

Mediating role of inflammatory indicators in the association between sleep status and blood pressure in centenarians: evidence from China Hainan Centenarian Cohort Study

Qiao LI^{1*}, Sheng-Shu WANG^{2*}, Guang-Dong LIU^{3,*}, Jian-Hua WANG², Ya-Li ZHAO⁴, Miao LIU^{3,✉}, Yao HE^{2,✉}, Shan-Shan YANG^{5,✉}

1. Jockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong, China; 2. Institute of Geriatrics, Beijing Key Laboratory of Aging and Geriatrics, National Clinical Research Center for Geriatrics Diseases, Second Medical Center, Chinese PLA General Hospital, Beijing, China; 3. Graduate School, Chinese PLA General Hospital, Beijing, China; 4. Central Laboratory of Hainan Hospital, Chinese PLA General Hospital, Sanya, China; 5. Department of Disease Prevention and Control, First Medical Center, Chinese PLA General Hospital, Beijing, China

*These authors contributed equally to this work.

✉ Correspondence to: liumiaolmbxb@163.com (LIU M); yhe301@x263.net (HE Y); shanqinhua001@163.com (YANG SS)
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ABSTRACT

Objectives To conduct a comprehensive analysis in Hainan centenarians on the link between sleep status and their blood pressure status. Furthermore, the study also aims to explore how inflammatory indicators may mediate the relationship.

Methods The China Hainan Centenarians Cohort Study (CHCCS) collected baseline data on sleep status, inflammatory indicators, and blood pressure data. The study used a mediation model to investigate how inflammatory indicators mediate the relationship between sleep status and blood pressure status.

Result In this study, a total of 967 centenarians were included. The prevalence of hypertension among the centenarians was 71.4%. The analysis showed that centenarians with poor sleep quality had a 43% higher risk of hypertension compared to those with normal sleep quality (OR = 1.43, 95% CI: 1.03-1.97). Additionally, centenarians with nighttime sleep durations of ≤ 6 h or > 9 h had higher proportions of high pulse pressure (PP), with OR values of 1.76 (95% CI: 1.18-2.63) and 2.07 (95% CI: 1.34-3.19), respectively. Mediation analysis illustrated that complement C3 played a mediating role in the relationship between sleep quality and hypertension, with an effect ratio of 2.4%. Similarly, lymphocyte count, the neutrophil-to-lymphocyte ratio (NLR), and the systemic immune-inflammation index (SII) were identified as mediating factors in the association between nighttime sleep duration and high PP, with effect ratios of 91.22%, 36.93%, and 0.20%, respectively.

Conclusion In centenarians, poor sleep quality raises the risk of hypertension, with complement C3 as a mediator. Additionally, nighttime sleep durations of ≤ 6 h or > 9 h increases the risk of high PP, mediated by lymphocyte count, NLR, and SII.

Hypertension is a major preventable risk factor for cardiovascular disease and is highly prevalent among the elderly, significantly impacting global public health.^[1] Also, hypertension is a critical risk factor for chronic kidney disease, and cognitive decline, significantly impacting the mortality and disability rates in the elderly population.^[2,3] Lifestyle factors, including high salt intake, alcohol consumption,^[4] tobacco exposure^[5] and physical inactivity,^[6] contribute signifi-

cantly to the development of hypertension. Notably, sleep, a critical aspect of one's lifestyle, has recently emerged as a factor closely linked to the onset and progression of hypertension.^[7] Sleep significantly influences the overall health of older adults and can be modified to improve their well-being. Maintaining functional health in the elderly is closely linked to quality sleep. Sleep issues in the elderly are frequently unnoticed and could be a common public health concern in numerous developing countries.^[8]

While several studies have demonstrated a U-shaped relationship between sleep duration and hypertension prevalence in adults,^[9] contradictory findings have been reported in other studies.^[10,11] Current researches showed that the relationship between sleep duration and hypertension was affected by factors like gender and age.^[12,13] Moreover, the relationship between sleep quality and hypertension continues to elicit debate among researchers.^[14,15] Limited research exists on the comprehensive evaluation of sleep duration, sleep quality, and their relationship with blood pressure, pulse pressure difference, and hypertension in centenarians.

A recent study found a link between blood pressure changes during sleep and inflammatory indicators, with neutrophil-to-lymphocyte ratio (NLR) indices negatively correlated with nighttime blood pressure dipping.^[16] A study utilizing mice demonstrated that alterations in sleep patterns can trigger inflammatory pathways, leading to changes in inflammation levels and impacting vascular elasticity.^[17] However, limited population-based evidence is available on this matter.

This study aims to comprehensively evaluate the relationship between sleep status (including sleep duration, sleep quality, and their cross groups) and blood pressure status (including blood pressure, pulse pressure difference, and hypertension) among centenarians. Further, the study aims to investigate how inflammatory indicators mediate this relationship.

METHODS

China Hainan Centenarians Cohort Study (CHCCS)

The CHCCS was conducted in Hainan Province, focusing on a fully sampled community population. The civil affairs bureau's household register in 2014 identified 1811 centenarians in the region. Subsequently, from June 2014 to December 2016, a comprehensive enrollment process took place wherein 1473 centenarians from 18 cities and counties in Hainan Province were included in the study based on their contact addresses. Following the initial recruitment, a total of 1002 centenarians underwent the survey, with exclusions applied to individuals whose age verification was below 100 years or those

whose family members declined participation in the physical examination and survey.^[18] The survey excluded 35 centenarians lacking complete sleep information or blood pressure data. Thus, a total of 967 centenarians were included in the study (Figure S1).

Research Variables

Sleep duration

The sleep duration of the centenarians and its recording process were detailed as follows: the unit of measurement used for tracking sleep duration was hours. Nighttime sleep duration was derived from a question in the Pittsburgh Sleep Quality Index Scale (PSQI), inquiring about the number of hour of actual sleep at night in the previous month. In contrast, daytime sleep duration was ascertained by responses to a question about the number of h spent sleeping during the day in the previous month. Both the centenarians and their family members provided self-reports to record the sleep duration. Finally, by combining the nighttime and daytime sleep durations, the total sleep duration for each participant was calculated.

According to results of the study on a representative elderly population in China aged between 80 and 105, this study classified total sleep duration into three categories: short (≤ 7 h), appropriate (7-9 h), and long (> 9 h) sleep duration.^[19] Furthermore, the duration of night sleep was also divided into three categories: ≤ 6 h (short night sleep duration), 6-9 h (appropriate night sleep duration), and > 9 h (long night sleep duration). Additionally, the daytime sleep duration was categorized as follows: no sleep, less than 1 h, ≥ 1 h but less than 2 h, and ≥ 2 h.

Sleep quality

The Chinese version of the PSQI.^[20] was utilized to assess the sleep quality of the centenarians. The total PSQI score, ranging from 0 to 21 points, was determined by summing the scores of its components. It is noted that higher scores on individual components or the overall scale signify poorer sleep quality. Past studies focusing on the elderly population in China have indicated that a PSQI score above 7 is indicative of poor sleep quality.^[21,22]



Blood pressure (BP) data

Participants' blood pressure (BP) values were carefully assessed by nurses during the study. The BP was measured twice, 10 min apart, using a stethoscope and a mercury-stand sphygmomanometer. The average of these measurements was calculated and recorded as the final BP value for each centenarian. Based on the results, centenarians with a systolic blood pressure (SBP) ≥ 140 mmHg and/or a diastolic blood pressure (DBP) ≥ 90 mmHg were categorized as having hypertension.^[23] Additionally, centenarians who had previously been diagnosed with hypertension in secondary hospitals or higher medical facilities were also considered to have hypertension.

Pulse pressure (PP)^[24] is calculated as the difference between SBP and DBP, serving as a marker for arterial stiffness, and PP > 60 mmHg was defined as high PP.

Inflammatory indicators

After participants signed the consent form, experienced nurses collected 8 ml of fasting blood using four vacutainer tubes, each with a 2 ml capacity. Two of these tubes were purple-top anticoagulant tubes containing ethylenediaminetetraacetic acid (EDTA), while the other two were yellow-top serum-separating tubes (SST). Following the blood collection, participants were provided with a complimentary breakfast before proceeding to complete the interview and the remaining components of the physical examination.^[18] This study measured various inflammatory indicators, such as neutrophils, lymphocytes, acute C-reactive protein (CRP), complement C3, complement C4, neutrophil-to-lymphocyte ratio (NLR) and systemic immune-inflammation index (SII). Neutrophils, lymphocytes, acute C-reactive protein (CRP), complement C3 and complement C4 were measured using standard reagent testing at the central laboratory of Hainan Hospital.^[18] The NLR and SII were calculated using these formulas: $NLR = \text{neutrophil count} / \text{lymphocyte count}$, $SII = (\text{neutrophil count} \times \text{platelet count}) / \text{lymphocyte count}$.^[25]

Covariates

The covariates adjusted in the study included age, sex, ethnicity, marital status, education level,

residential type, smoking status, alcohol consumption, physical activity level, central obesity, diet regularity and comorbidity. Central obesity is defined as a waist circumference of ≥ 90 cm for men and ≥ 85 cm for women.^[26] Comorbidity is defined as the presence of two or more diagnosed diseases (including conditions such as hypertension, coronary heart disease, diabetes, stroke, chronic obstructive pulmonary disease, tumors and abnormal blood lipids) at a secondary hospital or higher level.^[27]

Ethics

The study received approval from the Ethics Committee of Hainan Hospital at People's Liberation Army General Hospital (Approval No.: 301hn11201601), and all participants provided signed informed consent forms.

Statistical Analysis

Statistical analysis was carried out by inputting all data into Epidata 3.0 simultaneously by two individuals. Initially, continuous variables underwent normality assessment using the Kolmogorov-Smirnov method. The descriptive statistics of variables were reported based on their distribution. For variables following a normal distribution, the mean $\pm$ SD was calculated. The t-test was applied to compare two groups, and the one-way ANOVA was used for comparing three or more groups. On the other hand, for variables that did not conform to a normal distribution, the median (interquartile range) was used as a representation. Subsequently, pairwise comparisons between two groups were conducted using the Mann-Whitney *U* test, while comparisons involving multiple groups were made using the Kruskal-Wallis *H* test. Categorical variables were delineated in terms of frequency (%) and intergroup comparisons were conducted using the chi-square test. Logistic regression was utilized to investigate the association between sleep status (including sleep duration, sleep quality and their cross groups) and blood pressure status (hypertension, isolated systolic hypertension and high PP). The adjusted model considered various covariates: age, gender, ethnicity, marital status, education level, residential type, smoking status, alcohol consumption status, exercise status, central obesity, dietary habits and comorbidities. Additionally, mediation analysis



is (Model 4) was used to investigate the mediating effects of various inflammatory indicators in the link between sleep quality, sleep duration at night and hypertension, high PP. All statistical tests were conducted with a two-tailed approach, with significance set at $P < 0.05$, using SPSS 29.0 software for the analysis.

RESULTS

This study included 967 centenarians aged 100 to 116 years, with an average age of 102.79 ± 2.75 years, after excluding 35 individuals from the original pool of 1002 centenarians due to incomplete key variables. The sample consisted of 177 men (18.3%) and 790 women (81.7%) in CHCCS. Among these centenarians, only 250 were found to have normal blood pressure, while the majority, 717 centenarians (74.1%), were diagnosed with hypertension. Of those with hypertension, 527 centenarians (54.5%) had isolated systolic hypertension. Additionally, 742 centenarians (76.7%) exhibited a high PP.

In analyzing the basic information and sleep status of centenarians, Table 1 categorizes individuals into groups based on blood pressure levels and gender. Among centenarians with hypertension, a higher prevalence of central obesity (13.0% vs. 8.0%, $P = 0.035$), a more regular dietary pattern (95.5% vs. 91.6%, $P = 0.019$), and an elevated comorbidity rate (25.8% vs. 10.4%, $P < 0.0001$) were observed in comparison to centenarians with normal blood pressure.

Furthermore, when considering sleep quality, there was a greater occurrence of poor sleep quality among centenarians with hypertension (37.4% vs. 31.2%) and a relatively higher percentage experiencing both short and poor sleep duration (17.4% vs. 14.0%). However, it is important to note that there was no statistically significant difference found in this aspect.

Table 2 includes logistic models that used various sleep duration groups, sleep quality groups, and their cross groups as independent variables respectively. Adjusted for covariates showed in the Methods part, the relationship between sleep status and blood pressure status (hypertension, isolated systolic hypertension, and high PP) in centenarians in Hainan was assessed. After adjustment, centenarians with poor sleep quality show a 43% increased risk of developing hypertension (OR = 1.43, 95% CI: 1.03-1.97) compared to those with normal sleep quality. Moreover, those centenarians who have both a total sleep duration ≤ 7 h and poor sleep quality exhibit the highest likelihood of developing hypertension (OR = 1.75, 95% CI: 1.07-2.88) after adjustment, as compared to centenarians who get 7-9 h of sleep quality and have normal sleep quality. Notably, an association between sleep duration at night and isolated systolic hypertension is observed, with centenarians sleeping over 9 h at night showing a higher incidence of isolated systolic hypertension compared to those sleeping for 6-9 h at night (OR = 1.46,

Table 1 General and sleep characteristics of CHCCS.

	All (n = 967)	Without Hypertension (n = 250)	Hypertension (n = 717)	P	Men (n = 177)	Women (n = 790)	P
SBP	149.00 (134.00, 171.00)	126.00 (117.00, 132.00)	158.00 (147.00, 178.00)	< 0.001	145.00 (130.50, 162.50)	150.00 (135.00, 173.00)	0.005
DBP	75.00 (67.00, 83.00)	67.00 (59.00, 74.00)	78.00 (70.00, 86.00)	< 0.001	74.00 (66.50, 81.00)	76.00 (67.00, 84.00)	0.101
Pulse pressure difference	75.00 (62.00, 91.00)	58.00 (50.00, 66.00)	83.00 (70.00, 96.00)	< 0.001	71.00 (61.00, 87.00)	76.00 (63.00, 92.00)	0.010
PSQI Score (points)	6.00 (4.00, 9.00)	5.50 (4.00, 8.00)	6.00 (4.00, 9.00)	0.046	6.00 (4.00, 9.00)	6.00 (4.00, 9.00)	0.850
Sleep duration at night, h	8.00 (7.00, 9.00)	8.00 (7.00, 9.00)	8.00 (7.00, 9.00)	0.671	8.00 (7.00, 9.00)	8.00 (7.00, 9.00)	0.136
Daytime sleep duration, h	1.00 (0.50, 1.50)	1.00 (0.50, 1.50)	1.00 (0.50, 1.50)	0.281	1.00 (0.50, 1.50)	1.00 (0.50, 1.50)	0.612
Total sleep duration, h	9.00 (8.00, 10.25)	9.00 (8.00, 10.50)	9.00 (8.00, 10.25)	0.802	9.00 (7.00, 10.00)	9.00 (8.00, 10.50)	0.102
Neutrophils	0.56 (0.49, 0.63)	0.57 (0.48, 0.64)	0.56 (0.49, 0.63)	0.468	0.57 (0.48, 0.64)	0.56 (0.49, 0.63)	0.767
Lymphocytes	0.31 (0.25, 0.38)	0.30 (0.24, 0.38)	0.31 (0.25, 0.37)	0.373	0.28 (0.23, 0.34)	0.31 (0.25, 0.38)	0.002
C-reactive protein	0.19 (0.08, 0.55)	0.20 (0.08, 0.79)	0.19 (0.08, 0.47)	0.078	0.23 (0.09, 0.77)	0.18 (0.07, 0.49)	0.016
Complement C3	97.00 (85.00, 111.00)	96.00 (83.00, 109.25)	98.00 (86.00, 111.50)	0.065	93.00 (81.00, 107.00)	98.00 (86.00, 112.00)	0.004
Complement C4	22.80 (18.50, 27.90)	22.40 (18.78, 28.75)	22.60 (18.20, 27.50)	0.250	21.90 (18.10, 26.90)	23.00 (18.60, 28.00)	0.139

Continued

	All (n = 967)	Without Hypertension (n = 250)	Hypertension (n = 717)	P	Men (n = 177)	Women (n = 790)	P
NLR	1.79 (1.34, 2.49)	1.86 (1.30, 2.63)	1.77 (1.34, 2.46)	0.438	1.99 (1.45, 2.78)	1.76 (1.32, 2.46)	0.034
SII	383.05 (257.20, 587.40)	414.58 (259.96, 639.23)	375.96 (255.96, 572.87)	0.209	370.49 (263.75, 556.31)	386.86 (255.15, 589.64)	0.524
Age group				0.084			0.026
100-104 yrs	764 (79.0%)	194 (77.6%)	570 (79.5%)		147 (83.1%)	617 (78.1%)	
105-109 yrs	173 (17.9%)	43 (17.2%)	130 (18.1%)		30 (16.9%)	143 (18.1%)	
≥ 110 yrs	30 (3.1%)	13 (5.2%)	17 (2.4%)		0 (0.0%)	30 (3.8%)	
Sex				0.169			
Male	177 (18.3%)	53 (21.2%)	124 (17.3%)				
Female	790 (81.7%)	197 (78.8%)	593 (82.7%)				
Nationality				0.087			0.708
Han	850 (87.9%)	225 (90%)	625 (87.2%)		153 (86.4%)	697 (88.2%)	
Li	104 (10.8%)	25 (10.0%)	79 (11.0%)		22 (12.4%)	82 (10.4%)	
Others	13 (1.3%)	0 (0.0%)	13 (1.8%)		2 (1.1%)	11 (1.4%)	
Marital status				0.291			< 0.001
Married	96 (9.9%)	30 (12.0%)	66 (9.2%)		39 (22.0%)	57 (7.2%)	
Widowed	808 (83.6%)	201 (80.4%)	607 (84.7%)		121 (68.4%)	687 (87.0%)	
Divorced or never married	63 (6.5%)	19 (7.6%)	44 (6.1%)		17 (9.6%)	46 (5.8%)	
Education level				0.577			< 0.001
Illiterate	883 (91.3%)	231 (92.4%)	652 (90.9%)		120 (67.8%)	763 (96.6%)	
Primary school	65 (6.7%)	16 (6.4%)	49 (6.8%)		42 (23.7%)	23 (2.9%)	
Middle school or higher	19 (2.0%)	3 (1.2%)	16 (2.2%)		15 (8.5%)	4 (0.5%)	
Residential type				0.475			0.012
Living together with families	833 (86.1%)	212 (84.8%)	621 (86.6%)		142 (80.2%)	691 (87.5%)	
Living alone at home	134 (13.9%)	38 (15.2%)	96 (13.4%)		35 (19.8%)	99 (12.5%)	
Smoking status				0.002			< 0.001
Non-smoker	886 (91.6%)	216 (86.4%)	670 (93.4%)		117 (66.1%)	769 (97.3%)	
Former	51 (5.3%)	22 (8.8%)	29 (4.0%)		40 (22.6%)	11 (1.4%)	
Current	30 (3.1%)	12 (4.8%)	18 (2.5%)		20 (11.3%)	10 (1.3%)	
Drinking status				0.206			< 0.001
Non-drinker	840 (86.9%)	209 (83.6%)	631 (88.0%)		114 (64.4%)	726 (91.9%)	
Former	78 (8.1%)	25 (10.0%)	53 (7.4%)		34 (19.2%)	44 (5.6%)	
Current	49 (5.1%)	16 (6.4%)	33 (4.6%)		29 (16.4%)	20 (2.5%)	
Physical activity				0.635			0.022
Low	842 (87.1%)	222 (88.8%)	620 (86.5%)		143 (80.8%)	699 (88.5%)	
Medium	37 (3.8%)	8 (3.2%)	29 (4.0%)		10 (5.6%)	27 (3.4%)	
High	88 (9.1%)	20 (8.0%)	68 (9.5%)		24 (13.6%)	64 (8.1%)	
Central obese				0.035			0.025
No	854 (88.3%)	230 (92.0%)	624 (87.0%)		165 (93.2%)	689 (87.2%)	
Yes	113 (11.7%)	20 (8.0%)	93 (13.0%)		12 (6.8%)	101 (12.8%)	



Continued

	All (n = 967)	Without Hypertension (n = 250)	Hypertension (n = 717)	P	Men (n = 177)	Women (n = 790)	P
Diet regularity				0.019			0.913
Irregular	53 (5.5%)	21 (8.4%)	32 (4.5%)		10 (5.6%)	43 (5.4%)	
Regular	914 (94.5%)	229 (91.6%)	685 (95.5%)		167 (94.4%)	747 (94.6%)	
Comorbidity				< 0.001			0.053
No	756 (78.2%)	224 (89.6%)	532 (74.2%)		148 (83.6%)	608 (77.0%)	
Yes	211 (21.8%)	26 (10.4%)	185 (25.8%)		29 (16.4%)	182 (23.0%)	
Sleep quality				0.079			0.772
Normal	621 (64.2%)	172 (68.8%)	449 (62.6%)		112 (63.3%)	509 (64.4%)	
Poor	346 (35.8%)	78 (31.2%)	268 (37.4%)		65 (36.7%)	281 (35.6%)	
Sleep duration at night				0.535			0.422
6-9 h	556 (57.5%)	151 (60.4%)	405 (56.5%)		105 (59.3%)	451 (57.1%)	
≤ 6 h	213 (22.0%)	50 (20.0%)	163 (22.7%)		42 (23.7%)	171 (21.6%)	
> 9 h	198 (20.5%)	49 (19.6%)	149 (20.8%)		30 (16.9%)	168 (21.3%)	
Daytime sleep duration				0.266			0.511
None	187 (19.3%)	59 (23.6%)	128 (17.9%)		38 (21.5%)	149 (18.9%)	
< 1 h	146 (15.1%)	35 (14.0%)	111 (15.5%)		21 (11.9%)	125 (15.8%)	
≥ 1 h & < 2 h	184 (19.0%)	45 (18.0%)	139 (19.4%)		32 (18.1%)	152 (19.2%)	
≥ 2 h	450 (46.5%)	111 (44.4%)	339 (47.3%)		86 (48.6%)	364 (46.1%)	
Total sleep duration				0.632			0.308
7-9 h	340 (35.2%)	94 (37.6%)	246 (34.3%)		60 (33.9%)	280 (35.4%)	
≤ 7 h	205 (21.2%)	50 (20.0%)	155 (21.6%)		45 (25.4%)	160 (20.3%)	
> 9 h	422 (43.6%)	106 (42.4%)	316 (44.1%)		72 (40.7%)	350 (44.3%)	
Total sleep duration& sleep quality				0.327			0.670
7-9 h & Normal	217 (22.4%)	66 (26.4%)	151 (21.1%)		41 (23.2%)	176 (22.3%)	
≤ 7 h & Normal	45 (4.7%)	15 (6.0%)	30 (4.2%)		9 (5.1%)	36 (4.6%)	
> 9 h & Normal	359 (37.1%)	91 (36.4%)	268 (37.4%)		62 (35%)	297 (37.6%)	
7-9 h & Poor	123 (12.7%)	28 (11.2%)	95 (13.2%)		19 (10.7%)	104 (13.2%)	
≤ 7 h & Poor	160 (16.5%)	35 (14.0%)	125 (17.4%)		36 (20.3%)	124 (15.7%)	
> 9 h & Poor	63 (6.5%)	15 (6.0%)	48 (6.7%)		10 (5.6%)	53 (6.7%)	

Data are presented as M (Q1, Q3) or n (%). DBP: diastolic blood pressure; NLR: the neutrophil-to-lymphocyte ratio; PSQI: Pittsburgh Sleep Quality Index Scale; SBP: systolic blood pressure; SII: systemic immune-inflammation index.

95% CI: 1.04-2.04). Additionally, individuals with nighttime sleep durations either ≤ 6 h or > 9 h exhibit elevated proportions of high pulse pressure, with OR values of 1.76 (95% CI: 1.18-2.63) and 2.07 (95% CI: 1.34-3.19), respectively, in comparison to those sleeping for 6-9 h at night.

The gender-specific analysis revealed that the results for female centenarians mirrored those of the overall population. No association was found between sleep status and blood pressure in male cen-

tenarians after adjustments (Table S1).

In the mediation analysis model 4 conducted, hypertension was set as the dependent variable, while sleep quality grouping was designated as the independent variable. The mediation analysis included neutrophils, lymphocytes, CRP, complement C3, complement C4, NLR, and SII as mediator variables in the equation. The findings revealed that complement C3 acted as a mediator between sleep quality and hypertension. Specifically, complement C3 exhib-



Table 2 The association between sleep status and blood pressure status in centenarians.

	Hypertension		Isolated systolic hypertension		Large pulse pressure difference	
	Crude Model	Adjusted Model	Crude Model	Adjusted Model	Crude Model	Adjusted Model
Sleep quality						
Normal	1	1	1	1	1	1
Poor	1.32 (0.97-1.79)	1.43 (1.03-1.97)	1.10 (0.85-1.44)	1.13 (0.87-1.49)	1.15 (0.84-1.58)	1.29 (0.93-1.78)
Sleep duration at night						
6-9 h	1	1	1	1	1	1
≤ 6 h	1.22 (0.84-1.76)	1.33 (0.90-1.95)	1.24 (0.90-1.71)	1.26 (0.91-1.75)	1.66 (1.12-2.45)	1.76 (1.18-2.63)
>9 h	1.13 (0.78-1.65)	1.16 (0.78-1.70)	1.45 (1.04-2.02)	1.46 (1.04-2.04)	2.06 (1.35-3.16)	2.07 (1.34-3.19)
Daytime sleep duration						
None	1	1	1	1	1	1
< 1 h	1.46 (0.90-2.39)	1.41 (0.85-2.34)	1.28 (0.83-1.97)	1.28 (0.82-1.98)	1.08 (0.64-1.82)	1.05 (0.62-1.79)
≥ 1 h & < 2 h	1.42 (0.90-2.25)	1.20 (0.74-1.94)	1.34 (0.89-2.02)	1.30 (0.86-1.97)	1.11 (0.68-1.83)	1.03 (0.62-1.71)
≥ 2 h	1.41 (0.97-2.05)	1.39 (0.94-2.05)	1.36 (0.96-1.91)	1.37 (0.97-1.94)	0.85 (0.57-1.28)	0.82 (0.55-1.25)
Total sleep duration						
7-9 h	1	1	1	1	1	1
≤ 7 h	1.19 (0.80-1.76)	1.31 (0.86-1.981)	1.15 (0.82-1.63)	1.18 (0.83-1.69)	1.46 (0.97-2.21)	1.55 (1.01-2.37)
>9 h	1.14 (0.82-1.58)	1.12 (0.80-1.56)	1.17 (0.88-1.56)	1.17 (0.88-1.56)	1.39 (1.00-1.94)	1.35 (0.96-1.89)
Total sleep duration& sleep quality						
7-9 h & Normal	1	1	1	1	1	1
≤ 7 h & Normal	0.87 (0.44-1.73)	1.10 (0.53-2.26)	0.81 (0.42-1.53)	0.85 (0.44-1.63)	1.37 (0.64-2.93)	1.52 (0.70-3.33)
>9 h & Normal	1.29 (0.89-1.87)	1.31 (0.89-1.93)	1.15 (0.82-1.61)	1.16 (0.83-1.64)	1.39 (0.94-2.04)	1.39 (0.94-2.07)
7-9 h & Poor	1.48 (0.89-2.47)	1.67 (0.98-2.84)	1.00 (0.64-1.55)	1.05 (0.67-1.64)	1.11 (0.68-1.83)	1.28 (0.77-2.14)
≤ 7 h & Poor	1.56 (0.97-2.51)	1.75 (1.07-2.88)	1.28 (0.85-1.93)	1.33 (0.87-2.02)	1.56 (0.96-2.55)	1.76 (1.06-2.90)
>9 h & Poor	1.40 (0.73-2.67)	1.47 (0.76-2.87)	1.31 (0.74-2.31)	1.34 (0.75-2.37)	1.85 (0.91-3.78)	2.04 (0.99-4.20)

Data are presented as OR (95%CI). Adjust model: adjusted for age, sex, ethnicity, marital status, education level, residential type, smoking status, drinking status, physical activity level, central obesity, diet regularity, and comorbidity.

ited a mediating effect with an effect ratio of 2.4%, as shown in Table 3.

Mediation analysis model 4 was used to explore the mediating role of inflammatory indicators in the relationship between nighttime sleep duration and high pulse pressure. In this analysis, neutrophils, lymphocytes, CRP, complement C3, complement

C4, NLR, and SII were included as mediator variables. The findings revealed that lymphocyte count, NLR, and SII acted as mediators in the link between nighttime sleep duration and high PP. Specifically, the effect ratios for lymphocyte count, NLR, and SII were 91.22%, 36.93%, and 0.20%, respectively (Table 4 and Tables S2 and S3).

Table 3 Analysis of the mediating role of complement C3 in the association between sleep quality and hypertension.

Paths	Coefficient	Effect	Z	P
Hypertension = c'*sleep quality+b*Complement C3+e3	ab	0.0072	1.9674	0.0491
	c'	0.2930	2.7344	0.0062
Mediation effect ratio		0.0240		

Adjusted for age, sex, ethnicity, marital status, education level, residential type, smoking status, drinking status, physical activity level, central obesity, diet regularity, and comorbidity; The independent variable X is sleep quality, the mediator variable M is Complement C3, and the dependent variable Y is Hypertension; ab represents the mediating effect value, obtained by multiplying the values of a and b obtained from the equations Complement C3 = a sleep quality + e2 and Hypertension = c' sleep quality + b Complement C3 + e3, respectively; C' represents the effect of X on Y after controlling M; Mediation effect ratio = ab/(ab+c')



Table 4 Analysis of the mediating role of Lymphocytes in the association between sleep duration at night and PP.

Paths	Coefficient	Effect	Z	P
PP = c*sleep duration at night+b*Lymphocytes+e3	ab	22.5019	3.1401	0.0017
	c'	2.1661	2.5069	0.0124
Mediation effect ratio		0.9122		

Adjusted for age, sex, ethnicity, marital status, education level, residential type, smoking status, drinking status, physical activity level, central obesity, diet regularity, and comorbidity; The independent variable X is sleep duration at night, the mediator variable M is Lymphocytes, and the dependent variable Y is PP; ab represents the mediating effect value, obtained by multiplying the values of a and b obtained from the equations Lymphocytes = a sleep duration at night+e2 and PP = c' sleep duration at night+b Lymphocytes+e3, respectively; C' represents the effect of X on Y after controlling M; Mediation effect ratio = ab/(ab+c'). PP: pulse pressure.

DISCUSSION

The findings of the research demonstrate a significant link between poor sleep quality and hypertension among centenarians. Furthermore, the study identified a relationship between sleep duration at night and isolated systolic hypertension, as well as high PP in centenarians. The mediating role of complement C3 was observed in the association between poor sleep quality and hypertension. Additionally, lymphocyte count, NLR, and SII were identified as mediators in the relationship between nighttime sleep duration and high PP.

In CHCCS, the prevalence was 71.4% for hypertension and 54.5% for isolated systolic hypertension. Prior studies on hypertension in centenarians show varying prevalence rates, with rates reported at 19 percent in Finnish centenarians and 65 percent in both Hong Kong centenarians^[28] and Polish centenarians.^[29] In a study on Tokyo centenarians,^[30] it was found that over 95% of them had chronic diseases, with hypertension being the most commonly reported. This difference could be linked to genetic factors, living environment, and dietary habits.

This study indicates that centenarians with poor sleep quality are more likely to have hypertension, and those who sleep more than 9 h at night have an increased risk of isolated systolic hypertension. Previous studies on the association between sleep status and blood pressure have mostly focused on adolescents and middle-aged populations. This association in older adults has received limited attention compared to younger age groups. In 2005, a comprehensive epidemiological survey of older Chinese individuals^[31] found no statistically significant link between sleep quality and arterial blood pressure. Research involving individuals under the age of 60^[32] indicated that poor sleep quality was associated with an increased risk of hypertension. The variation

in findings may be attributed to the age gap among participants as well as potential survivor bias. The research focus on sleep duration, pulse pressure difference, and isolated systolic hypertension in the elderly population was not found.

Some potential mechanisms can explain this association, such as the total sleep duration, which may reflect that the body is in a pro-inflammatory state.^[33] Mouse-based studies have also shown that changes in sleep status can activate inflammatory pathways and affect vascular elasticity, potentially leading to cardiovascular disease.^[17] This study suggests that inflammatory indicators play a mediating role in the association between sleep status and blood pressure.

This study offers several significant advantages. Firstly, it is noteworthy that the study, carried out through the framework of the CHCCS, stands as the largest single-center full-sample centenarian study in Asia, equipped with valuable resources. The research delves into exploring the relationship between sleep status and blood pressure status among centenarians in Hainan. Moreover, this study provides important data for understanding the underlying mechanisms by examining the potential mediating role of inflammatory indicators in the relationships. Secondly, the research includes a carefully planned epidemiological investigation that incorporates strict quality control measures at each stage. By conducting thorough data analysis, the study guarantees the dependability and scientific integrity of its findings.

Several limitations need to be considered in this section of the study. Firstly, the cross-sectional nature of the research design inherently limits the ability to make causal inferences. This is compounded by the relatively small sample size of male centenarians, with only 179 individuals included in the

study. Such a limitation could lead to issues with multivariate analysis, particularly with wider confidence intervals for the effect estimates due to an insufficient sample size. Furthermore, all participants in the study were exclusively sourced from a specific island region, Hainan Province. This restriction significantly hampers the generalizability of the findings, cautioning against any broad extrapolation of the results. Despite attempts to mitigate recall bias through separate interviews with centenarians and their caregivers, residual recall bias may still be present in the data. Moreover, the reliance on self-reported sleep information from questionnaires without objective monitoring data introduces limitations in accurately assessing sleep patterns. Lastly, it is crucial to acknowledge the possibility of unadjusted factors in the multivariate analysis of association studies, potentially affecting the validity of the results.

In conclusion, this study using baseline data from CHCCS offers a detailed description of the sleep status and blood pressure status. The results indicated that poor sleep quality increases the risk of hypertension, and sleeping ≤ 6 h or > 9 h at night raises the risk of high PP in centenarians. Explored the association between sleep status and hypertension, isolated systolic hypertension, and high PP. Complement C3 mediates the relationship between poor sleep quality and hypertension, while lymphocyte count, NLR, and SII mediate the relationship between sleep duration at night and high PP. Therefore, for elderly people with poor sleep quality and long or short sleep duration at night, attention should be paid to their blood pressure status, and monitoring and protection of their body inflammation levels should be emphasized.

DECLARATIONS

Consent for publication

Not applicable.

Competing interests

None.

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Authors' contributions

Qiao LI, Shengshu WANG, Guangdong LIU, Yao HE and Shanshan YANG contributed to the data analysis and manuscript writing. Jianhua WANG, Yali ZHAO and Miao LIU contributed to the study design and data collection. All authors contributed to the manuscript revision and approved the final submission.

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