insomnia will have an impact on our analysis related to the short sleep duration of hypertension. However, the cross-sectional design of this study cannot reveal the causal role of serum uric acid in the development of hypertension. Increasing uric acid levels can cause vascular dysfunction, but after long-term exposure to high uric acid levels, the corresponding changes in the cardiovascular system will decrease over time [69].

Finally, the research subjects we analyzed were limited to the data from the MJ Health Examination Center in Taiwan from 2016 to 2018. The subjects were 101,566 (49,040 males and 52,526 females), and their ages ranged from 20 to 65 years old.

5 Conclusion

This study revealed that short sleep duration is associated with an increased risk of hyperuricemia and hypertension. Males and females who slept for less than 4 hours had a significantly increased risk of hypertension (Male: AOR = 1.131, 95% CI = 1.073-1.192; Female: AOR = 1.257, 95% CI = 1.190 -1.327) and hyperuricemia (Male: AOR = 1.657, 95% CI = 1.213-5.768; Female: AOR = 1.583, 95% CI = 1.050-3.660). Females who sleep more than 8 hours have a significantly increased risk of hyperuricemia (Female: AOR = 1.019, 95% CI = 1.007-2.143). Participants aged < 50 years who sleep less than 4 hours or 5 hours a day have a higher risk of hypertension and hyperuricemia than those of the ages of 50-75 and >75 years (Hypertension: slept ≤ 4 hrs: OR=1.349, 95%CI: 1.110-1.640; slept 5 hrs: OR=1.197, 95%CI: 1.080-1.327; Hyperuricemia: slept ≤ 4 hrs: OR=1.135, 95%CI: 1.012-1.272; slept 5 hrs: OR=1.387, 95%CI: 1.311-1.468). Short sleep duration may be a risk factor for hyperuricemia and hypertension.

We suggest that participants aged < 50 years in Taiwan should maintain a sufficient sleep duration. Furthermore, Ministry of Health and Welfare in Taiwan should pay close attention and publicize health damage caused by short sleep durations. Health care providers should pay close attention to the association between sleep duration with hyperuricemia and hypertension. Further longitudinal studies are needed to determine the association between sleep duration, hypertension and hyperuricemia.

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