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Original Research Article

Association of sleep disorders with non-lab-based CVD risk score among Indian population aged above 45 years: insight from Longitudinal Aging Study in India

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ABSTRACT

Background: Both sleep disorders and cardiovascular events have been found to increase with age. The current study aimed to find an association between the two.
Methods: The current analysis used data from Longitudinal Aging Study in India (LASI) (1st) conducted from April 2017 to December 2018 with sleep disorder as the output variable. Non-lab-based CVD risk score, defined by the WHO (2019) was explanatory variable. Possible confounders were also included in the secondary analysis.
Results: Sleep disorder was seen among 11.69%, higher in females, elderly >60 years, rural population, unemployed and those with limited physical activity and self-reported poor health. Increased CVD risk score was associated with higher odds of having sleep disorder [5-9: 1.19 (1.12-1.28), 10-19: 1.31 (1.22-1.40), 20-29: 1.24 (1.09-1.41)]. On stratified analysis, similar results were seen in males but showed higher odds in the highest risk score category in females.
Conclusions: Recognition and management of sleep disorders, especially those with cardiovascular comorbidities and risk factors is important.

Keywords: Elderly population, LASI, Non-lab CVD risk, Sleep disorders

INTRODUCTION

Sleep is an important component for health and wellness across the lifespan and is a critical health state and health-related behaviour. There is very limited literature guidance on sleep, possibly because of the complexity of sleep health as a multi-dimensional behaviour. However, with the fast pace of the modern life and an increasing workload, sleep duration and sleep patterns have been greatly altered. Sleep disorders have become a prevalent health problem, affecting an estimated 936 million adults aged 30-69 years. The highest number of affected individuals were seen in China, followed by the USA, Brazil, and India.[1,2]

The DSM-5 classification of sleep-wake disorders includes 10 disorders or disorder groups: insomnia disorder, hyper-somnolence disorder, narcolepsy, breathing-related sleep disorders, circadian rhythm sleep-wake disorders, non-rapid eye movement (NREM) sleep arousal disorders, nightmare disorder, rapid eye movement (REM) sleep behaviour disorder, restless legs syndrome, and substance/medication-induced sleep disorder.[3] These disorders involve problems with the quality, timing, and amount of sleep, which result in daytime distress and impairment in functioning.[4]

Cardiovascular disease (CVD) is among the leading causes of death and disability worldwide and in India. The age standardized CVD death rate in India is much higher than that of global average of 235. CVDs strike Indians a decade earlier than the western population.[5] Emerging research highlights the complex interrelationships between sleep-disordered breathing and cardiovascular disease.[6-8]

Most of the available literature propose sleep disorders as a predictor for cardiovascular disorders.[9] Insomnia, the most common of them, is associated with an increased risk for all cause and CVD mortality among older age population.[10] Even a shortened or a lengthened sleep duration is associated with an increased blood pressure leading to a higher risk of CVD. Metabolic dysfunctions and systemic inflammation seen with altered sleep duration may additionally work to increase the risk.[11]

A bidirectional relationship between CVD risks and sleep disorders has been postulated. While sleep disorders influence cardiovascular risk, the converse is also seen.[12-14] The dyspnoea induced due to circulatory congestion and the suppressed ventilatory drives due to the decreased arterial oxygen have been suggested or this. Simultaneously, risk factors for CVDs including obesity and diabetes also elevate the incidence of sleep disorders.[15-17] A longer sleep duration of sleep among males was also seen to be significantly associated with the intermediate to high risk as assessed by the Framingham risk score.[18,19]

Age plays a vital role in the deterioration of cardiovascular functionality, resulting in an increased risk of cardiovascular disease (CVD) in older adults.[20] Additionally, there are changes in circadian rhythm and sleep homeostatic mechanism which disturb sleep in elderly.[21] Thus sleep becomes more fragmented and lighter with an increase in the number of arousals and awakenings which result in reduced sleep efficiency and total sleep time.[22] So, with increasing age, disordered sleep may be a factor for an increased risk for CVD. The elderly population of India is currently one of the world's largest and is continuously growing.[23,24] As India undergoes demographic transition, it becomes increasingly important to focus on the comorbidities which plague its ageing population.

What we already know

Increasing age predisposes individuals to cardiovascular morbidities and sleep disorders. Evidence available on the causality of cardiovascular adverse events due to sleep disorders India's demographic transition is leading to a larger greying population and their chronic co-morbidities need to be detected early and managed.

What this article adds

Sleep disorder maybe indicative of underlying cardiovascular adverse event by using the cardiovascular risk score as a proxy. Recognition through screening and management of sleep disorders in any medical patient, especially those with cardiovascular comorbidities and risk factors is important. Reverse causality of sleep disorders due to cardiovascular morbidity maybe explored.

The LASI

The Longitudinal Aging Study in India (LASI) is an ongoing longitudinal survey with a purpose of collection of detailed information on the psychological, social, economic, and health aspects of ageing in India and generate a comprehensive and globally comparable survey data on ageing in India, conducted by The National Institute on Ageing, the Government of India's Ministry of Health and Family Welfare. The United Nations Population Fund all provided funding for the study. A large sample size of 66,606 Indian volunteers above the age of 45 were included in the current study.

The study followed a representative sample of the older adult population every two years for the following 25 years, with a revised sample size to account for attrition due to death, migration, non-reachable, and non-response.

The objective of the current study was to determine the association between sleep disorders and non-lab cardiovascular risk score in population aged more than 45 years based on the results from the LASI study.

METHODS

The current analysis used data from the 1st wave of LASI from 35 Indian states and union territories (UTs) (except for Sikkim). The study was conducted from April 2017 to December 2018.

Outcome variable

Sleep disorder was the explanatory variable of interest. It was derived from the Jenkins sleep scale, a four-item questionnaire which evaluates frequency of sleep problem during the previous month, which was used in LASI.[25] The Jenkins sleep scale is a 4 items instrument with a Likert scale of five response options [never (0), 1-3 days (1), 4-7 days (2), 8-14 days (3), 15-21 days (4), and 22-31

days (5)] to assess the frequency and intensity of sleep problems. Sleep disorder was classified as "yes" if the participant responded "frequently" to any of the item in the instrument.[26] Previous research has shown that JSS has high internal consistency, as evidenced by the Cronbach's alpha of 0.86. The scale provides good construct validity and excellent reliability.[27]

Explanatory variables

The input variable for this analysis was the non-lab based CVD risk score as defined by the WHO in the cardiovascular disease risk non-laboratory-based chart for South Asia, published in 2019.[28] It was calculated using the variables age, sex, smoking status, BMI category and systolic blood pressure category. Education, residence, MPCE (monthly per capita expenditure, health insurance, occupation, physical activity, self-rated health, alcohol consumption.

In this analysis, participants below 45 years were excluded. Because, LASI- first wave was conducted with the main focus on participants aged ≥45 years. While selecting the primary participants (≥45 years), their spouses were also selected from the same household. This led to a disproportionate distribution of participants aged <45 years in view of nationally representative data. After adjusting missing data by row wise deletion and excluding BMI outliers, we have included participants who documented their sleep disorder status. Details are provided in the supplement (Figure 1). Thus, this secondary study of LASI-first wave data included information from 59411 participants.

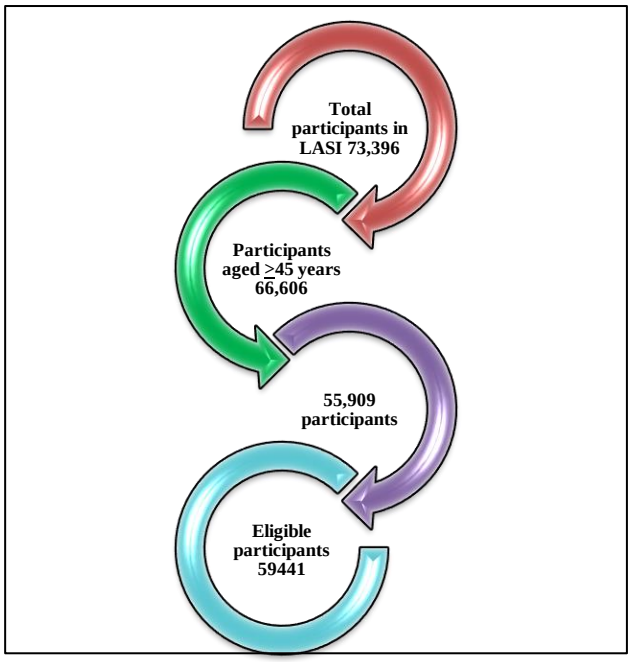

Figure 1: Study flow diagram- selection of the study participants.

Statistical analysis

Data was analysed in Stata version 17 (StataCorp. 2017. Stata Statistical Software: Release 17. College Station, TX: StataCorp LP.). Characteristics of participants were described as median (IQR) for non-parametric continuous variables frequencies and percentage for categorical variables [age-group, occupation, BMI (body mass index)] categories. Univariate logistic regression was conducted between outcome variable and each explanatory variable. To avoid multi-collinearity among explanatory variables VIF (variance inflation factor) was applied. VIF>5 indicates high correlation between a given explanatory variable and other explanatory variables in the model, which might create problems with the regression analysis. Marital status and self-rated health had VIF>5 and were excluded for final association. P value <0.05 were considered as statistically significant. P value <0.2 was taken for further multivariable logistic regression. Association was calculated in overall population and as per gender and age groups.

Ethics

Since this was a secondary analysis, ethical clearance was not required. Ethical approvals for the original study were obtained from the following collaborating organizations: Indian Council of Medical Research (ICMR), Delhi; IRB, International Institute for Population Sciences (IIPS), Mumbai; IRB, Harvard T.H. Chan School of Public Health (HSPH), Boston; IRB, University of Southern California (USC), Los Angeles; IRB, ICMR-National AIDS Research Institute (NARI), Pune; and IRB, Regional Geriatric Centres (RGCs), MoHFW. An anonymous dataset made available to the public has been used in the current study.

RESULTS

The participants had almost equal distribution among the age groups of 45-59 years and 60 years and above. A slightly higher proportion were females (53.7%). Almost half of the participants were illiterate and a majority of them (two-thirds) resided in the rural area. Most of the participants were currently married or had a history of ever being married. Most of the participants did not avail any form of health insurance and almost half of the participants were unemployed. Almost two-thirds of the participants never involved in any physical activity and about a fourth of the participants performed physical activity every day. Most of the participants self-reported their health to range between very good and fair and about 82% of the participants never indulged in alcohol abuse.

Majority (two-third) of the participants had a risk score of more than 5% and less than 20%. The median (IQR) CVD risk-score reflected the same and was 8 (2-34).

Table 1: Sociodemographic characteristics of eligible participants (n=59441).

Parameters	N	%
Age (years)		
45-59	31234	52.55
>60	28207	47.45
Sex		
Male	27541	46.33
Female	31900	53.67
Education		
Illiterate	28,046	47.18
Less than primary	6,938	11.67
Primary completed	7,922	13.33
Middle completed	5,691	9.57
Secondary school	5,223	8.79
Higher secondary	2,480	4.17
Diploma/graduate	3,141	5.28
Residence		
Rural	39133	65.84
Urban	20308	34.16
Marital status		
Unmarried	706	1.19
Married/in live-in	44879	75.5
Widow/separated/divorced	13856	23.31
MPCE quintile		
Poorest	11,783	19.82
Poorer	12,022	20.23
Middle	12,032	20.24
Richer	11,961	20.12
Richest	11,643	19.59
Health insurance		
No	58138	97.81
Yes	1303	2.19
Occupation		
Unemployed	30,178	50.77
Professional and semi-professional	1,342	53.03
Clerical and skilled	15,096	25.4
unskilled	12,825	21.58
Physical activity		
Everyday	14,366	24.17
More than once/week	4,201	7.07
Once/week	2,207	3.71
1-3 times/month	3,022	5.08
Never	35,645	59.97
Self-rated health		
Excellent	2,299	3.87
Very good	11,323	19.05
Good	23,442	39.45
Fair	16,552	27.85
Poor	5,813	9.78
Alcohol abuse		
No	48778	82.06
Yes	10663	17.94

Table 2: Univariate and multivariable logistic regression of sleep disorder and CVD risk score.

Characteristics	Univariate		Multivariable	
	Crude odds ratio (95% CI)	P value	Adjusted odds ratio (95% CI) Model 2	P value
Non lab based CVD risk score				
<5	Reference	-	Reference	-
5-9	1.22 (1.14-1.31)	<0.001	1.19 (1.12-1.28)	<0.001
10-19	1.43 (1.34-1.53)	<0.001	1.31 (1.22-1.40)	<0.001
20-29	1.40 (1.24-1.59)	<0.001	1.24 (1.09-1.41)	<0.001
≥30	0.80 (0.35-1.85)	0.610	0.70 (0.30-1.62)	0.408
Education (minimum)				
Illiterate	Reference	-	Reference	-
Less than primary	0.97 (0.90-1.05)	0.510	0.99 (0.92-1.08)	0.917
Primary completed	0.94 (0.87-1.02)	0.130	0.98 (0.91-1.06)	0.602
Middle completed	0.79 (0.72-0.87)	<0.001	0.84 (0.77-0.92)	<0.001
Secondary school	0.71 (0.64-0.78)	<0.001	0.74 (0.67-0.82)	<0.001
Higher secondary	0.65 (0.56-0.75)	<0.001	0.69 (0.59-0.80)	<0.001
Diploma/graduate	0.52 (0.45-0.60)	<0.001	0.56 (0.48-0.65)	<0.001
Residence				
Urban	Reference	-	Reference	-
Rural	1.21 (1.15-1.29)	<0.001	1.15 (1.08-1.22)	<0.001
MPCE quintile				
Poorest	Reference	-	Reference	-
Poorer	1.00 (0.92-1.08)	0.940	1.02 (0.94-1.10)	0.661
Middle	1.00 (0.92-1.08)	0.970	1.03 (0.95-1.12)	0.434
Richer	1.08 (0.99-1.17)	0.054	1.14 (1.05-1.24)	0.001
Richest	1.11 (1.02-1.20)	0.010	1.22 (1.12-1.32)	<0.001
Health insurance				
No	Reference	-	Reference	-
Yes	0.78 ()0.64-0.94	0.008	0.96 (0.79-1.17)	0.691
Occupation				
Unemployed	Reference	-	Reference	-
Professional and semi-professional	0.49 (0.40-0.60)	<0.001	0.70 (0.56-0.88)	0.002
Clerical and skilled	0.77 (0.72-0.82)	<0.001	0.83 (0.78-0.89)	<0.001
Unskilled	0.69 (0.65-0.74)	<0.001	0.75 (0.70-0.80)	<0.001
Physical activity				
Never	Reference	-	Reference	-
Everyday	1.03 (0.92-1.15)	0.652	1.01 (0.89-1.13)	0.907
More than once/week	1.17 (1.01-1.35)	0.033	1.13 (0.98-1.30)	0.095
Once/week	1.17 (1.03-1.32)	0.016	1.12 (0.99-1.27)	0.086
1-3 times/month	1.33 (1.25-1.41)	<0.001	1.19 (1.11-1.28)	<0.001
Alcohol consumption				
No	Reference	-	Reference	-
Yes	0.96 (0.90-1.02)	0.202	-	-

Adjusted (if individual univariate p value <0.20) for education, residence, mpce quintile, health insurance, occupation, physical activity. Classification accuracy= 88.31%. Pseudo R^2= 0.0112.

Out of 59441 participants studied, 6948 (11.69%) had a positive history of sleep disorder. Participants with a higher CVD risk score had a higher prevalence of sleep disorders but the prevalence was similar beyond the risk score of ten. There was a decrease in prevalence of sleep disorders beyond a risk score of 30. Compared to males, the females had a higher preponderance for sleep disorders (p<0.001). The population aged more than 60 years also had a higher prevalence of sleep disorders and the prevalence was consistently higher in females in both the age groups (p<0.001) The prevalence of sleep disorders was higher in population residing in rural areas, unemployed population, participants who provided no history of physical activity and who self-reported a poor health.

On performing logistic regression after adjusting for education, residence, MPCE quintile, health insurance, occupation, and physical activity the odds of a person having a sleep disorder progressively rises with increase in the CVD risk score followed by a fall after the risk score crosses 30. Better educational history was found to be protective against the chances of having a sleep disorder provided the participant had at least been educated till the middle school. The participants on the higher end of the wealth quintile distribution had progressively higher chances of having a sleep disorder.

To account for the sudden drop in odds of having a sleep disorder after the CVD risk score was above 30, a stratified analysis was performed with respect to age and sex. It was found that while in males the risk showed a similar pattern as seen in the overall population, for females the risk did progressively increase with the score. On stratifying for age, no clear trend was discernible.

Table 3: Univariate and multivariable logistic regression of sleep disorder and CVD risk score.

Characteristics		Univariate		Multivariable	
		Crude odds ratio (95% CI)	P value	Adjusted odds ratio (95% CI) Model-2	P value
Non lab based CVD risk score	**Overall (>45 years)[a]**				
	<5	Reference	-	Reference	-
	5-9	1.22 (1.14-1.31)	<0.001	1.19 (1.12-1.28)	<0.001
	10-19	1.43 (1.34-1.53)	<0.001	1.31 (1.22-1.40)	<0.001
	20-29	1.40 (1.24-1.59)	<0.001	1.24 (1.09-1.41)	<0.001
	>30	0.80 (0.35-1.85)	0.610	0.70 (0.30-1.62)	0.408
	As per gender[b]				
	Male				
	<5	Reference	-	Reference	-
	5-9	1.22 (1.08-1.39)	0.001	1.15 (1.01-1.30)	0.029
	10-19	1.54 (1.36-1.73)	<0.001	1.26 (1.11-1.42)	<0.001
	20-29	1.54 (1.36-1.73)	<0.001	1.16 (0.96-1.39)	0.122
	>30	1.76 (1.25-1.92)	0.481	0.50 (0.18-1.38)	0.182
	Female				
	<5	Reference	-	Reference	-
	5-9	1.30 (1.20-1.41)	<0.001	1.25 (1.15-1.35	<0.001
	10-19	1.52 (1.40-1.66)	<0.001	1.38 (1.27-1.51)	<0.001
	20-29	1.60 (1.30-1.97)	<0.001	1.41 (1.14-1.74)	0.001
	>30	3.48 (0.68-17.98)	0.136	3.03 (0.59-1.74)	0.186
	As per age group[c]				
	45-59 years				
	<5	Reference	-	Reference	-
	5-9	1.12 (1.04-1.41)	0.004	1.14 (1.06-1.23)	0.001
	10-19	1.02 (0.88-1.18)	0.784	1.07 (0.92-1.24)	0.374
	20-29	0.48 (0.12-1.99)	0.312	0.49 (0.12-2.05)	0.332
	>30	-	-	-	-
	>60 years				
	<5	Reference	-	Reference	-
	5-9	1.56 (0.47-5.10)	0.465	1.52 (0.46-5.00)	0.488
	10-19	1.64 (0.50-5.36)	0.415	1.59 (0.49-5.21)	0.444
	20-29	1.57 (0.48-5.16)	0.459	1.49 (0.45-4.91)	0.511
	>30	0.89 (0.21-3.77)	0.870	0.85 (0.20-3.62)	0.823

Adjusted (if individual univariate p value <0.20) for education, residence, MPCE quintile, health insurance, occupation, physical activity. Classification accuracy= a) 88.31%, b) 87.34%, c) 86.55%. Pseudo R^2= a) 0.0112, b) 0.0090, c) 0.0103.

DISCUSSION

The current study was performed to find an association between the cardiovascular risk factors and sleep disorders in population aged more than 45 years in the LASI population. The findings included a significantly higher prevalence of reported sleep disorders among participants with a higher CVD risk score, females, those in higher age group, participants residing in rural areas, the unemployed population, participants with no history

of physical activity and those who self-reported a poor health. Figure 2 showing graphical abstract of multivariable logistic regression between sleep disorder and CVD risk score.

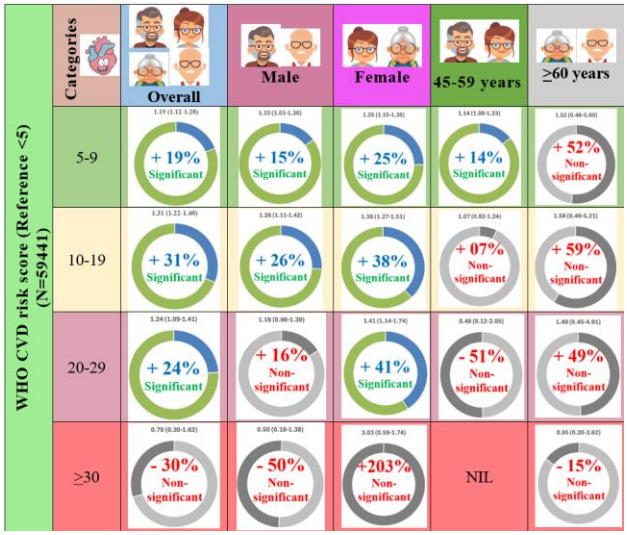

Figure 2: Graphical abstract showing multivariable logistic regression: (Adjusted odds ratio with 95% CI) between sleep disorder and CVD risk score.

It was found that 11.69% of the participants reported some form of sleep disorder. The available literature estimates the prevalence of sleep disorders between. Consistent with the current study, women had reported a poorer sleep quality than men according to the current available literature.[29] This has been attributed to influence of female gonadotropic hormones on sleep and the milestones related to these hormones, which in-turn is associated with physiological changes in other systems.[30]

The review by Guidozzi showed that sleep disturbances increase with increasing age in both males and females and become fairly common in the older community when compared to their younger counterparts. Even though these sleep disturbances increase with advancing age, there are nevertheless inherent differences in sleep disturbances between males and females. When compared to older men, older women have a longer sleep latency (number of minutes it takes to fall asleep), more daytime sleepiness, sleep about 20 minutes less per day, have less NREM stages 1 and 2 sleep, have more slow-wave sleep, and are more predisposed to REM sleep. Women have an increased risk for developing sleep disorders compared to men.[31] A cross-sectional study found association between sleep disturbances in patients and 10-year cardiovascular risk.

Sleep disorders have been found to be more common in older adults because the physiological aging process is associated with an increasing prevalence of multi-morbidity, polypharmacy, psychosocial factors affecting sleep, and certain primary sleep disorders. An increasing vulnerability of the regulatory system of the sleep-wake rhythm has also been postulated as a pathway.[32,33]

A previous study among elderly participants found that heart disease, marital status and being an income provider were strongly associated with the quality of sleep and sleep disorders.[34]

Findings from the sleep heart health study (SHHS) showed that some sleep disturbances may result from diabetes and associated cardiovascular risk factors through the deleterious effects of diabetes on central control of respiration.[35]

Some pathophysiological pathways have been proposed to explain the bidirectional relationship between CVD risks and sleep disorders. These include fluctuations of blood pressure in hypertensive individuals, which may induce obstructive respiratory events by a negative impact on the muscle tone of the upper airways.[36] Additionally, sleep fragmentation and intermittent hypoxia associated with OSAS may induce deleterious biological alterations. These alterations, such as hyperactivation of the sympathetic nervous system, deregulation of the renin-angiotensin system, endothelial dysfunction, activation of inflammatory mechanisms and metabolic dysregulation play a central role in the pathophysiology of hypertension.[37,38] Both sleep disorders and cardiovascular diseases share similar patho-mechanisms which include orexin, gut microbiome, and microparticles.

Studies have attempted to examine the bidirectional relationship between exercise or physical activity and sleep, especially in samples of older adults. Exercise promoted increased sleep efficiency and duration regardless of the mode and intensity of activity.[39]

The current study found that rural population had a poorer sleep quality than urban population. The available literature presents a variable picture regarding the place of sleep and the sleep quality. The reason for this may be the lifestyle difference among rural and urban populations. Easy availability of healthcare facility, level of awareness and more stress in urban life may be contributing factors. Tang et al found an increased prevalence rate of poor sleep quality among rural Chinese population, which may be due to higher demands for physical work, stress, poorer access to quality healthcare.[40]

There are certain limitations of the study. Firstly, the measure of sleep quality is subjective, retrospective and self-reported. Objective measures would offer more valid results, but the vast sample size would have made the process infeasible. The cross-sectional design does not allow us to infer causality in some associations. In addition to the high-risk factors studied CVD has many other high-risk factors, such as family history and diet habits which may also influence sleeping disorders. These factors were not studied in the LASI.

The large sample size and a structured method of collection for the data is one of the first in the older Indian population. The high rate of participation, the use of well-established instruments to examine sleep problems, and the questionnaire-based door-to-door physical interview are some of the other strengths of the study. A multistage, stratified sampling method was used to select a representative sample of the general population. That may help with the generalizability of this study.

CONCLUSION

Recognition and management of sleep disorders in any medical patient, especially those with cardiovascular comorbidities and risk factors is important. Similarly, screening for undetected medical conditions in patients presenting with sleep disorders might prove to be beneficial. Knowledge of the risk factors for the sleep disorders, especially the modifiable ones can form a principle of treatment by finding cause of the sleep disturbance and vigorously treat the co-morbid conditions causing the sleep disturbance.

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