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Title: Associations of sleep duration and disturbances with hypertension in metropolitan cities of Delhi, Chennai and Karachi in South Asia: cross-sectional analysis of the CARRS study

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Abstract:

Objectives: Sleep duration and disturbances may be risk factors for hypertension. Despite the high burden of hypertension in South Asia, little is known about this relationship in this region.

Methods: We analyzed population-level cross-sectional data from the Centre for Cardiometabolic Risk Reduction in South Asia (CARRS) study that recruited representative samples of adults ≥ 20 years from three cities- Delhi, Chennai (India) and Karachi (Pakistan) during 2010-11. We defined hypertension as self-reported treatment or measured blood pressure (BP) ≥140/90mmHg. Data on usual duration of sleep, insomnia and snoring were collected using "The Sleep Habits Questionnaire" and excessive daytime sleepiness (EDS) using Epworth Sleepiness Score. Logistic and linear regression were done with hypertension and BP as outcome variables, respectively. Age, sex, education, wealth index, family history, and body mass index (BMI) were included as covariates. We used multiple imputation to account for missing variables.

Results: Prevalence of hypertension was 30.1%. The mean (SD) sleep duration was 7.3 (1.2) hours. Insomnia, snoring and EDS were present in 13.6%, 28.7% and 4.6%, respectively. Moderate and habitual snoring were associated with increased odds of hypertension (OR=1.18, 95% CI [1.04, 1.33] and 1.47 [1.29, 1.67], respectively), after adjusting for covariates. Rare, occasional and frequent insomnia were associated with increased hypertension (OR 1.41, [1.12, 1.77], 1.39 [1.16, 1.67], 1.34 [1.09, 1.65], respectively). Sleep duration and EDS were not associated with hypertension.

Conclusion: Self-reported snoring and insomnia were associated with hypertension in South Asia. This relationship needs further exploration through robust longitudinal studies in this region.

Keywords: Hypertension, blood pressure, sleep duration, insomnia, snoring, daytime sleepiness, South Asia

Statement of Significance

This study addresses the important lacunae in population level sleep and health relationship in rapidly developing South Asian Cities. The study found high prevalence insomnia and self-reported snoring among adults in urban South Asia. The odds of hypertension were 18 and 47% higher for moderate and habitual snorers and 34-41% higher among participants with insomnia. Duration of sleep and excessive daytime sleepiness were not associated with hypertension.

Introduction:

Rapid unplanned urbanization and globalization in South Asia have resulted in adoption of lifestyles that includes high consumption of calorie dense foods, low physical activity, and psychological stresses leading to overweight and an increased susceptibility to hypertension, diabetes, and cardiac diseases.[1] Lifestyle changes, stress, and obesity are also risk factors for sleep loss and disturbances. [2,3] Urban lifestyles are associated with longer commutes to work, more hours spent watching television, and habitual internet use which can potentially result in shorter sleep duration and disturbances. Additionally, sleep duration[4,5] and disturbances are possible risk factors for hypertension.[6-8] Insomnia, a disorder in which there is difficulty in falling asleep or staying asleep or both, despite adequate opportunity to sleep,[9] is considered a risk factor for hypertension,[10] but the evidence for this is not consistent. [5,6,11,12] Snoring, a symptom of obstructive sleep apnea (OSA),[13,14] is identified as an independent risk factor for hypertension.[7,15-17] But, there is little evidence on independent associations between Excessive daytime sleepiness (EDS), another cardinal symptom of OSA, and hypertension.[15,18]

In South Asia, population data on usual duration and disturbances of sleep (insomnia, snoring, and EDS) are limited.[19,20] Nearly one third of the adult populations in countries like India and Pakistan are estimated to have hypertension.[21-23] Despite this high burden, the relationship of hypertension with sleep-duration and sleep-disturbances have remained largely unexplored. To address this gap, we examined potential associations between sleep parameters and hypertension by analyzing data from a cross-sectional representative survey of 16287 adults aged ≥20 years in three mega-cities (Chennai, Delhi and Karachi) of South Asia.

Methods:

We used data from the baseline survey of the Centre for Cardiometabolic Risk Reduction in South Asia (CARRS) study collected during 2010-11.[24] The methods, participant recruitment, data collection in CARRS cohort study are published in detail elsewhere [24] Briefly, participants were recruited by multi-stage cluster random sampling technique stratified by gender and city of residence. Primary sampling units(PSUs) were wards or larger municipal subdivisions for Delhi and Chennai respectively while, clusters were the PSUs for Karachi. At the time of data collection, the most recent census in each country (India-2001 census; Pakistan 1998 census) was used to randomly select the wards, clusters, or census enumeration blocks (CEB- smallest municipal subdivision in Indian cities), and households. In order to account for changes that may have happened in the interim, we manually listed and mapped all households in each CEB before randomly selecting them.[24,25] The "Kish Method", used in the WHO's STEPS surveys,[26] was used to select two participants (one male and one female), aged 20 years or older from each household. Pregnant women, bed-ridden individuals and persons unable to understand the questionnaire due to severe mental illness were excluded. Response rates were 94·7% for questionnaire completion and 84·3% for bio-specimens.[25]

Data were collected through personal interviews at the participants' homes using structured questionnaires. Blood pressure was measured twice at participants' homes by trained study staff using an electronic sphygmomanometer (Omron Dailan Co., Ltd, Dalian, Liaoning, China) in a seated position with a five-minute gap between measurements. A third measurement was obtained if the difference between the first two systolic (SBP) or diastolic (DBP) measurements was more than 10 mmHg or 5 mmHg, respectively. The time of blood pressure measurement varied between participants and was usually between 7am to 4pm. The mean of the first two BP measurements, or the second and third measurements if a third measurement was taken, were used for analyses. Participant was classified as having hypertension if SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg or self-reported hypertension medication.[27]

Data on sleep habits were collected using "The Sleep Habits Questionnaire" to assess usual sleep habits and sleep disorders including insomnia and snoring; this questionnaire has been used previously in Sleep Heart Health Study (SHHS).[28] The Epworth sleepiness scores (ESS) [29,30] was used to measure daytime sleepiness. The English questionnaires were translated to local languages (Tamil, Hindi and Urdu) and back translated to English. The questionnaires were piloted and interviewer debriefing method was used assess any difficulty or variation in understanding of the items in the questions and wordings of the questionnaire were modified accordingly. [24] To assess internal consistency (reliability) for insomnia and ESS, we measured Cronbach's alpha for overall population and subgroups (age, gender and city). Participants were asked about sleep duration (number of hours) during usual weekdays and weekends. The average duration of sleep per day was obtained by [(average of duration of sleep during weekdays * 6) + (average duration of sleep during weekends *1)]/7. Weekdays was multiplied by 6 because most establishments in South Asia have 6 working days a week. The average duration of sleep was categorized as <5, 5-5.9, 6-6.9, 7-7.9, 8-8.9 and ≥ 9 hours.[4] Participants were asked if they experience any of the following experiences of insomnia- "Have trouble falling asleep"; "Wake up during the night and have difficulty getting back to sleep" "Wake up too early in the morning and unable to get back to sleep"; and "Take sleeping pills or other medication to help you sleep" over past month. Insomnia was categorized into 'no', 'rare', 'occasional' and 'frequent' if the frequency of any insomnia was <2, 2-4, 5-15 and 16-30 nights/ month, respectively. If an individual had more than one symptom, insomnia was categorized based on the most frequent symptom.[4] The Cronbach's alpha for insomnia was 0.81, overall and varied between 0.78 and 0.85 for various subgroups.

Participants were asked if they ever snored and if yes, how often they snored. They were coded as non-snorer if they either never snored or did not snore anymore, moderate snorer if they said rarely or sometimes (up to two nights per week) and habitual snorer if they answered frequently, almost always or always to the question.[31] Regarding excessive daytime sleepiness (EDS), the Epworth Sleepiness Score (ESS) was used and categorized participant responses to chances (no chance=0; slight chance=1; moderate chance=2; high chance=3*)* of falling asleep in the following eight situations- sitting and reading; watching television; sitting inactive in a public place (such as a theatre or a meeting); riding as a passenger in a car for an hour without a break; lying down to rest in the afternoon when circumstances permit; sitting and talking to someone; sitting quietly after a lunch; in a car, while stopped for a few minutes in traffic. The scores for all items were added together. A participant was coded as unlikely sleepy, average day time sleepiness, excessive sleepiness depending on the situation, and excessive sleepiness if the total score was 0-7, 8-9, 10-15 and 16-24, respectively, based on ESS.[29] There were only 50 participants with ESS 16-24, therefore this category was merged with ESS 10-15 and renamed EDS. The Cronbach's alpha for daytime sleepiness was 0.80, overall and varied between 0.78 and 0.85 for various subgroups.

Regarding participant characteristics, self-reported age at baseline in completed years was used and categorized into three age groupings: 20-44, 45-59, and 60+ years. Participant-reported gender was used to code individuals as male or female. Self-reported highest education level attained was categorized into four categories - up to primary schooling; high or secondary schooling; up to university education; and university and higher. A wealth index based on different household amenities (separate cooking room and toilet facilities) and assets (television, refrigerator, washing machine, microwave, mixer-grinder, mobile phone, DVD player, computer, car, motor cycle, and bicycle) was used. Total scores were categorized into tertiles (lowest tertile representing poorest and highest tertile representing wealthiest).[25] Self –reported current use of smoked tobacco (both cigarettes and bidis), history of heart disease and stroke was obtained from questionnaire. We used a modified food frequency questionnaire, to estimate average servings of fruits and vegetable intake per day and coded these into <2, 2-4 and ≥ 5 servings a day.

Anthropometric parameters (height, weight, body composition, waist circumference, hip circumference, skin fold thickness) were measured using standard techniques either at participant's home or at a temporary blood collection clinics organized closer to participant's home. Measured height (meters) and weight (kilograms) was used to calculate body mass index (BMI) as weight / height^2. A 15 ml fasting venous blood sample was collected for biochemical measurements. Fasting plasma glucose (FPG) was estimated using hexokinase/kinetic methods and total cholesterol (TC) estimated by enzymatic colorimetric cholesterol oxidase peroxidase.[25,32]

Ethical issues:

The CARRS Surveillance study was approved by the independent ethics committees of Public Health Foundation of India, All India Institute of Medical Sciences, New Delhi, Madras Diabetes Research Foundation, Chennai, India, Aga Khan University, Karachi, Pakistan, and Emory University, Atlanta, US. The CARRS Study obtained informed consent from all participants.

Analysis:

This analysis included 16,287 participants. The number of missing values in CARRS dataset has been published previously.[25] In short, missing values in questionnaire data, blood pressure, BMI, blood biochemistry and overall were 0%, 4.9%, 23%, 15.8% and 25%, respectively. To account for the missing variables, we used multiple imputation using chained equation (MICE) for imputing all missing values across all variables to create ten completed datasets. All covariates and the outcome were included in the imputation model. Imputation methods are described in greater detail elsewhere.[25] Imputed values of missing continuous variables were modelled using linear regression and predictive mean matching, and imputed values of ordinal variables were modelled using ordinal logistic regression. Model convergence was checked, and diagnostics were performed on the imputed dataset. Sample weighting was taken into account in the data analysis using stata command svyset, with a 'ward' variable as primary sampling unit.[25,32,33] Standard weights and strata (6 strata of gender and age groups 20-44, 45-59, 60+ years) were used obtain weighted estimates. All analysis commands were prefixed with 'svy' to obtain weighted percentages, means, coefficients or odds ratios, and 95% confidence intervals (CI). The distribution of sleep variables by city and gender were assessed as percentages with 95% CIs.

We assessed collinearity between sleep variables by cross tabulation (results not shown) and found no significant collinearity between the sleep variables. For all regression analyses, 7-7.9 hours was used as the reference category for duration of sleep. We used logistic regression to model hypertension. Each sleep variable was modelled separately with hypertension to obtain unadjusted odds ratios (model-1). Individual sleep variables were then modelled adjusting for age as continuous variable and gender (model-2). In model-3, we further adjusted for socio-demographic variables- education, wealth index and city. In the model-4, we assessed for potential confounding by other variables (BMI, smoking, alcohol use, self-reported heart disease, stroke, family history of hypertension, fruits and vegetables intake, FPG and TC) using forward stepwise regression starting from the variables most strongly associated with hypertension in the bivariate analysis. Only BMI was found to confound the associations between sleep variable and BP categories, and therefore retained in model-4. Finally, we adjusted for other sleep variables in model-5. We further assessed the interaction between sleep duration and insomnia categories, and between snoring and EDS on their effects on hypertension. We computed predicted probabilities and 95% confidence intervals (using robust standard errors) of hypertension for each of the sleep categories using model-5. We assessed interaction of age (20-44, 45-59, ≥ 60 years), gender with sleep variables by introducing interaction term. We considered effect modification if the p-value of Wald test of interaction term was < 0.05. Further, we computed predicted probabilities and 95% confidence intervals (using robust standard errors) of hypertension for each of the sleep categories stratified by age and gender. BMI was one of the imputed variables, therefore stratification by BMI (which may vary between 10 imputed datasets) could have introduced bias. Hence, we were only able to assess effect modification of BMI by stratifying on BMI category (<18.5, 18.6-24.9, ≥ 25kg/m^2) for the non-missing complete cases. In addition, we assessed the independent effect of separate symptoms of insomnia: initial (have trouble falling asleep); middle (wake up during the night and have difficulty getting back to sleep); late (wake up too early in the morning and be unable to get back to sleep) and medication for insomnia on hypertension using logistic regression adjusting for each other, other sleep factors, age, gender, education, wealth index, city and BMI. None of the logistic regression models were adjusted for hypertension medication.

Further, we did two separate linear regressions with systolic and diastolic blood pressures as continuous outcome variables adjusting for medication for hypertension (model-1) and adding age, gender, education, wealth index, city, BMI and other sleep variables (model-2) using multiple imputed dataset. Forty-three observations (0.26%) who reported not knowing their snoring patterns were dropped from the analysis in all the models.

Finally, we performed a sensitivity analysis between the multiply imputed and complete case datasets. The weighted percentages (means, if continuous variable) of socio-demographic variables, exposures, and hypertension; and adjusted estimates of logistic and linear regression models in both datasets were compared. We used Stata 14.2 for all statistical analyses.

Results:

The number of participants recruited from Chennai, Delhi and Karachi were 6906, 5364 and 4017, respectively. Mean (standard deviation [SD]) age of participants total and city wise (Chennai, Delhi and Karachi) were 42.3 (12.6), 41.7 (12.2), 44.1 (12.2) and 41.7 (13.9) years, respectively.

Women constituted 52.4%, 53.9 %, 49.9 %, and 52.9% in overall, Chennai, Delhi and Karachi, respectively. The mean (SD) years of schooling in all, Chennai, Delhi and Karachi were 8.0 (5.0), 7.5 (4.2), 8.7 (5.4) and 7.1 (5.3), respectively. The complete description of CARRS population has been published previously.[25]

Table-1 shows the distribution of duration of sleep and sleep disturbances in the study population by gender and city. Overall, 5.5% and 1.9% of participants slept <5 and 5-6 hours, respectively. This distribution varied by city, with Chennai having lowest prevalence of short sleep and Karachi the highest. About 12.4% of participants slept greater than 9 hours on average. This again varied by city, with Delhi having lowest prevalence of long sleepers and Karachi the highest. The mean (SD) duration of sleep was 7.3 (1.2) hours in total population which was longest in Chennai women (7.7 [1.1] hours) and shortest in Delhi men (6.9 [1.1] hours). With respect to insomnia, about 12% of participants reported insomnia: either rare, occasional, or frequent. Women reported higher prevalence of insomnia than men in all three cities; the difference between genders was particularly striking in Karachi. Moderate and habitual snoring was reported by 14.5% and 14.2% of participants, overall. Snoring was more common among men than women overall. However, in Karachi, habitual snoring was more common among women compared to men. EDS was the least common sleep problem in these South Asian cities with 2.8% and 1.8% reporting average and excessive daytime sleepiness respectively. EDS was lowest in Chennai and highest in Karachi.

Table-2 presents the results of logistic regression analyses examining the relationships of sleep variables with hypertension. In unadjusted logistic regression (model-1), the odds of hypertension were higher with shorter duration of sleep and lower with longer duration of sleep when compared to 7-8 hours of sleep. However, this relationship did not hold after adjustment for sociodemographic variables and the fully adjusted model-5 showed no relationship between sleep duration and hypertension. Participants with rare occasional and frequent insomnia had significantly higher odds of hypertension compared to those with no insomnia. The effect size was slightly attenuated after adjusting for age and sex but remained significant. The magnitudes of these associations were unchanged in

the remaining adjusted models. The adjusted odds ratio of hypertension for early, middle, late and medication for insomnia were 1.09 (0.85, 1.39), 1.44 (1.06, 1.96). 0.87 (0.64, 1.20) and 1.85 (1.33, 2.59), respectively. (not in the table)
Both moderate snorers and habitual snorers had significantly higher odds of hypertension compared to non-snorers in model-1. However, the strength of this association was attenuated after adjusting for age and gender in model-2 and BMI in model -4. Adjusting for other sleep variables had no further substantial impact on the magnitude of associations (model-5). When assessing for patterns of relationships across snoring categories, there were significant associations between snoring categories and hypertension (Wald test p-value< 0.001 [data not shown]). In unadjusted models, the odds of hypertension were significantly higher if the participant had EDS; however, this association no longer existed after adjusting for age and sex in model-2, and remained non-significant in all further models (table-2).

Table-3 presents that association of sleep variables and hypertension, stratified by age groups. The associations between snoring and hypertension were more pronounced in young participants (20-44 years) and there was no association in the oldest group (≥ 60 years). There was a significant interaction between sleep duration and age groups. The odds ratio of hypertension was significantly higher among young adults who slept 6-6.9 hours but no significant association in other age groups. Additionally, associations between insomnia and hypertension were stronger in in middle and older age groups implying a significant interaction between age group and insomnia. And, the snoring and hypertension association were stronger in younger age groups (table-3). The association of sleep variables and hypertension were similar in both genders (table-4). We found no effect modification of BMI on sleep variables and hypertension relationship in the complete case analysis (supplementary table-3). We also found no significant interaction by insomnia for sleep duration and hypertension, nor by snoring for EDS and hypertension (data not shown).

In analyses using continuous SBP and DBP as outcomes, moderate and habitual snoring were significantly associated with higher SBP and DBP, even after adjusting for hypertension treatment. The associations were highly attenuated but remained significant after adjusting for other variables. We found no relationships between duration of sleep, insomnia, and EDS with either systolic or diastolic blood pressure (table-5).

In sensitivity analyses, we found that the complete case and MI datasets did not differ in any of the demographic, socio economic, behavioral, exposure, or outcome parameters (see supplementary table-1). The estimates from logistic and linear regressions were comparable between two datasets (see supplementary table-2).

Discussion:

In this representative adult population from three mega cities of South Asia, nearly a third of the population had either moderate or habitual snoring but only about 5% had daytime sleepiness. The percentage of adults sleeping longer than optimum hours were much higher than shorter duration of sleep. The principal findings in this large study of sleep and hypertension in South Asia was that self-reported snoring was associated with hypertension among urban adults. This association was independent of prominent risk factors for hypertension. Further, we noted significant associations across snoring categories with hypertension and linear associations with blood pressure. The associations were stronger in younger individuals and women.

The current study estimates are similar to the findings from a large cross-sectional study of 10413 adults (50-85 years) from Guangzhou in China, where daily snorers had higher odds of hypertension 1.37 (1.20-1.56) compared to non-snorers.[34] Similarly, a 10-year follow up study of 2451 Swedish men showed persistent snoring was independently associated with incident hypertension after adjusting for other risk factors among younger men (30-49 years at baseline) but not among older men (50-69 years at baseline).[16] However, in a population based survey of 6779 Swedish women, snoring was associated with hypertension only in presence of daytime sleepiness[15] while a smaller study among Hispanics Americans found no association between snoring and hypertension.[35] This indicates that there may be heterogeneity in snoring and hypertension relationships across populations. Nevertheless, a meta-analysis of longitudinal studies has confirmed that snoring is a risk factor for hypertension.[10]

While the direction of associations cannot be established in this cross-sectional study, the coexistence of snoring and hypertension has clinical implications. Although snoring is a symptom of OSA,[13] not all snorers may have OSA. Indeed, the relationships between snoring and cardio-metabolic disorders could be independent of OSA.[16] The relationships between OSA and hypertension may also be bidirectional [14]. Untreated coexistence of OSA may lead to uncontrolled hypertension despite medical treatment for hypertension.[36] Conversely, treatment of hypertension to a lower BP target may improve sleep apnea by improving upper airway tone.[14] Therefore, screening for snoring and OSA, and appropriate treatment among people with hypertension specifically among young adults and vice versa may help control both conditions.

The percentage of people reporting EDS in South Asian adults was small (4%). A smaller study from Chennai[20] which used snoring, tiredness during daytime, observed apnea, and high blood pressure (STOP) questionnaire[37] found 59% of adults had daytime sleepiness. However, the ESS instrument used in our study is more robust measure as it uses a comprehensive score and also was found to have higher specificity and positive predictive values compared to STOP.[38] We found no associations between EDS and hypertension in South Asian cities. This is unsurprising as previous studies showed EDS was associated with hypertension only in persons with OSA.[8]

The present analysis found that having insomnia, irrespective of the frequency was associated with about 40% higher odds of hypertension. These results contrast with a cross-sectional analysis of symptoms of insomnia and hypertension in 12,643 adults from the US' National Health And Nutrition Examinations Surveys (NHANES) which found no such association.[11] However, our findings are consistent with a meta-analysis of prospective studies that showed insomnia was positively associated with hypertension.[10] Another study from Finland, following employees with insomnia assessed during baseline found that odds of the use of antihypertensive medication was higher by 40% and 47% among persons with occasional and frequent insomnia respectively at the baseline[39]. The definition of frequent insomnia as defined in our study is in line with definition of insomnia disorder i.e. insomnia symptoms for at least three days a week. [9] We found the odds of hypertension in this group was similar to odds for rare or occasional insomnia. But, among the individual symptoms of insomnia, only medication used for insomnia remained significantly associated with hypertension indicating higher hypertension in severe insomnia. Disruptions in hypothamic-pituitary-adrenal axis and circadian rhythmicity, [40] sympathetic activation, oxidative stress, systemic inflammation and hypoxemia[40,41] are possible mechanisms on how insomnia might be related to elevated blood pressure. The cross-sectional analysis and lack of dose-response relationship makes it difficult to say definitively and to investigate the root causes of the relationships between insomnia and hypertension in our analysis.

We found no association between either short or long duration of sleep with hypertension after adjusting for other hypertension risk factors among South Asian adults. The Sleep Heart Health Study from the US, suggested a ''U" shaped relationship between duration of sleep and hypertension.[4] However, there is huge variation in duration of sleep and hypertension relationships by gender,[42] age groups,[43,44] and geographical regions.[2] Further exploration of the social context of sleep loss and the role of stress and other psychological factors in its occurrence may help explain these study and regional differences. Indeed, more open-ended and qualitative perspectives may be helpful in seeking the underlying causes of poor sleep patterns.

This study has several limitations that should be considered. First, this was a cross sectional study and therefore directions of association between sleep variables and snoring cannot be ascertained and there is a potential for reverse causality.[10] Second, self-reported sleep variables, specifically snoring, are subject to recall and information bias, and probably best asked of the participant's partner. Validation of sleep questions against roommate/partner's report in the United States found moderate to high correlation,[45] however no such validation studies exists in India, where cultural norms may influence participant responses differently to the USA. Nevertheless, any measurement error in exposure variables is likely to be non-differential (unlikely to be affected by hypertension status). If anything, this would possibly had pulled the associations towards the null and therefore the true relationships may have been underestimated rather than overestimated. Additionally, due to lack of objective measurements, it was not possible to differentiate between primary or simple snoring and snoring as marker of obstructive sleep apnea. [46] Third, the models were not adjusted for time of blood pressure measurement. Since time of blood pressure measurement varied between participants (between 7 AM to 4 PM), this may have non-differentially affected the sleep- blood pressure relationship. In future, ambulatory blood pressure measurements may be useful to further explain this relationship. Finally, the analysis was not adjusted for many other potential confounders such as physical activity, depression, and intake of caffeine or medications that are associated with poor sleep such as aspirin, non-steroidal anti-inflammatory drugs, and hormones. There may also be residual confounding by these variables which may have distorted the study results. However, the analysis was adjusted for the variables commonly included in publications examining associations between sleep and hypertension, and the associations reported above remained after adjustment for these variables.

The study also has several strengths. This was first study in South Asia reporting on the association between sleep factors and hypertension using large representative populations of three mega cities with such a high response rate. Secondly, the study used standardized protocol across all sites with stringent quality assurance and quality control. Thirdly, blood pressure, BMI, and biochemistry were all objectively measured. Fourth, the study reported on association between sleep variables with both hypertension and continuous measures of BP. Finally, we considered a large variety of potential confounders in order to minimize residual confounding.

Conclusion:

Moderate and habitual snoring was highly prevalent and was positively associated with hypertension, specifically in young adults and women in South Asian metropolitan cities. Any level of insomnia was also associated with higher odds of hypertension. Duration of sleep and daytime sleepiness were not associated with hypertension. Association of sleep variables with hypertension in this population needs further exploration through robust longitudinal studies in this region.

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Conflict of interest:

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Table-1: Distribution of sleep variables by gender and city (N=16287)

Sleep Variables	All			Chennai		Delhi		Karachi	
	Total	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**
Numbers*	**16287**	**7760**	**8527**	**3188**	**3788**	**2680**	**2684**	**1892**	**2125**
Duration of Sleep (hours)									
<5	**5.5 [5.0, 6.0]**	5.2 (4.5, 5.9)	5.8 (5.0, 6.5)	3.0 (2.2, 3.9)	2.2 (1.5, 2.8)	5.1 (3.9, 6.2)	6.2 (5.0, 7.4)	8.8 (7.3, 10.3)	11.4 (9.2, 13.7)
5-5.9	**1.9 (1.6, 2.2)**	1.8 (1.3, 2.2)	2.0 (1.6, 2.5)	0.8 (0.3, 1.4)	0.6 (0.2, 1.0)	2.5 (1.6, 3.3)	2.6 (1.9, 3.3)	2.3 (1.8, 2.8)	3.8 (3.0, 4.6)
6-6.9	**21.1 (19.9, 22.3)**	23.0 (21.2, 24.7)	19.4 (17.7, 21.1)	14.4 (12.2, 16.6)	11.4 (9.7, 13.2)	30.4 (27.8, 33.0)	24.6 (22.4, 26.8)	26.7 (24.5, 28.8)	26.5 (24.6, 28.5)
7-7.9	**28.4 (27.3, 29.4)**	27.9 (26.6, 29.2)	28.8 (27.2, 30.3)	24.7 (22.6, 26.8)	27.5 (25.5, 29.5)	35.9 (33.8, 38.0)	35.1 (32.4, 37.7)	21.8 (20.1, 23.5)	23.1 (20.7, 25.4)
8-8.9	**30.8 (29.0 ,32.6)**	31.3 (29.3, 33.3)	30.3 (27.5, 33.2)	41.4 (38.5, 44.4)	41.4 (38.8, 44.1)	20.9 (18.7, 23.0)	26.3 (23.2, 29.4)	29.4 (27.7, 31.1)	16.3 (14.1, 18.5)
≥9	**12.4 (11.4, 13.4)**	10.9 (9.6, 12.2)	13.7 (12.3, 15.1)	15.6 (13.4, 17.8)	16.9 (14.4, 19.4)	5.3 (4.0, 6.7)	5.2 (4.1, 6.4)	11.1 (9.5, 12.6)	18.9 (17.0, 20.7)
Mean (SD)	**7.3 (1.2)**	7.2 (1.2)	7.3 (1.2)	7.6 (1.1)	7.7 (1.1)	6.9 (1.1)	7.0 (1.1)	7.1 (1.2)	7.1 (1.2)
Insomnia (nights/month)									
No	**86.5 (85.2, 87.8)**	91.2 (90.4, 92.1)	82.2 (80.2, 84.1)	91.5 (90.3, 92.8)	89.0 (87.4, 90.5)	94.3 (93.2, 95.5)	83.7 (81.4, 86.0)	86.4 (84.5, 88.2)	68.4 (65.6, 71.2)
Rare	**4.9 (4.4, 5.4)**	3.0 (2.6, 3.5)	6.6 (5.8, 7.3)	3.3 (2.5, 4.1)	4.9 (3.8, 5.9)	2.0 (1.4, 2.7)	8.5 (7.2, 9.7)	4.1 (3.1, 5.1)	7.1 (5.7, 8.5)
Occasional	**4.7(4.0, 5.4)**	3.1 (2.5, 3.6)	6.1 (5.0, 7.3)	2.0 (1.3, 2.7)	2.2 (1.6, 2.8)	2.1 (1.5, 2.8)	4.1 (3.1, 5.2)	6.1 (4.9, 7.2)	15.5 (13.5, 17.6)
Frequent	**4.0 (3.5, 4.4)**	2.6 (2.2 ,3.1)	5.1 (4.5, 5.8)	3.2 (2.5, 3.8)	4.0 (3.1, 4.9)	1.5 (1.0, 2.1)	3.7 (2.9, 4.4)	3.4 (2.6, 4.2)	9.0 (7.4, 10.5)
Snoring frequency									
Non-snorer	**71.0 (69.8, 72.3)**	65.2 (63.3, 67.1)	76.4 (74.8, 77.9)	67.0 (64.3, 69.7)	83.1 (81.5, 84.7)	55.5 (52.0, 59.1)	67.2 (64.3, 70.1)	75.8 (72.6, 79.1)	76.3 (72.7, 79.8)
Moderate snorer	**14.5 (13.7, 15.3)**	17.9 (16.6, 19.1)	11.5 (10.6, 12.4)	20.0 (18.2, 21.9)	9.6 (8.3, 10.9)	18.3 (16.1, 20.4)	15.1 (13.0, 17.1)	13.7 (11.9, 15.4)	10.4 (8.9, 12.0)
Habitual snorer	**14.2 (13.3, 15.1)**	16.7 (15.3, 18.1)	11.9 (10.8, 13.0	12.4 (10.3, 14.5)	6.9 (5.8, 8.0)	26.1 (23.6, 28.7)	17.6 (15.7, 19.5)	10.4 (8.4, 12.5)	13.3 (10.8, 15.8)
Don't know	**0.2 (0.1, 0.3)**	0.3 (0.1, 0.4)	0.2 (0.1, 0.4)	0.6 (0.2, 0.9)	0.3 (0.1, 0.6)	0.0(0.0, 0.1)	0.2 (0.0, 0.4)	0.0 (0.0, 0.1)	0.1 (-0.1, 0.2)
Daytime sleepiness									
Unlikely	**95.4 (94.9, 96.0)**	96.1 (95.4, 96.8)	94.9 (94.0, 95.7)	98.2 (97.4, 99.1)	98.6 (97.9, 99.3)	95.7 (94.7, 96.7)	87.8 (85.9, 89.8)	93.0 (91.6, 94.4)	97.2 (96.3, 98.1)
Average	**2.8 (2.4, 3.2)**	2.2 (1.7, 2.6)	3.4 (2.7, 4.0)	0.9 (0.5, 1.4)	1.1 (0.4, 1.8)	2.2 (1.5, 2.9)	8.0 (6.2, 9.8)	4.1 (3.2, 5.0)	1.4 (1.0, 1.9)
Excessive^	**1.8 (1.5, 2.1)**	1.8 (1.4, 2.2)	1.8 (1.3, 2.3)	0.8 (0.2, 1.4)	0.3 (0.1, 0.4)	2.1 (1.3, 2.9)	4.2 (3.0, 5.4)	2.9 (2.2, 3.7)	1.4 (0.7, 2.1)

Notes: Estimates are in percentage and 95% confidence interval unless specified; *raw numbers; ^Excessive daytime sleepiness was defined as Epworth Sleepiness Score ≥ 10 because group ≥ 15 had only 50 observations and therefore was merged with 10-15 group

Table 2: Logistic regression models of association between sleep variables and hypertension (N=16244*)

Sleep variables	**Odds ratios (95% CI)**					**Predicted probability of hypertension from model- 5# % (95%CI)**
	Model-1 (Crude)	**Model-2 age and sex adjusted**	**Model-3 (model-2+ education, wealth index and city)**	**Model-4 (model-3+ BMI)**	**Model-5 (model- 4+ sleep variables)**	
Duration of Sleep (hours)						
<5	1.35 (1.15, 1.60)	1.03 (0.87, 1.22)	1.05 (0.88, 1.25)	1.07 (0.89, 1.28)	0.99 (0.82, 1.19)	29.9 (26.8, 33.0)
5-5.9	1.13 (0.86, 1.49)	1.12 (0.84, 1.50)	1.07 (0.80, 1.43)	1.08 (0.81, 1.45)	1.00 (0.74, 1.35)	30.1(24.7, 35.4)
6-6.9	1.10 (0.98, 1.23)	0.98 (0.87, 1.11)	0.97 (0.86, 1.10)	0.98 (0.86, 1.10)	0.97 (0.86, 1.10)	29.5 (27.9, 31.2)
7-7.9			reference			30.0 (28.4, 31.7)
8-8.9	0.90 (0.79, 1.01)	0.92 (0.81, 1.04)	0.99 (0.87, 1.13)	0.99 (0.87, 1.14)	1.01 (0.89, 1.16)	30.3 (28.4, 32.1)
≥9	0.79 (0.67, 0.94)	0.88 (0.75, 1.04)	0.99 (0.84, 1.16)	1.02 (0.86, 1.20)	1.02 (0.86, 1.21)	30.4 (27.7, 33.2)
Insomnia (nights/month)						
No			reference			29.2 (28.1, 30.4)
Rare	1.58 (1.29, 1.95)	1.46 (1.18, 1.80)	1.44 (1.17, 1.78)	1.41 (1.13, 1.77)	1.41 (1.12, 1.77)	35.5 (31.3, 39.6)
Occasional	1.61 (1.36, 1.91)	1.41 (1.20, 1.66)	1.44 (1.21, 1.70)	1.43 (1.20, 1.70)	1.39 (1.16, 1.67)	35.2 (31.8, 38.6)
Frequent	1.61 (1.30, 1.99)	1.3(1.06, 1.60)	1.38 (1.13, 1.68)	1.36 (1.10, 1.67)	1.34 (1.09, 1.65)	34.5 (30.5, 38.5)
Snoring frequency						
Non-snorer			reference			28.4 (27.2, 29.6)
Moderate snorer	1.81 (1.62, 2.02)	1.48 (1.31, 1.66)	1.43 (1.27, 1.60)	1.18 (1.05, 1.34)	1.18 (1.04, 1.33)	31.3 (29.2, 33.5)
Habitual snorer	2.72 (2.42, 3.05)	2.03 (1.80, 2.29)	1.87 (1.65, 2.12)	1.49 (1.31, 1.69)	1.47 (1.29, 1.67)	35.4 (33.2, 37.7)
Daytime sleepiness						
Unlikely			reference			30.1 (29.0, 31.2)
Average	1.21 (0.96, 1.53)	1.09 (0.85, 1.39)	0.97 (0.76, 1.23)	0.92 (0.72, 1.17)	0.91 (0.71, 1.16)	28.4 (24.3, 32.5)
Excessive	1.39 (1.07, 1.82)	1.15 (0.86, 1.52)	1.06 (0.79, 1.41)	1.02 (0.75, 1.38)	0.92 (0.68, 1.25)	28.7 (23.5, 33.8)

Notes: * Raw numbers, N= 16,244 as 43 observations who reported "don't know" for snoring were dropped from the analysis; # covariates used- age, gender, city, education, wealth index, body mass index and other sleep variables

Table-3: Logistic regression models$ of association between sleep variables and hypertension stratified by age group (N=16244*)

	Adjusted odds ratios (95% CI) $				**Predicted probabilities of hypertension % (95% CI) #**		
Sleep Characteristics	**20-44 years**	**45-59 years**	**≥ 60 years**	**p-value^**	**20-44 years**	**45-59 years**	**≥ 60 years**
Duration of Sleep (hours)							
<5	0.99 (0.75, 1.32)	1.10 (0.83 ,1.46)	0.65 (0.40, 1.08)		19.9 (15.7, 24.1)	48.1 (42.1, 54.1)	54.0 (43.4, 64.7)
5-5.9	1.46 (1.03, 2.09)	0.66 (0.43, 1.03)	0.31 (0.12, 0.80)		26.3 (19.6, 33.0)	36.7 (27.3, 46.0)	36.8 (16.5, 57.2)
6-6.9	0.96 (0.81, 1.14)	1.03 (0.85, 1.24)	0.92 (0.61, 1.38)		19.4 (17.5, 21.3)	46.5 (43.1, 50.0)	61.8 (54.5, 69.1)
7-7.9		reference			20.0 (17.9, 22.2)	45.8 (43.1, 48.6)	63.6 (57.4, 69.8)
8-8.9	0.98 (0.81, 1.18)	1.01 (0.84, 1.21)	1.02 (0.69, 1.50)		19.7 (17.6, 21.8)	46.0 (42.7, 49.4)	64.0 (57.6, 70.5)
≥9	0.85 (0.67, 1.08)	1.11 (0.83, 1.48)	1.38 (0.83, 2.31)	0.0135	17.7 (14.7, 20.8)	48.3 (42.2, 54.4)	70.3 (62.0, 78.6)
Insomnia (nights/month)							
No		reference			19.3 (17.9, 20.7)	44.2 (42.3, 46.1)	61.3 (56.7, 65.8)
Rare	1.34 (0.94, 1.92)	1.59 (1.16, 2.18)	1.67 (0.92, 3.06)		23.9 (18.4, 29.5)	55.0 (47.8, 62.3)	72.0 (61.5, 82.5)
Occasional	1.20 (0.92, 1.56)	1.58 (1.19, 2.09)	2.37 (1.20, 4.71)		22.1 (17.9, 26.2)	54.9 (48.6, 61.2)	78.2 (67.5, 89.0)
Frequent	1.11 (0.80, 1.54)	2.05 (1.53, 2.74)	0.74 (0.38, 1.41)	0.0071	20.8 (15.7, 25.9)	60.8 (54.2, 67.5)	54.3 (40.8, 67.8)
Snoring frequency							
Non-snorer		reference			17.6 (16.2, 19.0)	44.6 (42.4, 46.8)	63.6 (59.5, 67.6)
Moderate snorer	1.44 (1.21, 1.71)	1.08 (0.90, 1.30)	0.76 (0.49, 1.18)		23.2 (20.2, 26.2)	46.5 (42.9, 50.1)	57.4 (47.7, 67.2)
Habitual snorer	1.87 (1.56, 2.24)	1.30 (1.09, 1.54)	1.16 (0.77, 1.74)	0.0021	28.0 (24.9, 31.0)	50.7 (46.8, 54.6)	66.7 (58.7, 74.6)
Daytime sleepiness							
Unlikely		reference			19.7 (18.3, 21.0)	46.3 (44.5, 48.1)	63.1(59.4, 66.8)
Average	0.84 (0.54, 1.31)	1.05 (0.77, 1.43)	0.85 (0.43, 1.68)		17.3 (11.2, 23.3)	47.4 (40.4, 54.4)	59.5 (44.5, 74.4)
Excessive	1.04 (0.64, 1.70)	0.86 (0.56, 1.30)	1.02 (0.39, 2.66)	0.865	20.3 (13.3, 27.4)	42.7 (33.0, 52.5)	63.6 (42.0, 85.1)

Notes: * Raw numbers, N= 16,244 as 43 observations who reported "don't know" for snoring were dropped from the analysis; $ all models adjusted for age, sex, city, wealth index, education, body mass index and other sleep variables; ^ Wald test for effect modification of age group; # covariates used- age, gender, city, education, wealth index, body mass index and other sleep variables

Table-4: Logistic regression models$ of association between sleep variables and hypertension stratified by gender (N=16244*)

Sleep Characteristics	Adjusted odds ratios (95% CI)			Predicted probabilities of hypertension % (95% CI) #	
	Men	Women	p-value^	Men	Women
Duration of Sleep (hours)					
<5	0.94 (0.71, 1.24)	1.06 (0.83, 1.34)		32.6 (27.6, 37.6)	27.6 (23.8, 31.4)
5-5.9	0.97 (0.61, 1.55)	1.03 (0.70, 1.51)		33.2 (23.8, 42.6)	27.2 (21.1, 33.2)
6-6.9	0.98 (0.84, 1.15)	0.97 (0.80, 1.16)		33.4 (31.1, 35.7)	26.1 (23.8, 28.4)
7-7.9	reference			33.7 (31.0, 36.5)	26.7 (24.6, 28.7)
8-8.9	0.99 (0.83, 1.16)	1.04 (0.84, 1.29)		33.5 (30.9, 36.0)	27.4 (24.8, 30.0)
≥9	0.95 (0.74, 1.22)	1.09 (0.86, 1.37)	0.9277	32.7 (28.5, 36.9)	28.0 (24.4, 31.7)
Insomnia (nights/month)					
No	reference			33.1 (31.3, 35.0)	25.7 (24.4, 27.0)
Rare	1.19 (0.84 ,1.67)	1.52 (1.13, 2.04)		36.3 (30.1, 42.6)	32.9 (27.8, 38.1)
Occasional	1.23 (0.89, 1.70)	1.50 (1.20, 1.87)		37.1 (31.0, 43.2)	32.7 (28.8, 36.7)
Frequent	1.17 (0.82, 1.67)	1.44 (1.11, 1.86)	0.4649	36.0 (29.0, 43.1)	32.0 (27.2, 36.7)
Snoring frequency					
Non-snorer	reference			31.9 (30.0, 33.8)	25.4 (23.9, 26.8)
Moderate snorer	1.07 (0.91, 1.25)	1.33 (1.10, 1.61)		33.1 (29.9, 36.3)	30.3 (27.3, 33.2)
Habitual snorer	1.43 (1.19, 1.71)	1.50 (1.27, 1.78)	0.2090	38.8 (35.4, 42.1)	32.4 (29.4, 35.4)
Daytime sleepiness					
Unlikely	reference			33.5 (31.8, 35.3)	27.0 (25.7, 28.3)
Average	0.97 (0.67,1.39)	0.86 (0.61, 1.21)		32.9 (25.9, 40.0)	24.6 (19.5, 29.7)
Excessive	0.68 (0.42,1.10)	1.22 (0.83, 1.81)	0.1500	26.8 (18.9, 34.8)	30.5 (23.7, 37.2)

Notes: Estimates are in in odds ratio (95% confidence interval); $ all models adjusted for age, sex, city, wealth index, education, body mass index and other sleep variables; * Raw numbers, N= 16,244 as 43 observations who reported “don't know” for snoring were dropped from the analysis; ^ Wald test for effect modification of gender; # covariates used-age, gender, city, education, wealth index, body mass index and other sleep variables

Table 5: Linear regression models of association between sleep variables with systolic and diastolic blood pressures (N=16244*)

Sleep Characteristics	Systolic blood pressure (mm Hg (95%CI))		Diastolic blood pressure (mm Hg (95%CI))	
	Model 1$	Model 2@	Model 1$	Model 2@
Duration of Sleep (hours)				
<5	0.84 (-0.76, 2.44)	-0.30 (-1.77, 0.16)	-0.46 (-1.45, 0.54)	-0.52 (-1.45, 0.42)
5-5.9	-0.94 (-3.30, 1.43)	-0.68 (-2.72, 1.36)	0.07 (-1.39, 1.52)	0.14 (-1.24, 1.53)
6-6.9	0.94 (-0.02, 1.90)	-0.01 (-0.89, 0.87)	0.22 (-0.39, 0.83)	-0.09 (-0.66, 0.49)
7-7.9	reference			
8-8.9	-0.40 (-1.39, 0.59)	0.51 (-0.32, 1.34)	-0.55 (-1.18, 0.09)	0.00 (-0.57, 0.57)
≥9	-2.15 (-3.43, -0.86)	0.69 (-0.33, 1.71)	-1.65 (-2.42, -0.88)	-0.13 (-0.81, 0.54)
Insomnia (nights/month)				
No	reference			
Rare	-0.77 (-2.50, 0.95)	-0.50 (-2.15, 1.16)	-0.03 (-1.05, 0.99)	0.10 (-0.91, 1.12)
Occasional	-0.71 (-2.63, 1.21)	0.38 (-1.41, 2.16)	-0.45 (-1.58, 0.67)	0.35 (-0.76, 1.46)
Frequent	0.48 (-1.36, 2.31)	0.56 (-1.12, 2.25)	0.05 (-1.14, 1.24)	0.47 (-0.68, 1.62)
Snoring frequency				
Non-snorer	reference			
Moderate snorer	5.21 (4.21,6.21)	1.04 (0.08, 2.00)	3.78 (3.18, 4.38)	1.39 (0.78, 1.99)
Habitual snorer	7.90 (6.74,9.06)	2.34 (1.31, 3.36)	5.14 (4.49, 5.79)	1.97 (1.31, 2.62)
Daytime sleepiness				
Unlikely	reference			
Average	1.18 (-0.72, 3.08)	-0.49 (-2.27, 1.30)	1.00 (-0.23, 2.24)	-0.14 (-1.38, 1.10)
Excessive	2.16 (-0.26, 4.58)	-0.34 (-2.46, 1.78)	0.98 (-0.48, 2.44)	-0.31 (-1.70, 1.08)

Notes: Estimates are blood pressure in mm Hg; *Raw numbers, 16,244 as 43 observations who reported "don't know" for snoring were dropped from the analysis; SBP-Systolic Blood Pressure; DBP: Diastolic Blood Pressure; $Model 1: Adjusted for hypertension treatment; @Model 2: adjusted for hypertension treatment, age, sex, city, wealth index, education, body mass index and other sleep variables