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# Habitual sleep patterns and the risk of acute myocardial infarction: a case-control study in Andhra Pradesh, India

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***Abstract***
***Background****:Sleep is a daily process of physiological restitution and recovery. Reported literatures have shown that sleep deprivation has adverse effects on several cardiovascular disease (CVD) risk factors like blood pressure, glucose tolerance and sympathetic tone. Hence, this study was conducted in a tertiary care centre in Visakhapatnam to identify possible association between sleep patterns and acute myocardial infarction (AMI).*
***Materials and Methods****: A retrospective case-control study was conducted in Department of Cardiology, King George Hospital (K.G.H), Visakhapatnam, Andhra Pradesh. 100 first AMI cases and 100 controls matched to age, gender, presence of hypertension, diabetes mellitus, smoking and alcohol use were selected. Data on socioeconomic status, medical co-morbidities, smoking/alcohol/caffeinated drink use and sleep history was collected using a pre-tested questionnaire. Data was analysed using online statistical calculators on www.socscistatistics.com.*
***Results****: In this study, 62 cases had the habit of taking daytime naps compared to 27 controls (P<0.00001). Mean maximum nap duration among cases and controls was 54.6 ± 55.8 minutes versus 20.4 ± 42.6 minutes (P=0.0031). No significant difference was observed in sleep duration per night among cases and controls. Higher number of cases compared to controls, complained of feeling irritated and having headache on waking up (30 versus 16, P=0.019) and loss of sleep/disturbed sleep in the recent past (67 versus 28, P<0.00001).*
***Conclusion:****Significant association was found between increased day time nap duration, disturbed sleep, loss of sleep in recent past and occurrence of first AMI. Hence, sleep deprivation seems to be a potential risk factor for AMI.*

***Key words****:Acute myocardial infarction;Case-control study; India;Risk; Sleep.*

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## I. Introduction

In today's stressful lives, normal sleep patterns are adversely affected both in terms of quantity and quality. Fewer hours of sleep and increased sleep disturbances have become widespread - leading to increased complaints of fatigue, tiredness and excessive daytime sleepiness. It was reported that about 1/3rd of adult population sleep less than 6 hours per night, suggesting that we live in a "Sleep-deprived Society".[1] Factors responsible for this change may be due to (i) increased environmental light; (ii) longer workdays/commuting time; (iii) an increase in shift work and night work and (iv) the advent of television, radio, and the internet[2] – a consequence of Urbanization and Globalization.

Sleep is a daily process of physiological restitution and recovery of the body. Deprivation of sleep has adverse impact on the body's immunological, endocrine and metabolic activities.[3] Studies reported that an increased number of micro arousals per hour in a person is associated with an increase in blood lipid concentrations, cortisol levels and blood pressure.[4] Various studies have shown that short term sleep deprivation has adverse effects on body like decreased glucose tolerance and increased insulin resistance, sympathetic tone, and blood pressure[5,6,7]- all of which are known risk factors for cardio-vascular diseases (CVD).[8] Short term sleep deprivation results in elevated C- reactive protein, an inflammatory marker that is independently related to CVD.[9] Furthermore, another study showed that those with short sleep durations associated with sleep disturbances have greater risk of coronary heart disease (CHD) than those without sleep disturbances.[10] Hence, this shows that the habitual sleep patterns of present generation (both qualitative and quantitative) could be one of the contributing factors for CHD.

Previous studies evaluating this association were conducted in China, Japan and western countries but there is limited data available from the Indian sub-continent. Genetic and environmental differences prevent extrapolation of the results from these studies to Indian population. Hence, the present study was conducted at a

tertiary hospital setting in southern India with the aim to identify possible association between sleep patterns and acute myocardial infarction (AMI) by studying habitual sleep duration and disturbances.

## II. Material and Methods

This retrospective case-control study was conducted in King George Hospital (K.G.H), Visakhapatnam from May 2014 to July 2014. A total of 100 patients between the ages 20-80 years diagnosed with first AMI and 100 controls matched to age, gender, presence of hypertension, diabetes mellitus, smoking and alcohol use were selected for the study.

**Study design:** Retrospective case-control study
**Study setting:** This study was conducted in King George Hospital (K.G.H) which is an academic tertiary hospital centre in Visakhapatnam, Andhra Pradesh, India.
**Study duration:** May 2014 to July 2014
**Sample size:** 100 cases, 100 controls

**Study population:** 100 consecutive patients between the ages 20-80 years diagnosed with first AMI admitted to cardiology department of King George Hospital (K.G.H) were selected. 100 controls matched to age, gender, presence of hypertension, diabetes mellitus, smoking and alcohol use were selected for the study. Controls recruited were non-cardiac patients from other departments of K.G.H or healthy attendants of the patients admitted in the cardiology department without prior CVD.

**Inclusion criteria for cases:**Patients with first AMI diagnosed with chest pain suggestive of myocardial ischemia for >20min with electrocardiogram showing ST- segment elevation or ST- segment depression in two contiguous leads or elevation of cardiac enzyme (serum Creatine phosphokinase >171 U/l by optimised IFCC method, positive test result on qualitative Troponin T assessment by immunochromatography) or echocardiographic evidence of regional wall motion abnormality.

**Exclusion criteria for cases:**Patients on long-term sedatives or treatment for sleep disorders and those with prior history of CVD.

**Method of data collection:** A pre-tested questionnaire on sleep duration and quality was administered to all the cases and controls. The questionnaire recorded identification of the participants (name, age, gender), socioeconomic status (occupation, participation in night/rotating shifts), medical co-morbidities (hypertension, diabetes mellitus, other illness), smoking history, alcohol use, consumption of caffeinated drinks and sleep history. Histories of hypertension and diabetes mellitus were self-reported. When enquiring about caffeinated drink consumption, each participant was asked how many standard cups of caffeinated drinks (coffee, tea, cola) they consumed per day.

Sleep is a complex physiological process which can be influenced by several factors. This makes it highly difficult to study sleep patterns. For the sake of convenience, in the present study, sleep is assessed under three main categories. They are (i) Nap characteristics, (ii) Quantitative sleep characteristics and (iii) Qualitative sleep characteristics. The qualitative characteristics of sleep were determined under FIVE aspects. They are (i) Frequency of wake ups per night, (ii) Causes for waking up, (iii) Relative ease (subjective) of going back to sleep, (iv) participant's feeling on waking up from sleep in the morning and (v) any loss of sleep in the recent past (last one month).

Sleep history was elicited through the following questions. (i) The daytime sleep of participants was assessed by enquiring "whether they had the habit of taking naps". If yes, then the "minimum & maximum duration of naps per day" along with the "frequency of naps per week" was enquired. (ii) In order to assess the amount of sleep the participants get in one night, each participant was asked "at what time they would go to bed and at what time they would wake up along with the average minimum and maximum duration of sleep per night". (iii) In order to assess the qualitative sleep characteristics, each participant was asked "How many times do you wake up in the middle of night?" Further, only those participants who complained of waking up at night were asked for "the reasons for waking up" and also "how easily they go back to sleep after waking up in the middle of night". Additionally, each participant was asked "how they feel on waking up from sleep in the morning." Finally, each participant was asked "if they lost significant amount of sleep due to worries and had restless/ disturbed nights over the last one month."

**Ethical approval and Informed consent:** Informed consent was obtained from all participants prior to participation in the study. Approval from the Institutional Ethics Committee (IEC) was taken before beginning the study.

**Statistical analysis:** The results obtained from the questionnaire were compared using student T-test for means and Chi-square test for proportions. A 2-sided P-value < 0.05 was used to indicate statistical significance. The collected data was entered into an electronic spreadsheet in Microsoft Office Excel and the data was analysed with online statistical calculators on www.socscistatistics.com. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as percentages.

## III. Results

The general characteristics of participants are shown in Table no 1. The mean age of cases and controls was 56.72 ± 10.32 years and 56.1 ± 10.33 years respectively.

**Table no 1:** General characteristics of participants

| S.NO | CHARACTERISTICS | CASES (n=100) | CONTROLS (n=100) | P-value |
|---|---|---|---|---|
| 1 | Male sex | 63 | 63 | 1 |
| 2 | Mean Age (SD),years | 56.72 (10.32) | 56.1 (10.33) | 0.7 |
| 3 | Hypertension | 63 | 63 | 1 |
| 4 | Diabetes mellitus | 40 | 37 | 0.66 |
| 5 | Smoking habits | 45 | 45 | 1 |
| 6 | Alcohol habits | 32 | 29 | 0.64 |
| 7 | Rotating shifts/ Night shift jobs | 16 | 13 | 0.55 |
| 8 | Caffeinated products mean (SD), standard cups/day<br>• Minimum<br>• Maximum | <br>2.4 (1.69)<br>2.64 (2.16) | <br>2.38 (1.32)<br>2.65 (1.49) | <br>0.357<br>0.32 |

The nap characteristics of participants are presented in Table no 2. As shown in Table no 2, 62 cases had the habit of taking daytime naps as compared to 27 among controls (P<0.00001). Also, the mean maximum nap duration was found to be 54.6 ± 55.8 minutes in cases and 20.4 ± 42.6 minutes in controls (P=0.0031).

**Table no 2:** Nap characteristics of participants

| | CASES (n=100) | CONTROLS (n=100) | P- value |
|---|---|---|---|
| **Day time naps – Yes** | 62 | 27 | < **0.00001** |
| Mean minimum nap duration (SD), minutes | 48.6 (51.6) | 19.2 (41.4) | 0.088 |
| **Mean maximum nap duration (SD), minutes** | 54.6 (55.8) | 20.4 (42.6) | **0.0031** |
| Nap frequency (SD), per week | 4.1 (3.3) | 1.84 (3.1) | 0.1268 |

The quantitative sleep characteristics of participants are shown in Table no 3. As shown in Table no 3, though the minimum and maximum sleep duration per night was higher in controls compared to cases, these differences did not reach statistical significance.

**Table no 3:** Quantitative sleep characteristics of participants

| | CASES (n=100) | CONTROLS (n=100) | P-value |
|---|---|---|---|
| Mean sleep duration minimum per night (SD), hours | 7.26 (1.34) | 7.51 (1.36) | 0.848 |
| Mean sleep duration maximum per night (SD), hours | 7.81 (1.24) | 8.48 (1.42) | 0.9996 |

The qualitative sleep characteristics of participants are summarised in Table no 4. Based on the responses given by those participants who complained of waking up in the night (88 cases, 87 controls), the reasons for waking up were broadly classified into 3 categories- (i) Thoughts & other psychological disturbances, (ii) Urination/ Thirst/ Hunger, (iii) External Disturbances. When asked how the participant feel on waking up in the morning, based on the responses, 3 categories were made – (i) Tired/ Stressed, (ii) Irritating/ Headache and (iii) Relaxed/ Normal. As shown in Table no 4, there were no statistically significant differences between cases and controls in terms of frequency of wake ups per night. While the most common cause of waking up in both cases and controls was observed to be urination and thirst, it was found that wake ups due to thoughts and other psychological disturbances were numerically higher in cases compared to controls. Also, it was observed that higher number of cases complained of feeling irritated and having headache on waking up

when compared to controls (30 versus 16, P=0.019). Additionally, 67 cases and 28 controls complained of loss of sleep/disturbed sleep in the last one month (P<0.00001).

**Table no 4:** Qualitative sleep characteristics of participants

| **FREQUENCY OF WAKE UPS PER NIGHT** | | | |
|---|---|---|---|
| | **CASES (n=100)** | **CONTROLS (n=100)** | **P- value** |
| Mean minimum number of wake ups/ night(SD) | 1.84 (1.24) | 2.02 (1.65) | 0.702 |
| Mean maximum number of wake ups/ night (SD) | 2.18 (1.63) | 2.49 (2.14) | 0.803 |
| **CAUSES FOR WAKING UP** | | | |
| | **CASES (n=88)** | **CONTROLS (n=87)** | |
| Thoughts (%) | 17 (19.32) | 8 (9.195) | |
| Urination/ Thirst/ Hunger (%) | 80 (90.91) | 78 (89.66) | |
| External Disturbances (%) | 2 (2.27) | 9 (10.345) | |
| **EASE OF GOING BACK TO SLEEP** | | | |
| | **CASES (n=88)** | **CONTROLS (n=87)** | |
| Easy (%) | 66 (75) | 67 (77.01) | |
| Difficult (%) | 22 (25) | 20 (22.99) | |
| **PARTICIPANT'S FEELING ON WAKING UP FROM SLEEP IN THE MORNING** | | | |
| | **CASES (n=100)** | **CONTROLS (n=100)** | **P- value** |
| Tired/ Stressed (%) | 36 (36) | 35 (35) | 0.88 |
| **Irritating/ Headache (%)** | 30 (30) | 16 (16) | **0.019** |
| Relaxed (%) | 65 (65) | 69 (69) | 0.547 |
| **NUMBER OF PARTICIPANTS WHO LOST SLEEP IN THE LAST 1 MONTH** | | | |
| | **CASES (n=100)** | **CONTROLS (n=100)** | **P-value** |
| **Yes (%)** | 67 (67) | 28 (28) | < **0.00001** |

## IV. Discussion

In this study, we evaluated the association between habitual sleep patterns (quantitative and qualitative) and occurrence of first AMI. We observed that there was no statistically significant difference between cases and controls in terms of sleep duration per night. Hence, the null hypothesis of no association between sleep duration per night and the risk of AMI cannot be disproved with this study. However, several studies have shown that short sleeping hours is related to increased risk of AMI.[11, 12] The Fukuoka Heart study has shown that short sleep time (<= 5 hours per night) and frequent lack of sleep (2 or more days/week with <5 hours of sleep) were associated with a two to three fold increased risk of AMI.[13] This increase in risk of CVD in short sleepers was correlated with elevated C-reactive protein levels in their circulation – an inflammatory marker predictive of cardiovascular morbidity.[9] Some studies have shown that both longer and shorter sleeping hours are associated with increased risk of AMI suggesting a U-shaped association.[14, 15] In some other studies, only long sleeping hours was found to be associated with risk of AMI.[16, 17] It should be noted that although we did not find inter-group differences in sleep duration between cases and controls, average sleep duration was close to recommended 7-8 hours/day in both groups.

In the present study, we observed significantly higher number of cases had the habit of taking daytime naps as compared to controls. Also, a statistically significant difference in nap duration between cases and controls was observed. Based on these results, a significant association between increased day time nap duration and occurrence of first AMI was found to exist in this study. Our findings were consistent with several studies which have shown day time napping as an independent risk factor for cardiovascular deaths.[18, 19, 20] On the contrary, some studies showed negative association between day time nap and AMI.[21, 22] The morning time of the day has the highest risk for cardiovascular events due to a rapid rise in blood pressure caused by activation of the sympathetic nervous system.[23] Since blood pressure patterns during daytime napping are similar to nocturnal sleep,[24] a rapid rise in blood pressure after napping[25] could be associated with sympathetic nervous activation and AMI risk. The pro-thrombotic effects of an acute change in posture in the morning[26] could also occur after daytime napping and may play a role in triggering thrombotic cardiovascular events.

In our study, we observed that wake ups due to thoughts and other psychological disturbances were numerically higher in cases compared to controls. Also, it was observed that significantly higher number of cases complained of feeling irritated and having headache on waking up from sleep compared to controls. These findings suggest an association between disturbed sleep and occurrence of AMI. Similar to our findings, many studies have shown that sleep disturbances pose an independent risk in the causation of AMI.[10, 13] Further, some studies have shown that the risk of AMI is much higher in short sleepers who have concurrent sleep disturbances than those without sleep disturbances.[10, 27] The possible mechanism between disturbed sleep and risk of AMI may be explained as follows. Disturbed sleep leads to an inability to reduce sympathetic stimulation of cardiovascular system at night, thereby preventing adequate rest and restoration.[28] Disturbed sleep may also cause disturbances of immune function and promote inflammation in the blood vessels.[29] Disturbed sleep may also increase cholesterol concentrations, blood pressure and blood glucose concentrations,[30] all of which are risk factors for AMI.

Another important finding in our study is that a statistically significant association was found between those who have lost significant amount of sleep in the recent past (last one month) and occurrence of AMI. When enquired, the reasons for loss of sleep in the last one month were mostly work overload, loss of job/business failure, stress, exhaustion, family conflicts, divorce, death/major illness of spouse/close family member and several other psychosocial stressors. These findings are consistent with several studies which have shown strong association between recent loss of sleep due to various psychosocial stressors and the risk of AMI.[31, 32, 33] The Fukuoka Heart Study group has shown that lack of adequate rest in the very recent past may exert a trigger effect on the onset of AMI.[13] Lack of sleep increases activity in sympathetic nervous system, leading to an increase in blood pressure and heart rate.[34] Moreover, people with sleep deprivation were shown to be more likely to develop malignant hypertension than those without – which is again a risk factor for AMI.[35]

The strengths of our study are careful matching between cases and controls to avoid confounding from important cardiovascular risk factors like age, gender, smoking, hypertension and diabetes mellitus. The advantage of this case-control study was being resource, time and cost efficient.

Our study also has several important limitations. Firstly, the details of sleep obtained were subjective and based on the memory of the participant. This might lead to the possibility that accurate sleep patterns may not be reported by each participant. However, using the pre-tested questionnaire and thorough interviews, participants were asked to specifically report their habitual sleep duration and patterns. Also, there might be a problem of differential recall between cases and controls. However, when compared to the western world, the awareness of CVD prevention and health consciousness may not be as high in Indian population, making the likelihood of recall bias lower in the present study. Also, we excluded all those participants with any prior heart disease from the study. Secondly, this study was conducted in an urban tertiary-care hospital with participants drawn from coastal part of southern India. Hence, the study population may not be representative of the general Indian population as a whole. Thirdly, presence of hypertension and diabetes mellitus were determined based on patient reporting, thereby posing a risk of unmeasured confounding. Future larger studies within India should try to adequately address these biases. There is a wide scope for research in this area in order to evaluate the more exact associations between sleep and risk of AMI. Also, new study designs and methods need to be developed as the results of a study are highly dependent on the quality of study design.

## V. Conclusion

To conclude, in this study in Indian population, no association was found to exist between average sleep duration per night and occurrence of first AMI. However, increased day time nap duration was found to be associated with occurrence of AMI. In addition, significant association was found to exist between disturbed/ poor quality of sleep and risk of AMI. Also, it was found that loss of sleep in the recent past (last one month) was significantly associated with risk of AMI. So, sleep deprivation seems to be a potential risk factor for acute myocardial infarction. Hence, understanding underlying mechanisms linking sleep deprivation to AMI can help better understand the patho-physiologic mechanisms leading to the development of AMI.

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