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### RESEARCH ARTICLE

#### EFFECT OF TREATMENT OF OBSTRUCTIVE SLEEP APNEA UPON COMORBID HYPERTENSION AND CARDIAC ARRHYTHMIAS.

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Obstructive sleep apnea, hypertension, cardiac arrhythmias, atrioventricular blocks, continuous positive airway pressure.

#### Abstract

**Background:** There is an established relation between obstructive sleep apnea (OSA) and various cardiovascular consequences.

**Objectives:** To study the relation between obstructive sleep apnea, hypertension and cardiac arrhythmias and to see the effect of treatment of sleep apnea on these associations.

**Methods:** Sixteen subjects, 11 (68.7%) males and 5 (31.2%) females with mean age of 48.12±9.3 years were diagnosed to have OSA and concomitant hypertension, cardiac arrhythmias and atrioventricular blocks. The diagnosis of OSA was established on the basis of clinical picture, Epworth Sleepiness Scale and Polysomnography.

**Results:** Hypertension was observed in all subjects. It was found to be associated with severe OSA having apnea hypopnea index (AHI) of 31.2±2.12 bearing high statistical significance (OR 1.98, p < 0.001). Various arrhythmias included ventricular premature complexes (50%), paroxysmal supraventricular tachycardia (12.5%), atrial fibrillation (25%), and atrioventricular block was found in 12.5% patients. Treatment with nocturnal continuous positive air pressure (CPAP) significantly improved hypertension and arrhythmias and completely reversed AV blocks, bearing high statistical significance.

**Conclusion:** Obstructive sleep apnea bears a strong relation with hypertension, cardiac arrhythmias and AV blocks and treatment almost abolishes these illnesses. Large sample studies are needed to further substantiate these observations.

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#### Introduction:-

There is enough evidence supporting the association between obstructive sleep apnea (OSA) and cardiovascular morbidity and mortality.<sup>1</sup> OSA is characterized by repetitive episodes of occlusion or near occlusion of the upper airway at the level of oropharynx despite increasing inspiratory efforts.<sup>2</sup> These episodes of hypopnea / apnea periods are terminated by brief arousals resulting in sleep fragmentation. Inspiratory efforts against an occluded airway result in large intrathoracic pressure swings with eventually increased sympathetic nervous system activity, fluctuations in parasympathetic tone, changes in heart rate, arterial and pulmonary vasoconstriction, hypertension and increase in cardiac preload and after load.<sup>3,4,5</sup> It is a well known fact that intermittent hypoxia or experimentally

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induced OSA can lead to persistent daytime hypertension, and it is significant to mention that nighttime systolic and diastolic blood pressure (BP) carry greater long-term cardiovascular risk than daytime [24 hour ambulatory BP recordings have shown this].<sup>6,7</sup> Again, by several mechanisms OSA initiates atrial or ventricular arrhythmias, including wall stretch, abrupt increase in intrathoracic pressure, myocardial ischemia secondary to ischemia induced intermittent hypoxia, and activation of cardiac inflammatory properties.<sup>8</sup> Studies have demonstrated that arrhythmias provoked by OSA are reversible after use of continuous positive airway pressure (CPAP).<sup>9</sup>

On the basis of these established facts we conducted the present study regarding impact of treatment of OSA on hypertension and cardiac arrhythmias and stands first of its kind in the Jammu and Kashmir State.

## **Material and Methods:-**

### **Study Sample:-**

This prospective, random-sample study was conducted at the Postgraduate Department of Medicine of Government Medical College, Srinagar – a tertiary health care center of Jammu and Kashmir. This included 16 subjects of obstructive sleep apnea with cardiovascular comorbidities studied from June 2015 to March 2017. Each study subject was interviewed, examined and evaluated after obtaining valid consent. All those who refused to furnish reliable information or who failed to cooperate for investigations and regular follow up were excluded from the study.

### **Diagnosis of Cardiac Disease:-**

The study sample was taken from the population who had established evidence of cardiac disease and hypertension (not attributed to any known cause) on the basis of history, clinical examination, baseline electrocardiography and other related baseline investigations. Those who had high clinical possibility of OSA were validated on the basis of Epworth Sleepiness Score as used in previous studies.<sup>10</sup> Those carrying a score of more than 10 were further evaluated for OSA. Other causes of hypertension and cardiac arrhythmias were excluded.

### **Diagnosis of Obstructive Sleep Apnea:-**

The subjects suspected to have OSA on the basis of clinical picture and Epworth Score were subjected to overnight polysomnography, either hospital attended (n=9), or at patients home (n=7) by board certified sleep technologists. The data was interpreted and final scoring and diagnosis was made by board certified sleep specialist, strictly as per the recommendations of the American Academy of Sleep Medicine.<sup>11</sup> Apnea-hypopnea index (AHI), meaning number of apneas and hypopneas per hour of sleep of more than 5 events was considered diagnostic of obstructive sleep apnea.

### **Statistical Analysis:-**

The data of demographic profile, questionnaire variables and polysomnography parameters were analyzed with SPSS version 20. Qualitative variables were expressed as percentages and the quantitative ones as mean $\pm$ SD. Percentages were compared by using standard chi-square test and means by the student 't' test. P values of less than 0.005 were considered to be significant.

## **Results:-**

Overall the study included 16 subjects, 11 (68.7%) males and 5 (31.2%) females with mean age of 48.12 $\pm$ 9.3 years. 12 patients belonged to Srinagar city, and 4 subjects were from other districts of Kashmir valley. Majority of the subjects were obese with BMI of over 30kg/m<sup>2</sup> (Table 1). No subject had mechanical cause of OSA. Arterial hypertension was present in all on presentation that was not controlled with one anti-hypertensive agent. Epworth score was suggestive of OSA. Keeping in view high clinical probability of OSA, the subjects were subjected to polysomnography. Severe form of OSA was confirmed in patients of hypertension, carrying high statistical significance. Similarly, arrhythmias and atrioventricular conduction blocks were associated with moderate – severe OSA (Table 2). While analyzing effect of continuous positive airway pressure (CPAP), hypertension was normalized within 3 to 6 months of treatment carrying high statistical significance. Ventricular premature complexes were not seen after third month of treatment (Table 3), atrioventricular conduction blocks disappeared within first month after CPAP, however only one patient of atrial fibrillation continued to have this electrocardiographic abnormality, who was further controlled by adding pharmacotherapy. Overall the results of CPAP application significantly reduced hypertension, cardiac arrhythmias and conduction blocks.

**Table 1:-** Patient characteristics (n=16)

Age, mean±SD	48.12±9.3
BMI (kg/m <sup>2</sup> ), mean±SD	31.5±2.8
Arterial hypertension number %	16 (100%)
Neck circumference (inches) mean±SD	18.1±1.2
Epworth Sleepiness Score, mean±SD	14.8±6.1

**Table 2:-** Relationship between obstructive sleep apnea, hypertension and cardiac arrhythmias

Disease	AHI mean±SD	OR	p value
Hypertension	31.1±2.12	1.98	<0.001
Ventricular premature complexes	30.0±3.11	0.69	<0.005
Paroxysmal supraventricular tachycardia	27.0±3.43	1.04	0.003
Atrial fibrillation	34.0±1.11	2.01	0.033
Atrioventricular conduction block	32.0±4.13	1.91	<0.01

AHI, apnea-hypopnea index; OR, odds ratio

**Table 3:-** Effect of treatment of OSA on diseases (n=16)

Disease		Duration of Treatment			OR	p value
		1 month	3 months	6 months		
HTN	Systolic	140±9.9	130±4.2	120±1.3	1.99	0.001
	Diastolic	113±3.9	101±2.2	80±7.1	0.82	<0.001
Ventricular premature complexes		8 (50%)	4 (25%)	1 (6.25%)	1.01	<0.032
Paroxysmal supraventricular tachycardia		2 (12.5%)	1 (6.25%)	-	1.91	<0.001
Atrial fibrillation		4 (25%)	1 (6.25%)	1 (6.25%)	1.06	<0.001
Atrioventricular conduction block		2 (12.5%)	-	-	0.91	<0.001

OR, Odds ratio

### Discussion:-

So far large epidemiological studies have demonstrated a strong and consistent relation between OSA and hypertension.<sup>12,13,14</sup> Obesity has been the most prominent risk factor for OSA<sup>12</sup>, similar was the situation in our study, although a very small sample where all the study subjects had BMI near or over 30kg/m<sup>2</sup>. Though the causative pathways remain debatable, cross-sectional analysis of several studies suggest that OSA is an independent risk factor for high mean, systolic and diastolic blood pressure.<sup>15,16</sup> Several mechanisms have been proposed for occurrence of hypertension due to OSA. These include increase in sympathetic activity secondary to micro-arousals at night, nocturnal fluctuations in catecholamines, and endothelial dysfunction leading to failure of endothelial dependent and independent vasodilatation of vessels with eventual increase in peripheral vascular resistance and hypertension.<sup>17,18,19</sup> All of the subjects in our study were having hypertension. Cardiac arrhythmias do occur more frequently in subjects with OSA especially during sleep and increase with the severity of disease. Bradycardia, first to third degree arterioventricular blocks during sleep have been reported in OSA patients.<sup>20,21</sup> In our study, the arrhythmias were more frequent with moderate to severe forms of sleep apnea (Table 2). There are several mechanisms that could lead to either bradyarrhythmias or tachyarrhythmias in OSA. In the initial phase of apnea there is predominance of vagal tone. Towards the end of apnea there is substantial increase in sympathetic activity. These neurohumoral factors as well as the mechanical stress on the myocardium from the intra thoracic pressure changes are potentially arrhythmogenic. Epidemiological data suggest significant association between atrial fibrillation and OSA.<sup>22</sup> Mehra and co-workers found that subjects with OSA were five times more likely to have AF compared to non-OSA patients.<sup>23</sup> In our study, both hypertension, arrhythmias and atrioventricular blocks significantly improved after institution of nocturnal continuous positive airway pressure (Table 3). Previous studies have well demonstrated that application of nocturnal CPAP abolishes majority of these arrhythmias.<sup>24,25</sup> Becker and co-workers<sup>26</sup> observed that sinus arrest and atrioventricular blocks got reversed by treatment with CPAP.

To summarize, our study showed significant effect of treatment outcome of hypertension and arrhythmias, and these findings are consistent with findings of previous studies. Large sample studies are needed in future to substantiate this association and treatment outcome, that may have significant impact on improvement of patient care.

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