Short Report

Prevalence of obstructive sleep apnoea among patients admitted with acute coronary syndrome in a hill state of northern India

SANYAM K. MAHAJAN, BALBIR S. VERMA, SUNIL SHARMA, KUNAL MAHAJAN, BALRAJ SINGH

ABSTRACT

Background. Obstructive sleep apnoea (OSA) is one of the emerging non-traditional cardiovascular risk factors. Studying OSA may contribute towards a better understanding of current concepts of atherogenesis and in guiding therapy.

Methods. We conducted this cross-sectional study among 66 patients with acute coronary syndrome (ACS) in a tertiary care hospital from 1 January 2019 to 30 June 2020. We included patients of ST elevation myocardial infarction (STEMI)/ non-STEMI (on achieving Killip class I/II) and unstable angina and performed in-hospital overnight polysomnography (PSG) within 8 weeks of index event. Apnoea–hypoapnoea index (AHI) value 5–<15 was defined as mild OSA, AHI 15–<30 as moderate OSA and AHI ≥30 as severe OSA. We analysed data using Epi Info version 7.2.4 for Windows.

Results. The 66 patients had a mean (SD) age of 57.7 (11.1) years and 54 (81.8%) were men. Forty-three (65.1%) patients had STEMI, 19 (28.7%) had non-STEMI and 4 (6%) had unstable angina. On PSG, the prevalence of OSA (AHI≥5) was 78.8% (95% CI 67.0–87.9). Of these, AHI ≥15 was significantly associated with diabetes, hypertension and different measures of obesity ($p \leq 0.05$).

Conclusions. This study, conducted in a hill state of northern India, showed a high prevalence of OSA in patients with ACS. Obesity, diabetes mellitus and hypertension were significantly associated with severity of OSA (AHI≥15).

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INTRODUCTION

Obstructive sleep apnoea (OSA) is characterized by episodic collapse of the upper airway during sleep, which results in periodic reduction or cessation in ventilation, with consequent hypoxia, hypercapnia or arousals from sleep.[1] The common symptoms include excessive daytime sleepiness, fatigue, non-refreshing sleep, nocturia, morning headache, irritability and memory loss. Overnight polysomnography (PSG) is the gold standard to make a diagnosis of OSA.[2]

The presence of hypertension, dyslipidaemia, diabetes mellitus, smoking, physical inactivity and obesity are the main modifiable cardiovascular (CV) risk factors and their targets are set in the national and international guidelines.[3]

OSA is one of the emerging non-traditional CV risk factors, and studying OSA may contribute towards a better understanding of current concepts of atherogenesis as an aetiology and in guiding therapy.[4,5]

OSA shares an interesting relationship with coronary artery disease (CAD). The underlying mechanisms are not entirely understood, the repetitive apnoeic/hypoapnoeic events along with ensuing arterial desaturation and hypercapnia cause activation of the sympathetic nervous system leading to development or exacerbation of hypertension. The intrathoracic pressure changes, oxidative stress and vascular inflammation resulting from the nocturnal hypoxia and reoxygenation cycles have been postulated to be the contributing factors.[6] The disorders of coagulation, endothelial damage and platelet activation in patients with OSA have also been implicated.[7] If not treated, this cascade of events can eventually lead to overt CV morbidity.[6]

Arzt *et al.* reported that the patients of acute MI with sleep disorder breathing (SDB) experience prolonged myocardial ischaemia, less salvaged myocardium and impaired left and right ventricular remodelling even after successful percutaneous coronary intervention when compared with those without SDB.[7]

Fan *et al.* found that among patients with OSA, death due to CV disease, myocardial infarction, stroke, revascularization after ischaemia or hospitalization for unstable angina or heart failure were significantly higher in those with acute coronary syndrome (ACS).[8]

OSA is a modifiable risk factor and treatment with continuous positive airway pressure (CPAP) may reduce the early signs of endothelial dysfunction and atherosclerosis and may improve CV outcomes.[2]

The topography of Himachal Pradesh is predominantly hilly with mountains ranging from 350 to 7000 m above mean sea level and 90% of the population resides in rural areas. People have to walk long distances to carry out routine activities. These characteristics make this population unique with potential implications on lifestyle diseases. Our study was conducted at a tertiary care centre situated at 2200 m above mean sea level, keeping in view the limited availability of data on association of OSA with ACS in the Indian literature and non-availability of data on prevalence of OSA in ACS in populations residing in hilly terrains of India.

METHODS

This cross-sectional study was done at a tertiary care hospital from 1 January 2019 to 30 June 2020.

Patients with ACS aged ≥18 years who gave consent to undergo PSG were included in this study. The exclusion criteria

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were: (i) cardiac arrest on admission or during hospitalization; (ii) severe insomnia, chronic sleep deprivation and abnormal circadian rhythm (sleep duration <4 hours/night); (iii) previous or current use of CPAP; (iv) pregnancy; (v) severe comorbid conditions, e.g. malignancy (life expectancy <2 years); (vi) psychiatric comorbid conditions such as bipolar disorder and schizophrenia; (vii) patients not willing to participate in the study; and (viii) patients on hypnotics/sedatives in the past 24 hours.

Patients who had ST elevation myocardial infarction (STEMI)/non-STEMI (on achieving Killip class I/II) and unstable angina were subjected to PSG within 8 weeks of the index ACS, after obtaining informed consent. On the day of PSG, a list of all eligible patients was prepared, and among the available patients, one was selected by a lottery method to undergo PSG. If the selected patient refused to undergo PSG, the lottery was drawn again until a patient willing to undergo PSG was found. The criteria for obesity as standard prescribed for waist–hip ratio, waist circumference and neck circumference were predefined.[9,10]

The study was approved by the Institutional Ethics Committee and informed consent was taken. The patients were provided with complete information about the study.

Polysomnography

All patients underwent overnight 16-channel PSG in the sleep laboratory using Alice LE-6 version machine (Philips Respironics). Recorded sleep data were scored manually according to American Academy of Sleep Medicine (AASM) version 2012 criteria with 3% oxygen desaturation. We followed diagnostic criteria for OSA in adults adapted from International Classification of Sleep Disorders, 3rd edition (ICSD-3).[11]

Apnoea and hypopnoea were defined according to the AASM criteria.[12] Apnoea–hypoapnoea index (AHI) <5 was defined as no OSA, AHI value 5–<15 was defined as mild OSA, AHI 15–<30 was defined as moderate OSA and AHI ≥30 was defined as severe OSA.

Statistical analysis

The data were entered in MS Excel sheet and Epi Info version 7.2.4 for Windows was used to calculate the prevalence (%) of OSA along with its 95% confidence interval (CI). We calculated the proportions of qualitative variables and constructed 95% CIs around the point estimates. For continuous variables, we calculated mean (SD). To compare means across groups, we used Student *t* test if variables were normally distributed or Mann–Whitney U test, if variables were not normally distributed. A value of $p \leq 0.05$ was considered statistically significant.

RESULTS

Of the 66 patients in the study group, 54 (81.8%) were men. The mean (SD) age of the patients was 57.7 (11.1) years. Patients were residing from 375 to 3750 m above mean sea level. Fifty-six (84.8%) patients resided at an altitude ≥1000 m above mean sea level, 45 (68.1%) ≥1500 m and 23 (34.8%) ≥2000 m above mean sea level.

Fifty-nine (89.3%) patients presented with chest pain and, of them, 30 (45.4%) presented within 6 hours of onset of symptoms. Forty-three (65.1%) patients had STEMI, 19 (28.7%) had non-STEMI and 4 (6%) patients had unstable angina. Thirty-six (54.4%) were managed with medical treatment and 30 (45.4%) underwent revascularization.

On PSG, 52 (78.8%) patients had evidence of OSA (AHI ≥5). Of these, 43 (82.6%) were men and 9 (17.3%) were women (Table I).

TABLE I. Prevalence of obstructive sleep apnoea (OSA) among the study participants (*n*=66)

Variable	*n* (%)	95% CI
No OSA (AHI <5)	14 (21.2)	12.1–33.0
Mild OSA (AHI 5–<15)	21 (31.8)	20.9–44.4
Moderate OSA (AHI 15–<30)	17 (25.8)	15.8–38.0
Severe OSA (AHI ≥30)	14 (21.2)	12.1–33.0
All grades of OSA	52 (78.8)	67.0–87.9

CI confidence interval AHI apnoea–hypoapnoea index

Thirty-five (81.4%) of 43 patients with STEMI, 14 (73.3%) of 19 patients with non-STEMI and 3 (75%) of 4 patients with unstable angina had OSA. Forty-six patients were in the age group of 51–70 years and 37 (80.4%) of them had OSA.

The highest prevalence of OSA was in the age group of 61–69 years, 21 (80.7%) of 26 patients in this age group had OSA and 14 (66%) of them had moderate-to-severe OSA.

On PSG, 35 (89.7%) of 39 patients with BMI >23 kg/m^2 whereas 17 (62.9%) of 27 patients with BMI <23 kg/m^2 and all 20 (100%) patients with neck circumference above cut-off limits, had OSA.

Of the 66 patients in our study group, modified Mallampati score was available in 61 patients and of them, 47 (77%) had OSA. Of these 47 patients, 30 (63.8%) had modified Mallampati score III or IV (p=0.043; risk ratio 2.2; 95% CI 0.9–5.3) and 26 (86.6%) of these 30 patients had OSA.

Sixty-four (96.9%) patients had increased waist–hip ratio, 51 (79.6%) of them had OSA and 41 (62.1%) of 66 patients had higher waist circumference than the cut-off value for obesity, 36 (87.8%) of these 41 obese patients had OSA.

The prevalence of hypertension, diabetes mellitus, smoking, recurrent CAD and their relationship with OSA in the study group is given in Table II. Regional wall motion abnormality (63.6%), left ventricular diastolic dysfunction (19.7%), left ventricular hypertrophy (19.7%) and left ventricular clot (6%) were noted on echocardiography.

The comparison of various parameters between patients of ACS with AHI <15 with those with AHI ≥15 is given in Table III.

DISCUSSION

In our study, the prevalence of OSA was significantly higher in patients with higher BMI, higher modified Mallampati score, increased neck circumference and increased waist–hip ratio and these parameters were significantly associated with severity of OSA. Namtvedt *et al.* reported a high prevalence of obesity in OSA; both are associated with endothelial dysfunction and precede the development of atherosclerosis. The presence of OSA is said to be associated with endothelial dysfunction independent of obesity and conventional risk factors.[13]

In our study, the presence of diabetes mellitus was significantly higher in patients with moderate-to-severe OSA. OSA can increase the risk of diabetes and glucose dysregulation, independent of obesity.[14]

We found hypertension was significantly higher in patients with moderate-to-severe OSA. Nieto *et al.* reported that the prevalence of hypertension increased significantly with increasing SDB irrespective of sex, age groups, ethnic groups and body weight.[15]

TABLE II. Distribution of medical disorders among study participants and relationship with obstructive sleep apnoea (OSA) (*n*=66)

Variables	*n* (%)	OSA, *n* (%)	Mild OSA, *n* (%)	Moderate OSA, *n* (%)	Severe OSA, *n* (%)
Current smokers	33 (50)	21 (63.6)	10 (47.6)	4 (19)	7 (33.3)
Hypertension	21 (31.8)	20 (95.2)	6 (30)	8 (40)	6 (30)
Current alcohol consumption	18 (27.2)	16 (88.8)	4 (25)	9 (56.2)	3 (18.7)
Diabetes mellitus	18 (27.2)	17 (94.4)	4 (23.5)	8 (47.1)	5 (29.4)
Recurrent coronary artery disease	10 (15.1)	9 (90.0)	3 (33.3)	4 (44.4)	2 (22.2)

TABLE III. Association between apnoea–hypoapnoea index (AHI) score and different variables of interest studied (*n*=66)

Item	Total (*n*=66)	AHI <15 (*n*=36)	AHI ≥15 (*n*=30)	p value*
General characteristics				
Mean (SD) age (years)	57.7 (11.1)	57.7 (10.8)	57.8 (11.8)	0.98
Men, *n* (%)	54 (81.8)	28 (77.8)	26 (86.7)	0.27
Mean (SD) body mass index (kg/m^2)	23.9 (4.4)	22.3 (3.7)	25.7 (4.6)	0.001
Waist–hip ratio	1.01 (0.08)	0.98 (0.07)	1.03 (0.08)	0.01
Mean (SD) neck circumference (cm)	35.5 (3.5)	34.2 (3.1)	37.2 (3.2)	<0.001
Mallampati score III–IV, *n* (%)	34 (51.5)	15 (41.7)	19 (63.3)	0.04
Cardiovascular risk factors, n (%)				
Diabetes mellitus	19 (28.8)	5 (13.9)	14 (46.7)	<0.01
Hypertension	21 (31.8)	7 (19.4)	14 (46.7)	0.01
Smoking (current or ex-smokers)	48 (72.7)	28 (77.8)	20 (66.7)	0.23
Acute coronary syndrome, n (%)				
STEMI	43 (65.1)	24 (66.7)	19 (63.3)	
NSTEMI	19 (28.8)	10 (27.8)	9 (30)	0.09
Unstable angina	4 (6.1)	2 (5.5)	2 (6.7)	
Killip class III–IV	15 (24.2)	9 (26.5)	6 (21.4)	0.8
RWMA on echocardiography	44 (66.7)	24 (66.7)	20 (66.7)	0.5
LVEF <45%	21 (31.8)	13 (36.1)	8 (26.7)	0.3
Clinical features (mean [SD])				
Pulse rate (per minute)	84.9 (19.9)	86.25 (18.9)	82.9 (21.4)	0.6
Systolic blood pressure (mmHg)	129.1 (21.1)	128.9 (21.1)	129.3 (22.1)	0.9
Diastolic blood pressure (mmHg)	78.9 (11.6)	80.3 (11.7)	76.8 (11.4)	0.3
Abnormal chest auscultation, *n* (%)	23 (34.8)	12 (33.3)	11 (36.7)	0.4
Laboratory parameters				
Troponin-I, median (IQR) (ng/ml)	7425 (920–33 815)	8213 (812–29 642)	7040 (1593–38 381)	0.69
Haemoglobin, mean (g)	14.6 (2.1)	14.6 (2.2)	14.5 (1.9)	0.8
RBS, median (IQR) (mg/dl)	118 (95–152)	110 (95–151)	126 (97–160)	0.6
Serum creatinine, mean (mg/dl)	0.89 (0.35)	0.88 (0.28)	0.92 (0.44)	0.8
LDL cholesterol, mean (mg/dl)	122.1 (39.5)	125.3 (40.3)	118.2 (39.1)	0.5
HDL cholesterol, mean (mg/dl)	40.5 (14.1)	40.8 (8.9)	40.2 (18.6)	0.2

STEMI ST elevation myocardial infarction NSTEMI non-ST elevation myocardial infarction RWMA regional wall motion abnormality LVEF left ventricular ejection fraction IQR interquartile range RBS random blood sugar LDL low-density lipoprotein HDL high-density lipoprotein

In a study by Sílvia *et al.*, OSA was diagnosed in 63% of patients admitted for ACS and they concluded that OSA was an underdiagnosed disease and recommended establishing screening protocols for identifying patients with unfavourable prognosis.[16] Leao *et al.* reported a high (63.0%) prevalence of OSA in patients with ACS and found that after a median follow-up of 75 months, patients with severe OSA showed a significantly higher incidence of death, myocardial infarction and revascularization.[17]

Martinez *et al.* assessed the association between sleep apnoea and CAD, after adjusting for usual CAD risk factors in 55 patients. They excluded patients older than 65 years, with BMI >40 kg/m^2, with diabetes and with history of smoking in the past year. Of 55 patients, 28 had AHI >14 (odds ratio 8.7 for CAD). Patients without (*n*=29) and with CAD (*n*=26), showed a mean (SD) AHI of 11 (11) and 23 (14), respectively (p=0.001). In a binary logistic regression to predict CAD, controlling for all the above risk factors, the only variables entered in the stepwise model were AHI (either as continuous or categorical variable) and uric acid. They concluded that in a sample without smokers, morbidly obese patients or people with diabetes, AHI was the main predictor of CAD and sleep apnoea should integrate the set of risk factors routinely assessed in clinical investigation for CAD risk stratification.[4]

In our study, 31 (46.9%) patients had moderate-to-severe OSA (AHI ≥15). Schäfer *et al.* noted OSA in 30.5% patients of angiographically proven CAD in contrast to 19.7% in controls on screening 223 men and observed that OSA of moderate severity (AHI ≥20) was independently associated with myocardial infarction.[5]

In our study, 78.8% of the patients with ACS had OSA and 21.2% severe OSA. A meta-analysis by Le Grande *et al.* reported that at any time after hospital admission for ACS, the pooled prevalence was 22% for severe OSA and 70% for mild OSA.[18]

Limitations

This study was conducted in a single centre on a small sample size and without follow-up data. All patients, who were subjected to PSG, were in Killip class I/II. The patients with higher Killip class (III and IV) were subjected to PSG only after improvement of their Killip class I/II. The patients with higher Killip class could not be recruited as some of them did not report for PSG or might not have survived, thus leading to recruitment of patients with only less severe ACS.

Conclusions

In this study, on gold standard, in-hospital overnight PSG, there was a high prevalence of OSA in patients with ACS. Further, obesity (as measured by BMI, neck circumference and waist–hip ratio), diabetes mellitus and hypertension were significantly prevalent with OSA (AHI ≥15) in these patients. The long-term effects of OSA and impact of treatment of OSA with CPAP therapy on long-term outcomes of ACS need further evaluation.

Conflicts of interest. None declared

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