Original Research

A PROSPECTIVE OBSERVATIONAL STUDY OF POTENTIAL CORRELATION BETWEEN INFLAMMATORY BIOMARKERS CRP, IL-6, TNF–ALPHA AND SEVERITY OF OBSTRUCTIVE SLEEP APNEA

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ABSTRACT

Background: OSA is defined by the presence of repetitive episodes of upper airway obstruction during sleep. OSAS promotes persistent low intensity inflammatory state. Obsructive sleep apnea is classified as mild, moderate, severe according to apnea hypopnea index. 5-14 AHI is mild, 15-30 AHI is moderate, more than 30 is severe. Correlation between AHI severity index and inflammatory biomarkers like CRP, IL-6, TNF-α is assessed. **Methods:** This is a 18 months prospective study of 50 patients done in Coimbatore medical college. Patients with symptoms of OSA is screened with STOP BANG score and subjected to overnight polysomnogram and AHI is obtained. Blood samples collected and sent for biomarkers CRP, IL-6, TNF-α from patients with AHI ≥ 5. **Results:** Severity of OSA based on AHI was, Mild in 5 patients, Moderate in 17 patients, Severe in 28 patients. CRP was high in 2 patients which belongs severe category, IL-6 was high in 21 patients in which 7 belongs to moderate and 14 to severe category, TNF-α was high in 9 patients in which 3 belongs to moderate and 6 to severe category. **Conclusion**: There is evidence that moderate and severe AHI is associated with increased inflammatory cytokines particularly IL-6, TNF-α.These patients prone to develop complications like metabolic syndrome, cardiovascular events, CVA. Studies shown that cytokines significantly reduced with CPAP therapy. Due to limitations in our setup, patients non affordability, CPAP therapy and thereby reduction in cytokines levels could not be assessed.

Keywords: CRP, IL-6, TNF-alpha, Severity of OSA.

INTRODUCTION

Obstructive sleep apnea (OSA) is a common disorder affecting about 4% of middle-aged males and 2% of middle-aged women in the developed world[1] and is a significant source of morbidity and mortality. Recurrent bouts of upper airway collapses during sleep are a hallmark of OSA.

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Obstructive sleep apnea is the most prevalent of sleep-disordered breathing. Obstructive sleep apnea affects 24% of men, 9% of women in the general population. An estimated 82% of men 92% of women with moderate to severe obstructive sleep apnea have not been diagnosed.[2,3] In OSA repeated episodes of partial and complete collapse cause a reduction or total cessation of airflow during sleep resulting in oxygen desaturation and arousals from sleep. OSA leads to excessive daytime sleepiness, unrefreshing sleep, poor concentration and fatigue. The frequent occurrence of upper airway collapse events is typically accompanied by desaturation of hemoglobin and terminated by brief arousals. This

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leads to significant fragmentation of sleep and persistent excessive daytime sleepiness (EDS). Consequently, there is a disruption in endothelial function, a prolonged sympathetic nervous system activation, and an upregulation of systemic inflammatory markers. Since chronic inflammatory responses are key players in atherosclerosis, many of these physiologic and biochemical abnormalities are linked to the etiology of cardiovascular and cerebrovascular disorders.[4-6] OSA is a serious condition that diminishes quality of life and is associated with many co-morbidities. Patients with OSA will have increased incidence of coronary artery disease, systemic hypertension, congestive cardiac failure, cerebrovascular disease, metabolic syndrome. There is enough evidence that pro inflammatory cytokines levels increased in OSA patients. In this study we tried to find out correlation between severity of apnea-hypopnea index and inflammatory biomarker levels.[7-9]

MATERIALS AND METHODS

This is a prospective observational study done in Coimbatore medical college during 18 months period between May 2023 to October 2024. Patients who attended our outpatient department in whom obstructive sleep apnea suspected are screened with STOP BANG score, those had moderate and high risk for OSA were taken for overnight polysomnography and AHI recorded. Blood sample was collected for biomarker levels CRP, IL-6, TNF-α and correlation was analysed.

RESULTS

In our study of 50 patients, number of male patients were 28 and female were 22 (Table 1). Comorbidities in our population are diabetes (n=16), hypertension (n=21), hypothyroid (n=6), coronary artery disease (n=8), COPD (n=1). We screened with STOP BANG score in which one had intermediate risk and 49 had high risk for obstructive sleep apnea and patients were taken for overnight polysomnography and severity of OSA categorised based on AHI. Mild AHI observed in 5 patients, moderate in 7 patients, severe in 38 patients. Blood samples were collected for biomarkers (CRP, IL-6, TNF-α) levels and its correlation with severity with AHI was analysed. Mean levels of biomarkers were increased as the severity of AHI increased.

Table 1: Sex Distribution

Sex	Number of Patients	Percentage
Male	28	56%
Female	22	44%

Table 2: Age Distribution

Age in Years	Number of Patients	Percentage
Less Than 40	3	6%
41-50	14	28%
51-60	19	38%
More Than 60	14	28%

Table 3: Comorbidities in Study Population

Comorbid	Number of patients
Diabetes mellitus	16
Hypertension	21
Hypothyroidism	6
Coronary artery disease	8
COPD	1
CVA	1

Table 4: Risk for OSA based on STOP BANG score

Stop Bang Score	Number of Patients	Percentage
Intermediate Risk	1	2%
High Risk	49	98%

Table 5: Severity of OSA based on AHI

AHI Category	Number of Patients	Percentage
Mild	5	10%
Moderate	7	14%
Severe	38	76%

Table 6: Table Showing Signifance between CRP Levels and Severity of Disease Based on AHI Category

AHI Category	C Reactive Protein	
	Mean	SD
Mild	0.6	0.28
Moderate	0.71	0.36
Severe	1.34	0.4

Table 7: Significance between the IL-6 Levels and Severity of Disease

AHI Category	Interleukin -6	
	Mean	SD
Mild	1.25	0.26
Moderate	1.41	0.38
Severe	1.84	0.36

Table 8: TNF-A Levels in Significance with Severity of OSA

AHI Category	TNF-α	
	Mean	SD
Mild	0.23	0.1
Moderate	0.35	0.08
Severe	0.49	0.34

DISCUSSION

In our study coming to age distribution, most of them were in 51-60 years of age (38%) followed by more than 60 years (28%) and 41- 50 years (28%) and only 6% were less than 40 years (Table 2).The comorbidities in our study population are shown in table 3. In our study group, only 1 (2%) had intermediate risk of OSA and 49 (98%) had high risk of OSA (Table 4) based on stop bang score. In our study 5(10%) of patients had mild OSA, 7(14%) of patients had moderate OSA and rest 38 (76%) of patients had severe OSA (Table 5). Coming to important part of our study the inflammatory markers, In our study except for 2 patients all patients had normal CRP levels. The mean score among our study population is 1.18 with SD of 0.48. When compared to AHI severity though most of them had normal levels, there was increase in c reactive protein levels as severity increases.[10] In mild OSA patients, it was 0.6 ± 0.28, in moderate OSA patients it was 0.71±0.6 and severe OSA patients it was 1.34±0.4, this was statistically significant too with a p value of 0.001(Table 6). Next, we evaluated Interleukin -6 and the mean score was 1.51 with SD of 0.35. When compared to AHI severity there was increase in interleukin 6 levels as severity increases.[11] In mild OSA patients, it was 1.25 ± 0.26, in moderate OSA patients it was 1.41 ± 0.38 and severe OSA patients it was 1.84 ± 0.36, this was statistically significant too with a p value of 0.001(Table 7). Finally we evaluated Tumour necrosis factor –alpha and among our study population the mean score was 0.39 with SD of 0.31. When compared to AHI severity there was increase in TNF-alpha levels as severity increases.[12] In mild OSA patients, it was 0.23 ± 0.1, in moderate OSA patients it was 0.35 ± 0.08 and severe OSA patients it was 0.49 ± 0.34, this was statistically significant too with a p value of 0.001(Table 8). We did Pearson correlation for all three markers with AHI severity score and all three showed positive correlation, which was statistically significant. On analysing the correlation of these biomarkers with comorbid population in our study, we found that mean CRP and TNF-α levels increased with AHI in diabetes and hypertension, mean levels of all three markers increased with AHI in coronary artery disease.

CONCLUSION

Our study found that compared to patients with mild or moderate OSA, those with severe OSA had higher levels of systemic inflammatory markers. Future studies are necessary to determine whether these markers can serve as predictors of the course or outcome of the disease.

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