

Sleep Status and its Relationship with Other Coronary Artery Diseases Risk Factors: Findings of a Community-based Study in South East of Iran

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Abstract

Introduction: Coronary artery diseases (CADs) are one of the main causes of mortality and morbidity in Iran. Due to the shortage of information regarding sleep status in the area and also the close relation between CADs and sleep health, this study attempted to examine sleep status in a large urban area of southeast Iran in order to find its relation with CADs risk factors such as anxiety and depression, hypertension, blood glucose level, smoking, low physical activity, and obesity.

Method: A Single-stage cluster sampling cross-sectional study was carried out on 5900 people aged 15 to75 in Kerman city to examine the CAD risk factors (KERCADR study). Alongside, sleep screening and a physical activity (PA) questionnaire regarding their sleep quantity and PA level were also used. Beck Anxiety and Beck Depression Inventories (for anxiety and depression assessment), medical examination and fasting blood sample were taken to collect the participants' demographic and blood glucose data.

Findings: From 3238 (54.9%) women and 2662 (45.1%) men who participated in this study 30.5% suffered from abnormal sleep (11.5% from insomnia and 19% from hypersomnia). 39.3% of the men and 45.1% of the women had low physical activity. There was a significant relationship between smoking (p=0.02), anxiety and depression (p<0.001), hypertension (p=0.03) and low PA (p=0.01) with sleep disorders.

Conclusion: the results showed that nearly one-third of the adult population suffered from abnormal sleep. Also, the prevalence of hypersomnia was 1.65 times more than that of insomnia. This issue along with the high prevalence of low physical activity exposed the population to different diseases.

Keywords: Insomnia; Hypersomnia; Anxiety; Depression; Physical activity; Obesity; High blood pressure; Kerman

Introduction

Sleep is one of the circadian cycles and is a basic human need which is necessary to maintain energy, happiness and physical well-being [1]. Sleep is a process which the brain requires in order to function properly. It is not merely a passive process; in fact, it is related to high brain activity [2]. According to DSM-5 there are different forms of sleep disorders such as insomnia-hypersomnia, narcolepsy, breathingrelated, circadian rhythm-related and somatic-related diseases or substance abuse related disorders.

Sleep disorders, in terms of pathology, are interconnected with other psychiatric disorders like depression-anxiety or other somatic diseases [3]. Hence, a smaller part of sleep disorders, which is primary as 25% of the patients who refer to sleep disorder clinics, suffer from a psychiatric disorder - half of whom have a mood disorder [4].

Sleep disorders are dangerous and costly as well. The direct cost per annum of sleep disorders in the United States is estimated at 16 billion dollars, with indirect costs ranging up to 100 billion dollars. Men over 30 years or older who slept less than 4 hours per night were 2.8 times more likely to die within 6 years than were those who slept 7 to 8 hours per night. Also, men who slept more than 10 hours per night had a higher death rate (1.8 times) than normal sleepers [5]. Studies show that there is a relation between obstructive sleep apnea and high blood pressure, heart failure, and heart attack (which are among the main causes of mortality and morbidity in developing countries such as Iran). Different factors can cause reduction in sleep. An anxietyarousing experience or expecting a stressful event such as the loss of a dear one, can be associated with insomnia [2]. Poor sleepers commonly complain from daytime fatigue, disturbed mood, faulty memory, trouble in thinking and concentration, restlessness and irritability, stress intolerance and lack of energy in performing innovative and complex tasks [4]. Some studies consider sleep deprivation as a risk factor for depression, anxiety and substance abuse in the future; also, frequent absences from work and increased direct and indirect medical costs are also some of its negative effects [6].

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Insomnia influences cognitive functioning, neuroendocrine, immune and inflammatory systems as well [7]. Recent studies show that sleep deprivation increases insulin resistance, compensatory hyperinsulinemia and the risk of diabetes among young adults with familial history of type 2 diabetes [8]. In a study doneby Gohansson et al. people with insomnia had increased variability in heart rate and blood pressure - which are risk factors for cardiovascular diseases. In addition, studies have shown that smokers suffer more from insomnia disorders [9]. Ohayon and Lemoine reported that the prevalence of insomnia was 20-40% in Western Europe and showed that it was more common among women and elderly people [10].

Another issue related to sleep disorder is hypersomnia. A longitudinal study carried out on 1200 men and women showed that people who slept more than 8.5 hours per night had 15% higher risk of death than those who slept 7 hours per night [6]. The lifetime prevalence of hypersomnia was found to be 8.2%. In a study done by Shirakawa and Takahashi, the rate of sleep disorder was reported to be 44% among the Japanese [11].

The studies devoted to sleep rate in Iran have been so far limited, and they are more frequently conducted to examine the sleep status in specific groups. In a study done in 2008 in Kashan-Iran, the prevalence of insomnia was reported to be 59% which had been more prevalent among women and middle-aged people [12]. In another study on students in Kurdistan University of Medical Sciences, the prevalence of insomnia was 57.4% [13]. This is why the sleep duration in the general population has been less investigated. Given the importance of sleep, its effects upon mental and general health, and its relation with cardiovascular diseases, the sleep status has not been investigated so far in southeast Iran according to the existing resources. As coronary artery diseases (CADs) are among main causes of mortality and morbidity in Iran and due to the shortage of information regarding the sleep status in the area, and also the close relation between CADs and sleep health, this study attempted to examine the prevalence of two main sleep disorders symptoms(insomnia and hypersomnia)in the general population of Kerman (the largest city in southeast Iran) and their relation with CADs risk factors such as anxiety and depression, hypertension, blood glucose level, smoking, low physical activity, and obesity. Also, in low and middle income countries, the sleep duration is affected by occupation as some people are obliged to have more than one job to manage their living expenses and the rate of unemployment is also high, the relation between sleep disorders and occupation was also investigated.

Methods

The present paper is a sub-analysis of data collected in a study which focused on the risk factors of coronary artery diseases (i.e. Kerman Coronary Artery Disease Risk Factor Study; KERCADRS). Four of these risk factors were the sleep status, the physical activity level, smoking, and obesity. The study was carried out on 5900 individuals ranging from 15 to 75 years old in 2010-2011on an urban population in South East of Iran. The study protocol was approved by the ethical committee of Kerman University of Medical Sciences, Iran (Permission No. 88/110KA). The unit of sampling was households who have been living in Kerman for at least one year prior to the interview. Using the zip code in the mail office as the sampling frame, we marked 250 post codes and approached the households in the area to recruit around 6000 individuals in the twelve strata of age and sex. The recruited people were invited to complete the informed consent and participate in the research. They were investigated in a clinical study site located in Kerman downtown where they went through several steps of in-person interview to disclose their demographic characteristics, occupation and CAD risk behaviors. They were also asked to report some possible factors influencing sleep such as their mental status (anxiety and depression), physical activity and smoking. A fasting blood sample was taken from each participant at the time of their attendance. The blood samples were then centrifuged and after 20 minutes of clotting time to separate the serum components, the glucose level was measured in a clinical laboratory by commerciallab kits. Details of this procedure are provided in another publication [14].

The blood pressure (BP) was measured by the physician using Rishter mercury BP manometer (RishterCo, Germany) after at least five minutes of rest, while the participant was required to hold his/her right arm in a sitting position. Also, participants with self-reported history of hypertension or anti-hypertensive drug used by participant were considered as hypertensive. More details are provided in another paper [15].

A sleep screening questionnaire was used by the interviewer to quantify the participants' sleep duration. Insomnia is defined to be the difficulty that one undergoes when initiating sleep or maintaining sleep, or having non-restorative sleep. Hypersomnia defined to be the excessive quantity of sleep, the deteriorated quality of wakefulness and sleep inertia [3]. Based on the American sleep association (A.S.A) an average of 7-8 hours of sleep is the best length of time for an adult [3]. In this study, cases with one hour less and one hour more than the normal range were placed in the following two groups respectively: insomnia and hypersomnia.

Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI) [16], were translated and adapted for use in Iran. questionnaires were completed by trained interviewers. Beck Anxiety Inventory (BAI) is designed to quantify the anxiety level and contains 21 phrases (each phrase describes one of the symptoms of anxiety with severity ranged from 0 to 3). The total score of the inventory is 63. For depression, the Beck Depression Inventory (BDI) includes 21 groups of statements and each statement has 4 responses with severity ranged from 0 to 3. The total score of the inventory is 63. In the present study, based on the score of the inventories, the anxiety and depression level of the participants were divided into 3 levels: mild, moderate and severe. The score range for the different levels of anxiety was as follows: scores 0-7, normal; 8-15, mild anxiety; 16-25, moderate anxiety; and 26-63, severe anxiety.

The score range for the different levels of depression was as follows:

Scores 0-15, without symptom; 16-30, mild depression; 31-46, moderate depression and 47-63, severe depression.

Daily physical activities at home and workplace were recorded using WHO Global Physical Activity Questionnaire (GPAQ). To evaluate the intensity of the physical activities, metabolic equivalent (MET) was used. MET is the amount of energy an individual adult uses while s/he is sitting. Moderate physical activities are believed to consume four times the energy used while sitting, and intense physical activities consume eight times more. Low physical activities are believed to consume energy less than four times in proportion to the amount used while sitting.

About smoking, by use of an interview-assist questionnaire, we asked about the number of cigarettes that the participants smoked per day and those who smoked at least one cigarette per day were considered as cigarette smokers.

Body mass index (BMI) was calculated by dividing the participants' weight in kg to their height in meters squared (kg/m2) and based on the WHO definition, BMI was classified into three categories of normal [BMI 18.5-24.9 kg/m2], overweight [BMI 25-29.9 kg/m2], and obese [BMI \geq 30 kg/m2].

The study Methodology has been explained more precisely in a previous publication [17].

Statistical analysis

The prevalence of Insomnia and hypersomnia were compared between the subjects with and without disorders using Chi square test. The prevalences were standardized according to Kerman's population distribution in 2006. We fitted univariate and multivariate (adjusted for age, gender, job and level of physical activity) Poisson regression models to show the crude and adjusted associations between the sleep disorders and other cardiovascular risk factors. Risk ratio (RR) is defined as the proportion of the existance of one risk factor in a case group to the existance of the same risk factor in the control group (crude RR). Adjusted RR is RR when the effect of the related confounding factors (such as the effect of aging on hypertension and diabetes) on the relationship/association was omitted by statistical methods (multivariate analysis). All the analyses were performed under survey data analysis considering the households as primary sampling units. Data analysis was conducted using STATA v.P value less than 0.05 was considered statistically significant.

Results

Out of 5900 participants in this study, 3238 (54.9%) and 2662 (45.1%) were men and women, respectively. Low physical activities were observed in 32.9% of the males (95% CI=37.9-40.6) and 45.1% of the females (95% CI=43.8-46.4). On the whole, 1800 (30.5%) had abnormal sleep. Accordingly, the prevalence of insomnia and hypersomnia were 11.5% and 19%, respectively; and their prevalence was more in the females than in males (p<0.001). In terms of occupation, the least prevalence of insomnia was related to employees (prevalence: 13.8%; 95% CI=8.3-21.9%) and the highest prevalence of hypersomnia was observed among the unemployed, retired individuals (prevalence: 43.2%; 95%Cl, 36.8-50.4%) and housewives. A significant relationship was found between smoking and sleep disorder (p<0.02), and the prevalence of hypersomnia was significantly higher in smokers (45.2%; 95%Cl: 38.3-52.4%) than in non-smokers (35.4%; 95%Cl: 33.5%-37.4%). In terms of physical activity, the prevalence of hypersomnia was significantly higher in those individuals who had low physical activity (37.9%) (95% CI: 34.9-40.9%) than in those with high physical activity (29.6%) (95% CI: 27.2-32.0%) (P=0.01). The prevalence of insomnia in anxious and depressed participants and the prevalence of hypersomnia in the participants having high blood pressure were significantly higher than in the people in good health (Table 1). The prevalence of insomnia and hypersomnia in the obese participants (BMI>30) was not significantly different from the others (p=0.09).

Disorders		Prevalence (95%Cl) of insomnia (<6 hours)	Prevalence (95%Cl) of hypersomnia (>9hours)	P-Value	
Depression	Yes(BDI>15) (N=2283)	18%(15.8-20.4)	34.7%(31.4-38.3)	<0.0001	
	no (N=3571)	7.7%(6.8-8.8)	37.1%(34.9-39.3)		
Anxiety	Yes(BAI>7) (N=4499)	12.8%(11.7-14)	35.6%(33.4-37.7)	0.0006	
	no (N=1352)	6.7%(5.2-8.4)	38.5%(34.5-42.6)	-	
Hypertension	Yes(BP>140/80 or taking drug) (N=1321)	14.4%(9.4-21.6)	45.4%(37.4-53.7)	<0.0001	
	no (N=4531)	11.4%(10.4-12.5)	35.7%(33.8-37.6)	-	
Obesity	Yes(BMI>30) (N=1043)	9.8%(7.6-12.4)	41.9%(35-49.2)	0.09	
	no (N=4731)	11.6%(10.6-12.7)	35.3%(33.4-37.3)		

Table 1: The prevalence of different sleep disorders in relation to depression, anxiety, hypertension and obesity.

Sleep time	Disorders							
	Depression(BDI>15)		Anxiety(BAI>7)		Hypertension		Obesity (BMI>30)	
	Crude RR	Adjusted RR	Crude RR	Adjusted RR	Crude RR	Adjusted RR	Crude RR	Adjusted RR
	(p-value)	(p-value)	(p-value)	(p-value)	(p-value)	(p-value)	(p-value)	(p-value)
6-9hours (ref)	1	1	1	1	1	1	1	1

<6 hours	1.77 (<0.0001)	1.59 (<0.0001)	1.16 (<0.0001)	1.14 (<0.0001)	1.39 (<0.0001)	1.10 (0.1)	1.23(0.01)	1.05(0.5)
>9hours	1.06 (0.2)	0.99 (0.9)	1.01 (0.6)	0.99 (0.8)	1.01 (0.9)	1.14 (0.03)	1.13(0.1)	1.15(0.06)

Table 2: Crude and adjusted risk ratios (p-value) among sleeping time and other disorders BDI: Beck Depression Index; BAI: Beck Anxiety Index; Hypertension: (BP>140/80 or taking drug).

In a multivariate analysis carried out on people having insomnia, the risk of anxiety and depression increased up to 14% and 59% after adjusting the variables of age, gender, occupation and physical activity level (p<0.0001)(Table 2).

Also, the risk of hypersomnia was higher (12% more) in people with low physical activity (p=0.01) (Table 3). On the other hand, hypersomnia raised the risk of high blood pressure (above 140/80 mm Hg) up to 14% which was statistically significant (p<0.03). In addition, the risk ratio between obesity and insomnia and hypersomnia were 1.05(p=0.5) and 1.15 (p=0.06), respectively (Table 2).

In comparison with those having normal sleep, the mean of fasting blood glucose (FBG) in people having insomnia was 2.2 mg/dl more, and among people having hypersomnia it was 0.8 mg/dl lesser. However, none of these differences were significantly different (P=0.3 and P=0.5, respectively).

Sleep time	crude RR	p- value	Adjusted RR*	p-value
<6 hours	1.1	0.09	1.03	0.6
>9 hours	1.13	0.006	1.12	0.01

Table 3: Crude and adjusted associations between sleep disorder and low physical activity (*controlling demographic and clinical characteristics).

Discussion

The findings of this study showed that nearly one-third of the 5900 participants in this study had sleep disorders whose rate was higher among the females. The results corresponded to the results of Shirakawa and Takahashi's study which indicated that the prevalence of sleep disorders was 44% in Japan [11], and it was also in line with another study done in Kashan, Iran in 2008 with the prevalence of insomnia being 59% in which the highest rate was related to the women [12]. Ohayon et al. carried out a research on French individuals who were between 14-96 years of age. It was observed that the prevalence of sleep disorders was higher in the females than in the males. The overall prevalence of sleep disorders in the population was 36.2% [10]. A variety of factors influence females' sleep including stress, illness, changes in the level of female hormones, sleeping environment, and being overweight [18]. In another study conducted in Tabriz on people having mental disorders and on general population [19], it was concluded that the prevalence of sleep disorders was 35.2% in the general population which is a little higher than that of Kerman.

In this study, the prevalence of hypersomnia in smokers increased significantly which corresponded with the study done by Zarowski [20] and Wetter [21], in which smokers suffered from sleep disorders more than non-smokers. The risk of anxiety and depression increased significantly after the variables of age, gender, occupation and physical activity level were adjusted in the multivariate analysis. This confirmed the studies in which insomnia was recognized as a risk factor for depression and anxiety [5]. In their study, Saleh et al. found that there was a relationship between reduced sleep quality and abnormal anxiety [22]. Also, a significant and direct relation was found between the scores of sleep disorders and those of depression intensity in the participants. There were also serious disorders in all aspects of sleep quality and quantity in the patients suffering from depression [3]. It is important to note that it was not possible to determine whether insomnia caused anxiety and depression or it was the consequence of anxiety and depression since having sleep disorders can be the main symptom of depression [3]. In other words, it is possible that this problem occurs as a result of reverse causality, and this requires an independent research.

In this study, hypersomnia increased the risk of high blood pressure after the confounding factors were adjusted. In a study done by Gohansson et al. [9] in Finland the increased variability of heart beat and blood pressure among the patients having insomnia had been recognized as a risk factor for cardiovascular diseases. Both hypersomnia and insomnia may increase the blood pressure, however, with different mechanisms. Of course, lifestyle especially one's diet, level of physical activity and daily stresses are important factors influencing the blood pressure, and these factors vary in different countries. The overall 19% hypersonnia along with 18.4% prevalence of hypertension (HTN)and 35.5% prevalence of pre-HTN in the study population[15] while considering the fact that hypersomnia had a significant association with hypertension (Table 2) would render this population at a high risk of suffering from cardiovascular diseases in the future. Especially, when we found that smoking, anxiety, and obesity were the most significant predictors for HTN [15].

Although, insomnia and hypersomnia increased the risk of obesity more than 5% and 15% respectively, none of these associations were statistically significant. However, the P value of 0.06 regarding the association of hypersomnia with obesity (Table 2) is close to the significant level. The global prevalence of 9% diabetes and 18.7% prediabetes that we observed in our study population [14] in conjunction with 42.1% prevalence of low physical activity (unpublished observation), and significant association of hypersomnia with LPA (Table 2) are also important cautions for general health in the studied population. Compared with normal sleepers, fasting blood glucose was higher in insomnia sufferers and lower in hypersomnia sufferers (although not statistically significant). According to a previous study, sleep deprivation increases insulin resistance, compensatory hyperinsulinemia and also the risk of diabetes among young adults with familial risks for type 2 diabetes [23], or makes a significant relationship between one's overall sleep status and the disturbances in one's glucose metabolism and increased circulating insulin levels [23]. Also, a review of different studies shows a bidirectional relation between sleep status and diabetes, and it notes that the reduced sleep duration paves the way for diabetes type 2among females [24]. This relationship can be justified by referring to the fact that sleep

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reinforces neuro-hormonal receptors that control blood glucose [3]. Thus, pathophysiologic changes related to sleep disorders seem to lead to the development of type 2 diabetes. Keeping the results of the above mentioned studies at mind, the difference in the relation between insomnia and the risk of diabetes in the present study may be due to the higher susceptibility of the individuals with familial risk of having diabetes to fall sick when exposed to stress.

Regarding the significant association between insomnia and anxiety/depression (Table 2), it may note that it is required to have normal mental function in order for one to have normal sleep. And it is acceptable that individuals who are anxious or depressed may have shorter sleep durations. Due to the effect of stress hormones on other body functions, such as the effect of cortisol and sympathetic hormones on glucose metabolism, anxiety and depression, this may cause insomnia on one hand and lead to diabetes on the other hand. In this regard, we found that the maximum prevalence of co-morbidities among the patients with diabetes were anxiety (87.5%), depression (57.9%) and overweight/obesity (47.1%) [14].

One of the limitations of the present study is that it was crosssectional. It also used simultaneous data collection concerning risk factors and their outcomes, which prevents an exact examination of the temporal transposition between them. In other words, we cannot be sure whether the higher prevalence of CAD risk factors leads to sleep disorders, or sleep disorders account for the increase of the prevalence of CAD risk factors. In order to find an answer to this, it is required to conduct a prospective longitudinal study on this issue. We have now commenced the second phase of KERCADR study as a longitudinal cohort to answer such important questions.

Conclusion

Given the high prevalence of abnormal sleep among nearly onethird of the population in this study and its relation with smoking, anxiety, depression, low physical activity and high blood pressure, (which are among the main risk factors of coronary artery diseases) and also by considering the fact that these diseases are currently the main causes of mortality and morbidity in Iran, it is suggested that necessary measurements should be considered to improve sleep health in the population. The prevalence of hypersomnia was concluded here to be 65% higher than the prevalence of insomnia. This along with high prevalence of low physical activity and body weight would render individuals exposed to various metabolic and cardiovascular diseases in the future.

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Conflict of Interest

The authors declare that there is no conflict of interest in this study.

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