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Obesity and Cardiovascular Risk Factors in Obstructive Sleep Apnea Syndrome:A Cross-sectional study

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Research Article

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Abstract

Objective: To study the association between obesity and cardiovascular risk factors among Obstructive sleep apnea syndrome (OSAS).

Methods: A prospective study was conducted in patient with excessive day time sleepiness, heavy snoring, air obstruction, breathlessness, and had never been treated for OSAS and were taking no medications were included in the study and they underwent polysomnography

Results: We have included eighty nine OSAS patients with apnea-hypopnea index (AHI)≥5 events/hr (72 Men and 17 Women). In the study population male patients were comparatively higher 80.89% than female patients (19.10%). The predominance of the disease in male (n=72) with average age of 46.82 ±10.91, but the severity of the disease was same in both male and female. We have examined cardiovascular risk factors, total cholesterol (TC), low density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), triglyceride (TG), fasting blood sugar (FBS) and C-reactive protein (CRP) levels of study population. The mean serum level of FBS was 107.75 ± 1.86 mg/dl (Mean ± SE), triglyceride was 186 ± 7.93 mg/dl, LDL-c was 118.17 ± 3.38 mg/dl, HDL-c was 33.38 ± 0.96 mg/dl, CRP was 7.33 ± 0.33 mg/L. The Pearson correlation coefficient of AHI with BMI was found to be 0.423 (P<0.0001) with FBS 0.222 (P=0.036), with LDL-c 0.231 (P=0.028) with TG 0.218 (P=0.039). AHI showed a significant positive correlation with BMI, FBS, CRP, TG, and LDL-c. Elevated levels of CRP were found in 64% (n=57) of population in our study.

Conclusion: Our study confirms the other reports to increasing BMI, the prevalence of elevated CRP levels. Our results show that OSAS is associated not only with BMI but also with increased CRP concentrations and elevated Triglycerides and LDL-c, FBS.

Keywords: Apnea-hypopnea index, obstructive sleep apnea, cardiovascular risk factors, Obesity, CRP.

Introduction

Obstructive sleep apnea syndrome (OSAS) is a chronic respiratory disorder which can cause significant morbidity and mortality.[1)] the condition, which includes one or two of the following symptoms: severe snoring, nocturnal respiratory arrest, repeated nocturnal awakening, nonrecuperative sleep, diurnal fatigue and altered concentration. Previous studies demonstrated that an association between OSAS and the risk for cardiovascular disease, such as arterial hypertension, congestive heart failure and coronary artery disease, which may also contribute diabetes mellitus, dyslipidemia and thyroid disorders.[2)] Body mass indexes (BMI), Serum Cholesterol, C reactive protein (CRP) are known risk factors for cardiovascular morbidities. Also several studies suggested blood glucose, interleukin (IL)-6, tumor necrosis factor (TNF)-α and homocystine are other important risk factors for atherosclerosis, stroke, and cardiovascular disease.[3,4)] Obesity is one of the most important risk factor for the development of OSAS.[5)] OSAS is associated with multiple casual factors of endothelial damage and atherosclerosis [6)] and it has been suggested that OSAS-related to hypoxia and systemic inflammation might be associated with the progression of atherosclerosis and thus might increase the risk for cardiovascular and cerebrovascular morbidity in patients with OSAS [7,8)] Elevated levels of CRP, IL-6, and TNF-α in OSAS was reported in many studies. [9,10)] CRP is a prototype inflammatory marker, which may play a direct role in atherogenesis and thrombus formation. In addition to OSAS, several other conditions that are associated with increased levels of CRP include chronic inflammation, obesity, metabolic syndrome, type 2 diabetes mellitus and hypertension. [11)] Little information exists regarding body fat distribution and body composition in person with OSAS ie, the extent of upper-body versus lower body (gluteofemoral, peripheral) fat deposition and the relative amounts of adipose versus lean body mass. Fat deposit in the neck has been implicated in the pathogenesis of OSAS. [12-14)] There was a conclusive evidence linked lipid abnormalities and diabetes mellitus to the development of cardiovascular diseases, studies of serum lipids and glucose tolerance have not been reported in detail in patients with OSAS.[15)] The present study was aimed to study the association between obesity and total cholesterol, low density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), triglyceride, fasting blood sugar (FBS) & CRP [16)] in patients with obstructive sleep apnea syndrome in south Indian population.

Methodology:

Patients and Methods

Study Design

This prospective study was conducted from May 2009 to September 2009 at Interventional Pulmonology & Sleep Medicine department, Kovai Medical Center and Hospital, Coimbatore, India.

Participants

Patient with excessive day time sleepiness, heavy snoring, air obstruction, breathlessness, and had never been treated for OSAS and were taking no medications were included in the study and they underwent polysomnography. Patients with other co morbidities were excluded. This study protocol was approved by the Ethics Committee of Kovai Medical Center and Hospital and written informed consent was given by all patients prior to enrollment.

Polysomnography

All enrolled subjects were underwent an overnight sleep study started at 10 pm and ended at 6 am with the use of a computerized polysomnogram system (Somnologica). The surface electrodes were applied using standard techniques and following signals (EEG), Electrooculogram (right & left): Submental electromyogram, and anterior tibialis electromyogram additionally, EEG and heart rate were recorded simultaneously. Snoring was recorded by a microphone placed at the jugular vein, and airflow was recorded combined oronasal thermistors, while arterial oxyhemoglobin saturation was recorded by a finger pulse oximeter. Thoracic cage and abdominal motion were recorded by inductive plethysmography.

Apnea was defined as a complete cessation of air flow lasting >10s: Hypopnea was defined as discernible fall in air flow lasting ≥ 10s accompanied by a decrease in oxygen saturation of atleast 3% or by an EEG-recorded arousal. Apnea Hypopnea Index (AHI) was defined as the total number of apneas and hypopneas occurring per hour of EEG sleep. Patients with pure or mainly central apneas were excluded from the study.

Patients and Predictive Factors

A total of 98 subjects underwent polysomnography and subjects with Apnea Hypopnea Index ≥5 are considered as OSAS and AHI<5 are Non-OSAS. In our study we found that 89 subjects were obstructive sleep apnea syndrome and 9 subjects were Non-OSAS. The remaining 9 subjects with AHI<5 were excluded. The relationships between AHI and cardiovascular risk factors were analyzed among the 89 sleep apneics. Total 89 patients demographic data, laboratory investigations such as serum CRP, Fasting blood sugar and Lipid profile were performed. The BMI for each patient was obtained by dividing weight in kilograms by height in meters squared. Based on the world health organization for the South East Asia region BMI ≥ 25kg/m^2 were considered as obese. [24)]

Blood Collection

All venous blood samples were collected at (8am to 10 am) the fasting state just after polysomnography was performed by phlebotomist. Then the samples were centrifuged immediately at 3000g for 5 min. After centrifugation the serum aliquots were frozen and stored at –80°C. The subjects did not perform any specific exercise or apply any specific diet.

Biochemical Analysis

Serum cholesterol, Triglyceride, HDL-c, LDL-c and FBS were analyzed by Semi-automatic, single-beam filter photometer with commercially available kits (Photometer 5010 $_{V5+}$ German). A serum level of CRP was done by immunoturbidimetry assay. For blood sample analysis following cutoff values was defined as abnormal: Total cholesterol ≥ 200mg/dl (TC) Ttriglycerides≥200mg/dl (TG); High Density Lipoprotein Cholesterol ≤ 40mg/dl (HDL -c); Low density lipoprotein cholesterol ≥100mg/dl (LDL -c); Fasting blood sugar level 80-100mg/dl; CRP > 6mg/L (CRP).

Statistical Analysis

The statistical package Prism 5 for Windows 2007 was used for statistical analysis. Significant level was set 5%. Results are expressed as mean ± standard error (SE) for continuous variables. χ^2 test and Pearson correlation coefficient was performed to study the association of cardiovascular risk factors among study population.

Results:

Eighty nine OSAS patients with AHI ≥5 (72 Men and 17 women) were included in the study From September 2009 to June 2010 at Interventional Pulmonology and Sleep Medicine department, Kovai Medical Center and Hospital, Coimbatore, India. Subjects with AHI<5 (n=9) were excluded from the study. From the total study population patient categorized based on AHI as Mild (13%), Moderate (22%) and Severe (64%) (Table: 1).

Table: 1 Average AHI of total study population

Category	I (n=12)	II (n=20)	III (n=57)
AHI	Mild(5-14.9)	Moderate(15-29.9)	Severe ≥30
Mean± SE	10.99±0.62	23.25±1.19	56.84±2.48

Data are presented as Mean ± SE values

Our study revealed 12.46% were smokers and 22.72% were alcoholic patients. It was found that 25.53% were had family history of snoring.

Among 89 patients only 6 had BMI<25. The average BMI of all 89 subjects were 30.13 ± 0.60. In the study population (n=89) male patients were comparatively higher 81% than female patients (19%). There were patients of all age group from 27 to 78 majorities of patients with age group of 40 to 60. From the observation no neonatal, pediatric and adolescent subjects were

treated for OSAS. Further, Chi square test was computed to study the difference in normal and abnormal among male and female patients. The results revealed that,

S.N	Variables	Relative Risk	95% CI	Odds Ratio	95% CI	*p*-value
1	BMI (kg/m^2)	0.989	0.864 to 1.131	0.838	0.091 to 7.679	1.000
2	CRP (mg/L)	1.110	0.720 to 1.709	1.316	0.446 to 3.880	0.779
3	TC (mg/dL)	1.087	0.779 to 1.515	1.373	0.423 to 4.450	0.754
4	TG(mg/dL)	3.424	0.904 to 12.97	5.058	1.075 to 23.81	0.045*
5	LDL –C (mg/dL)	2.361	1.230 to 4.532	9.167	2.838 to 29.60	0.002*
6	HDL –C(mg/dL)	1.692	0.865 to 3.311	2.718	0.904 to 8.173	0.103
7	FBS (mg/dL)	1.855	1.036 to 3.322	4.622	1.525 to 14.01	0.007*

TABLE: 2 Gender wise Association of variables in study population (*p< 0.05)

there was significant difference in FBS, LDL-c and TG at p< 0.05 level. The result indicates that FBS, LDL-c and TG were main triggering factors in OSAS patients. There was no significant difference in CRP, HDL-c, TC and BMI (Table: 2).

Cardiovascular risk factors

We have evaluated cardiovascular risk factors total cholesterol, LDL-c, HDL-c, triglycerides, fasting blood sugar and C-reactive protein. The mean serum levels of fasting blood sugar was 107.75 ± 1.86 mg/dl, triglyceride was 186 ± 7.93 mg/dl, LDL-c was 118.17 ± 3.38 mg/dl, HDL-c was 33.38 ± 0.96 mg/dl, CRP was 7.33 ± 0.33 mg/L. About 70% (n=68) were found abnormal levels of total cholesterol and 55% (n=49) of patients had HDL-c below

S.No.	Variables	Mean ± SE	r value	*p*-value
1	**BMI (kg/m^2)**	**30.13 ± 0.60**	**0.4236**	**0.001***
2	**CRP (mg/L)**	**7.33 ± 0.33**	**0.2114**	**0.047***
3	**TC (mg/dL)**	**234.04 ± 5.59**	**0.1901**	**0.074**
4	**TG(mg/dL)**	**186 ± 7.93**	**0.2183**	**0.039***
5	**LDL –C (mg/dL)**	**118.17 ± 3.38**	**0.2319**	**0.029***
6	**HDL –C(mg/dL)**	**33.38 ± 0.96**	**0.0908**	**0.398**
7	**FBS (mg/dL)**	**107.75 ± 1.86**	**0.2225**	**0.036***

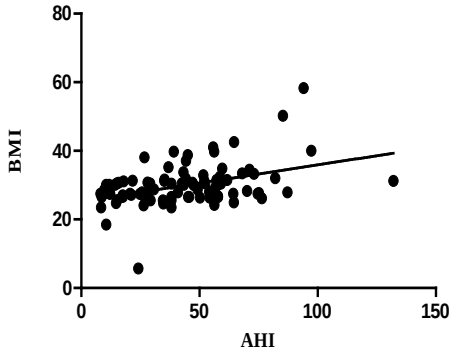
TABLE: 3 Association of Apnea Hypopnea Index with Cardiovascular risk factors (*p< 0.05)

the normal range. The Pearson correlation coefficient of AHI with other variables as follows with BMI 0.423 (P<0.0001) with FBS 0.222 (P=0.036) with LDL-c 0.231 (P=0.28) with TC; 0.190 (P=0.074) with HDL-c 0.090 (P=0.39) and with CRP 0.211 (P=0.046). AHI showed a significant positive correlation with BMI, FBS, LDL-c, TG, and CRP. Significant independent negative correlation for AHI was observed with Total Cholesterol, and HDL-c etc (Table: 3).

Discussion:

We conducted an observational study involving in patients with OSAS. Factors associated with cardiovascular risk were evaluated and effect of obesity on the disease were analysed. We observed the

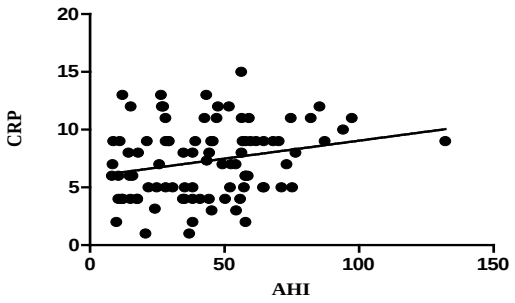
Figure: 1. Pearson correlation between AHI and BMI



r = 0.423, P value <0.0001

predominance of the disease in male (n=72) with average age of 46.82 ± 1.29, but the severity of the disease was same in both male and female. The prevalence of OSAS in the literature reported from 2:1 to 9:1 Male/female [23] where as in our study population it was found that 2:1 with adolescence to old age group. Female patients (n=17) with average age of 48.6 ±2.80. The mean age of our study group (49.06 ± 1.24) was similar to that reported in other studies.[16, 17, 18] Studies reported that alcohol consumption, smoking and physical inactivity appear to increase the occurrence of the OSAS disorder. A disproportionate craniofacial anatomy is also a risk factor for familial group with obstructive sleep apnea patients.[19,20]

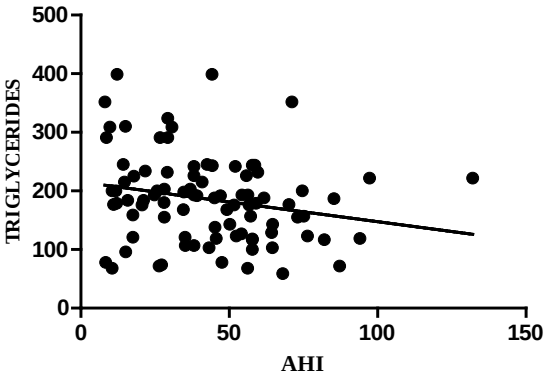
Figure: 2. Pearson correlation between AHI and CRP



r = 0.211, P value=0.04

A number of studies have found confounding role of obesity and indicated a significant correlation of OSAS with elevated levels of AHI.[11,21] Apnea hypopnea index was significant determinant of C-reactive protein. It was reported that in predicting cardiovascular risks of Obstructive sleep apnea syndrome, both hypoxia and obesity should be considered in middle aged group where as nocturnal respiratory disturbance are important in elderly group.[22] The degree of obesity, as calculated by BMI had the greatest impact on AHI. A clear correlation was shown between AHI and BMI. (r=0.423 P<0.0001). Obesity is probably the most important risk factor for OSAS. [23]

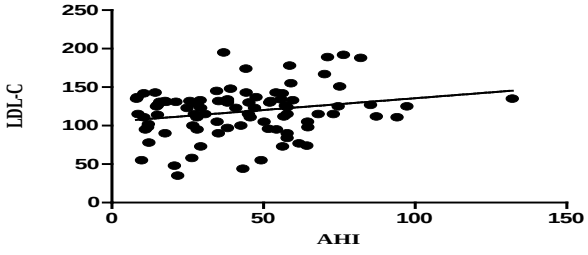
Figure: 3. Pearson correlation between AHI and Triglycerides



r = 0.218, P value=0.0399

In our study population 93% of OSAS patients were obese. The exact mechanisms underlying the effect of obesity on the risk of OSAS are still unclear. It may results fat deposition on upper airway wall or change in upper airway function.

Figure: 4. Pearson correlation between AHI and LDL-C

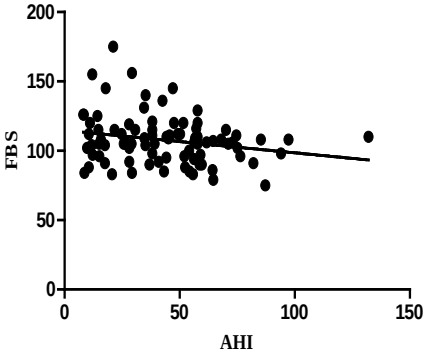


r = 0.231, P value=0.028

Conclusion

A recent epidemiologic study has shown that enhanced levels of CRP are a strong independent predictor of risk to myocardial infarction, stroke, peripheral arterial disease and vascular disease.[24] Elevated levels of CRP (>0.6mg/Ll) were found in 64% (n=57) patient population in our study. Our result shows that OSAS is associated not only with BMI but also with Fasting blood sugar levels, triglycerides, LDL-c and increased CRP concentrations. (r=0.211 P=0.046).

Figure: 5. Pearson correlation between AHI and FBS



r = 0.222, P value=0.0361

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AUTHORS' CONTRIBUTIONS

Athors contributed equally to all aspects of the study.

PEER REVIEW

Not commissioned; externally peer reviewed

CONFLICTS OF INTEREST

The authors declare that they have no competing interests