ORIGINAL ARTICLE

Relationship of Obstructive Sleep Apnoea and Metabolic Syndrome: A Study in a South Indian Population

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Abstract

Background/Objectives: The metabolic syndrome (MS) and obstructive sleep apnoea (OSA) are associated with an increased risk for cardiovascular disease. There are a number of studies investigating the relationship of OSA and MS, but the literature from India is scarce. This study aimed to investigate the relationship of OSA and MS in Indian subjects. The aim of this study is (1) the prevalence of MS in patients with OSA, (2) whether the presence of MS correlates with the severity of OSA, and (3) the association of OSA and the components of MS.

Methods: A cross-sectional, prospective study in which 110 adult patients undergoing overnight polysomnography was conductedand analysed for the presence of MS. OSA was defined as apnoea–hypopnoea index (AHI) =5 events/h. MS was diagnosed as per the definition by National Cholesterol Education Program, Adult Treatment Panel III criteria. Subjects were assessed for presence of OSA, MS, and correlation of severity of OSA with MS and association of each of the component of MS with OSA.

Results: Out of the 110 subjects, 81 were found to have OSA; the remaining 29 subjects were taken as controls. Out of 81 subjects with OSA, 61 (75.30%) had MS and 9 (31.03%) out of 29 controls had MS.

Interpretations/Conclusions: Subjects with OSA (1) had significantly higher prevalence of MS as compared to controls, (2) had higher systolic and diastolic blood pressures, (3) had hyperglycaemia, (4) had lower HDL cholesterol level, and (5) had differences in triglycerides and waist circumference that was not statistically significant.

Keywords: Metabolic syndrome, Obstructive sleep apnoea (OSA)

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Introduction

The metabolic syndrome (MS) is a disorder characterized by abdominal obesity, arterial hypertension, increased blood triglycerides, decreased HDL cholesterol, and increased blood glucose[1,2].The MS is correlated with an increased risk for cardiovascular disease and type 2 diabetes mellitus[3,4].The predominant underlying risk factors for the syndrome appear to be abdominal obesity[5] and insulin resistance[6]; other associated conditions can be physical inactivity[5], aging[7], and hormonal imbalance[8]. The National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) criteria for diagnosis of MS were further modified in 2005 by the American Heart Association / National Heart, Lung, and Blood Institute of Scientific Statement maintaining the ATP III criteria with minor modifications (Table 2) [9].

In 1965, Gastaut et al.[10] and Jung and Kuhlo[11] simultaneously described obstructive sleep apnoea (OSA) for the first time. Various global epidemiologic studies have shown the prevalence of OSA syndrome (with day time sleepiness) varies from 0.3 to 5.1%[12,13] whereas its prevalence in adult Indian population is approximately 3.5%[14-16]. OSA is considered an independent risk factor for development of systemic hypertension and cardiovascular events[17]. Predisposing factors are obesity, congenital or acquired craniofacial and neck defects, endocrine abnormalities, and menopause, whereas smoking and alcohol use can precipitate the disorder.

A few recent studies show that sleep apnoea could be a manifestation of the metabolic syndrome[18,19]. It has been suggested that the metabolic syndrome "syndrome X" should include obstructive sleep apnoea and must then be renamed "syndrome Z"[20]. Even though there is circumstantial evidence to implicate OSA in the development of MS, the causal relationship remains unproven. Hence, it remains unclear whether OSA leads to MS or vice versa. There are a number of studies investigating the relationship of OSA and MS, but the literature from South India is scarce. This study aimed to address the same issue in the patients all of which were of South Indian descent.

Materials and Methods

This study was a descriptive study conducted between June 2009 and May 2011 in the departments of Internal Medicine and Respiratory Medicine, Kerala Institute of Medical Sciences, Thiruvananthapuram, Kerala, India.

Study participants: All successive adult patients (age = 18 years) who were referred to the sleep laboratory for overnight polysomnography (PSG) by their respective physicians for various symptoms or signs are recruited. Exclusion criteria for the study: (1) Patients with known diabetes mellitus, hypertension, dyslipidaemia; (2) Significant liver, cardiac, renal, endocrine or other systemic disorders; (3) Subjects with total sleep duration <6 hours during PSG,and (4) Those unwilling to participate in the study. Informed written consent was taken from patients and their close relatives and documented in patient's record in accordance with the institutional policy.

All study participants had their basic physical assessment prior to PSG. It included age, sex, height, weight, BMI (BMI was defined as weight (kg)/height2 (m)), neck circumference (measured to the nearest 0.1 cm just below the laryngeal prominence (Adam's apple) in both sexes), and waist circumference (measured midway between the lower rib and iliac crest, in cm). Subjective day time sleepiness was assessed by Epworth Sleepiness Score (ESS)[21].History of smoking, alcohol use and medications used regularly was sought and documented.

Polysomnography: All patients underwent overnight PSG at a hospital-based sleep laboratory using Embla S4500 (Natus Neurology, Wisconsin, USA). All studies included 2 channels of electroencephalogram, electro-oculogram, submental electromyogram, nasal-oral airflow measurement by pressure transducer, chest and abdominal wall motion by respiratory inductive plethysmography, oximetry, single-lead electrocardiography, and electromyogram of both anterior tibialis muscles. Apnoea and hypopnoea were de?ned according to the Chicago criteria as recommended by the American Academy of Sleep Medicine[22]. Apnoea-Hypopnoea index (AHI) was calculated.OSA was de?ned as AHI =5 events/h[23]. Severity of OSA was graded as, mild OSA: AHI =5 and <15 events/h, moderate OSA: AHI =15 and <30 events/h, and severe OSA: AHI =30 events/h[24].

Biochemical tests: At the end of the sleep study on the next morning, blood samples were taken (12 hours fasting state) from each subject and the following tests were done: fasting blood glucose (hexokinase method), serum triglyceride (TG) (glycerol-3-phosphate oxidase (GPO) enzymatic method), and high density lipoprotein cholesterol (HDL) (homogenous enzymatic colorimetric

method) (using Cobas®6000 analyser; Roche, Germany).

Metabolic syndrome: MS was defined as per the American Heart Association/National Heart, Lung, and Blood Institute modified criteria of NCEP-ATP III guidelines[9] (Table 1).

Statistical analysis:Sample size calculation was done as per the mentioned formula:

$$N = \frac{(Za)2 \times p \times q}{d2}$$

(N = sample size, Za = confidence level at 95% (standard value of 1.96) for a = 0.05 (*a* error is 5%), *p* = prevalence of disease, *q* = (1-p), d = precision (15% of the prevalence). The values were as follows: *p* = 70% (assuming prevalence of MS to be 70 % in OSA as per the previous studies reviewed during this study); *q* = (1-0.7) = 0.3. With power of 80% and alpha error of 5% it was estimated that a sample size of about 74 would be sufficient. Data was analyzed using computer software, Statistical Package for Social Sciences (SPSS) version 10.0. Probability (P) values of < 0.05 were taken as statistically significant. In the inferential part, comparisons were done using unpaired t tests, Mann-Whitney test, and ÷2 tests as appropriate. In the multivariate analysis, association of obstructive sleep apnoea with components of the metabolic syndrome was tested after adjusting for age, BMI, and smoking status (multiple regression analysis).

Evaluation of Outcomes:Patients with OSA were compared to those without OSA for the presence of MS. Patients with OSA were compared to those without OSA for each component of MS, namely, central obesity, hypertension, impaired fasting blood glucose, and dyslipidaemia. Multiple regression analysis was performed to remove the effects of obesity (BMI), smoking, and age while comparing the two groups. Patients with OSA were divided into three groups depending on the severity of OSA, i.e., mild, moderate, and severe and were compared with the control group.

Results

A total of 110 patients were included in the study. Of the 110 subjects, 62 (56%) were male and 48 (44%) were female. The groups with and without OSA (controls) were comparable in terms of age, smoking status,and alcohol intake status (Table 2).The paricipants in the OSA and control group were similar in respect to age (P=0.857), sex distribution (P=0.557), smoking status (P=0.73), and alcohol consumption (P=0.993). The mean body mass index was higher in OSA group as compared to controls (27.93 vs 24.38; P=0.0001). The mean waist circumference was higher in OSA group as compared to controls (91.80 cm vs 85.62 cm; P=0.0001). The mean neck circumference was higher in OSA group as compared to controls (38.80 cm vs 37.45 cm; P=0.04). The mean AHI and ESS were higher in OSA group as compared to controls (25.16 vs 22.40; P=0.0001 and 10.85 vs 7.45; P=0.0001, respectively).

Out of 110 subjects, 81(73.63%) (47 males and 34 females) subjects were found to have OSA and 29 (23.36%) (15 males and 14 females) did not have OSA (controls). The prevalence of metabolic sydrome was higher in OSA group (61 out of 81) as compared to controls (9 out of 29) (75.3% vs 31.03%; P=0.0001).On the other hand, out of the 70 subjects which were found to have MS, 61(87.14%) had OSA.

The number of patients with mild, moderate,and severe OSA was 26 (32.09%), 33 (40.74%),and 22 (27.16), respectively. 55 out of 81 patients with OSA (67.9%) and 13 out of 29 controls (44.8%) were obese. 45 of the patients with OSA (55.55%) and 6 of the controls (20.68%) had fasting hypergylcaemia. Distribution of subjects with hypertension (HTN), dyslipidaemia (DLP) (low HDL-cholesterol or high triglycerides (TG)), hyperglycaemia, and metabolic syndrome (MS) according to OSA statusis given in Table 3.

Comparison of components of metabolic syndrome: The mean systolic and diastolic blood pressures, mean fasting blood glucose,and mean triglyceride levels were higher in OSA group as compared to controls (Table 4). The mean HDL level was lower in the OSA group as compared to controls.

The association of OSA with various components of MS after adjusting for confounding factors by multiple regression analysis is given in the Table 5. After adjustment for age, BMI and smoking history, followed by stepwise multiple regression analysis, systolic and diastolic blood pressure, HDL cholesterol, fasting blood glucose and, Epworth sleepiness scale score levels were independently associated with a diagnosis of OSA. Waist circumference and triglyceride levels did not reach statistical significance.

Table 6 shows the comparison of various components of MS in groups with mild, moderate and, severe OSA as compared to controls. Some of the interesting findings are as follows: There was no significant difference in triglyceride (TG) levels in the groups with mild and moderate OSA as compared to controls (P>0.05) and the p value was borderline for severe OSA vs control group (P=0.05). Fasting blood glucose (FBG) level was significantly higher in the group with mild and moderate OSA as compared to controls (P<0.05 for both groups) but surprisingly, P value did not reach statistically significant level when group with severe OSA was compared to controls, for FBG level (P>0.05).

Table 1: Criteria for clinical diagnosis of metabolic syndrom[9]

Measure (any 3 of 5 constitute MS)	Categorical cutpoints
Elevated WC*	≥102 cm (=40 inches) in men ≥88 cm (=35 inches) in women
Elevated triglycerides	≥150 mg/dL (1.7 mmol/L) or on drug treatment for elevated TG‡
Reduced HDL-C	<40 mg/dL (1.03 mmol/L) in men <50 mg/dL (1.3 mmol/L) in women or on drug treatment for reduced HDL-C‡
Elevated blood pressure	≥130 mm Hg systolic blood pressure or ≥85 mm Hg diastolic blood pressure or on antihypertensive drug treatment in a patient with a history of hypertension
Elevated fasting glucose	≥100 mg/dL or on drug treatment for elevated glucose

*Lower waist circumference (WC) cutpoint (eg, =90 cm in men and =80 cm in women) appears to be appropriate for Asians.
‡Fibrates and nicotinic acid are the most commonly used drugs for elevated TG and reduced HDL-C. Patients taking one of these drugs are presumed to have high TG and low HDL.

Table 2: Demographics of the subjects with and without OSA (controls)

OSA (*n*=81)	Control (*n*=29)	Difference (95% CI)	*P*	
Age	51.42(±9.4)	51.79(±10.03)	0.37(-3.73, 4.48)	0.857
Males: no.(%)	47 (58.02)	15 (51.72)	chi-square=0.35	0.557
BMI* (kg/m2)	27.93(±3.32)	24.38(±3.39)	3.55(-4.98, -2.12)	0.0001
WC** (cm)	91.80(±7.59)	85.62(±6.0)	6.18(-9.27, -3.08)	0.0001
NC† (cm)	38.80(±3.49)	37.45(±1.31)	1.35(-2.26, -0.45)	0.044
Smokers:no.(%)	28.0(34.46)	9.0(31.03)	chi-square=0.12	0.730
Alcohol:no.(%)	28.0(34.56)	10.0(34.48)	chi-square=0.00	0.993
AHI (/h) ††	25.16(±16.51)	2.76(±0.87)	22.40(-26.07, -18.74)	0.0001
ESS¶	10.85(±2.87)	7.45(±1.27)	3.4(-4.19, -2.62)	0.0001

* Body Mass index, ** Waist circumference, † Neck circumference, †† Apnoea-hypopnoea index (events per hour), ¶ Epworth Sleepiness Score, chi-square:- Pearson Chi-Square

Table 3: Distribution of subjects with hypertension (HTN), dyslipidaemia (DLP) (low HDL-cholesterol or high triglycerides (TG)), hyperglycaemia and metabolic syndrome (MS) according to OSA status

Parameter	Controls, no. (%)	Mild OSA no.(%)	Mod. OSA no.(%)	Severe OSA no.(%)
HTN	18 (62.06)	19 (73.07)	30(90.90)	19(86.36)
DLP	13(44.82)	19(73.03)	23(69.70)	19(86.36)
Hyperglycaemia	6(20.68)	12(46.15)	21(63.63)	12(54.54)
MS	9(31.03)	19(73.07)	24(72.72)	18(81.80)

Table 4: Comparison of the components of metabolic syndrome

	OSA (*n*=81)	Control (*n*=29)	Difference (95% CI)	*P*
SBP*(mm Hg)	146.57(±12.9)	131.79(±8.37)	14.77(-18.9, -10.56)	0.0001
DBP†(mm Hg)	87.44(±7.06)	81.10(±4.19)	6.34(-8.54, -4.14)	0.0001
HDL†† (mg/dl)	43.01(±6.3)	47.69(±6.5)	-4.68(1.94, 7.41)	0.001
TG¶ (mg/dl)	162.62(±25.7)	147.79(±16.43)	14.82(-23.15, -6.50)	0.005
FBG¶¶ (mg/dl)	103.06(±12.65)	94.41(±11.67)	8.65(-13.97, -3.33)	0.002
MS**: no.(%)	61(75.3)	9(31.03)	chi-square=18.08	0.0001

* Systolic blood pressure, † Diastolic blood pressure, †† High density lipoprotein, ¶ Triglycerides, ¶¶ fasting blood glucose, ** Metabolic syndrome, chi-square:- Pearson Chi-Square

Table 5: Association ofobstructive sleep apnoea with components of the metabolic syndrome after adjusting for age, BMI and smoking status (multiple regression analysis)

Dependent variable	ß Coefficient (95% CI)	P
Systolic blood pressure (mmHg)		
F4, 105= 16.36, P =0.0001	-9.49 (-14.65, -4.37)	0.0001
Diastolic blood pressure (mmHg)		
F4, 105=11.12, P<0.0001	-3.57 (-6.41, -0.73)	0.014
Waist circumference (cm)		
F4, 105=41.41, P<0.0001	-0.67 (-2.99, 1.64)	0.567
HDL (mg/dl)		
F4, 105=6.89, P<0.0001	3.16 (0.28, 6.04)	0.031
TG (mg/dl)		
F4, 105=4.59, P=0.002	-7.69 (-18.62, 3.24)	0.166
FBG (mg/dl)		
F4, 105=3.34, P=0.013	-8.67 (-14.57, -2.77)	0.004
ESS		
F4, 105=13.23, P=0.0001	-2.62 (-3.78, -1.45)	0.0001

HDL: High Density Lipoprotein, TG: Triglycerides, FBG: fasting blood glucose, ESS: Epworth Sleepiness Score

Table 6: Comparison of the components of MS in relation to severity of OSA (*vs* control)

	Control	Mild OSA	Moderate OSA	Severe OSA	F
Age	51.7(±10.03)	51(±8.92)*	50.97(±10.11)*	52.59(±9.20)*	0.16
BMI	24.38(±3.39)	27.30(±3.32) †	27.63(±3.41) †	29.11(±3.02) †	9.53
WC	85.62(±6.0)	89.23(±7.0) *	92.26(±8.15) ¶	94.14(±6.75) †	7.40
NC	37.45(±1.31)	37.69(±3.65) *	38.73(±3.46) *	40.23(±2.93) ¶	4.34
SBP	131.7(±8.3)	146.7(±13.9)†	144.24(±11.5) †	149.8(±13.4) †	12.02
DBP	81.10(±4.19)	84.69(±6.69) *	87.36(±6.21) †	90.82(±7.50) †	11.45
HDL	47.69(±6.58)	45.46(±6.16) *	42.24(±5.77) †	41.27(±6.62) †	6.04
TG	147.7(±16.4)	160.7(±22.2) *	162.2(±27.7) *	165.3(±27.2) ^	2.90
FBG	94.41(±11.67)	103.6(±16.01)¶	103.6(±12.03)¶	101.5(±8.98) *	3.55

BMI: Body Mass Index, WC: Waist Circumference, NC: Neck Circumference; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HDL: High Density Lipoprotein; TG: Triglycerides;
FBG: Fasting Blood Glucose. *P>0.05, ¶P<0.05, †P<0.01, ^P=0.05

Table 7: Parish et al.[32]

Parameter	Controls (%)	MildOSA (%)	Mod. OSA (%)	Severe OSA(%)
HTN	54	58	68	88
DLP	52	58	49	60
Hyperglycaemia		28	25	32 35
MS	43	49	49	70

Table 8: For male subjects, Sasanabe et al.[33]

Parameter	Controls (%)	MildOSA (%)	Mod. OSA (%)	Severe OSA(%)
HTN	40.7	50	64.7	76.6
DLP	45.7	56.9	61.4	71.1
Hyperglycaemia	11.9	11.8	23.5	27.7
MS	22	27.1	44.4	59.0

Table 9: For female subjects, Sasanabe et al. [33]

Parameter	Controls (%)	MildOSA (%)	Mod. OSA (%)	Severe OSA(%)
HTN	26.7	34.3	48	80
DLP	26.7	60	48	65
Hyperglycaemia	13.3	17.1	16	25
MS	6.7	20	20	50

Table 10: Independent association between obstructive sleep apnoea and metabolic syndrome (after adjustments for age, BMI)

Parameter	*P*	Odds ratio (95% confidenceinterval)
Metabolic syndrome	0.024	3.39 (1.179, 9.786)

Discussion

Obstructive sleep apnea is an increasingly prevalent condition that is characterized by repetitive upper airway obstructions resulting in intermittent hypoxia and sleep fragmentation caused by arousals. As described earlier, MS is a condition in which there is a constellation of obesity, insulin resistance, hypertension, and dyslipidaemia; factors which increase the risk of atherosclerotic vascular disease thus increasing the risk of cardiovascular and cerebrovascular events.

Recently, there has been growing interest in the interaction between OSA and metabolic dysfunction. In particular, OSA has been independently associated with insulin resistance, suggesting that OSA may be an important factor for the development of type 2 diabetes and the so called MS.

Though there is circumstantial evidence to implicate OSA in the development of MS, the causal relationship remains unproven. It has been hypothesized that in the setting of OSA and MS, there probably exists feed-forward relationship between the two which leads to further aggravation of both disorders. It has been proposed that the OSA may be one of the manifestations of MS[18,19]. Though several human studies suggest that the OSA is independently associated with insulin resistance and other components of the MS, published data are conflicting[25,26,27–31].

Parish et al.[32] and Sasanabe et al.[33] analyzed the severity of OSA and the proportion of subjects with hypertension (HTN), dyslipidaemia (DLP), hyperglycaemia, and metabolic syndrome (MS). The results are given in Tables 7, 8 and 9.

Our study reveals that with increase in severity of OSA the odds of having metabolic syndrome and hypertension increases. This is in par with the other 2 studies mentioned above. The prevalence in DLP also increases with increase in severity of OSA, though not in a linear fashion; this is again in par with the studies mentioned above.

In this study, each component of MS in relation to OSA has been studied. The aim was to recognize the component(s) of MS that is (are) most commonly associated with OSA. Clinically this would help to investigate patients with those clinical features of MS which might be due to underlying OSA.

A high index of suspicion is the most important factor to recognize OSA. Patients complaining of un-refreshing sleep, snoring, tiredness, poor concentration systemic hypertension, coronary vascular disease, congestive heart failure, cerebrovascular disease, glucose intolerance, impotence, obesity, pulmonary hypertension, gastro-oesophageal reflux, and dyslipidaemia should be enquired about sleep history. A simple method to assess daytime sleepiness would be the Epworth Sleepiness Score. In our study we found that ESS is a good tool to screen patients for OSA. In our study, the ESS was significantly higher in patients with OSA (P=0.0001). The results of ESS in subjects with OSA and controls are varying in different studies. Coughlin et al.[25] andGruber et al[26]. found significantly higher ESS in subjects with OSA as compared to controls while Sasanabe et al[33]. and Papanaset al.[34] found no such difference.

Systemic hypertension has been associated with OSA in many studies[17,28] including the Wisconsin Sleep Cohort study[27]. The Sleep Heart Health Study demonstrated convincingly that OSA is an independent risk factor for hypertension and all cardiovascular disease[32]. A few studies studied systolic and diastolic blood pressures separately. Systolic blood pressure (SBP) was found to be higher in subjects with OSA in some studies[25,33] and higher but not statistically significant in others[26,34,35]. Systolic blood pressure was significantly higher in subjects with OSA as compared to controls in our study (146.56 vs. 131.79; P=0.0001). Diastolic blood pressure (DBP) was also significantly higher in subjects with OSA in our study, though less significant as compared to SBP (87.44 vs. 81.10; P=0.014). DBP was found to be significantly higher in subjects with OSA in some studies[25,33,35] and not statistically differentin some studies[26,34].

There are studies quoting elevated fasting blood glucose (FBG)[34] and no elevation of FBG in subjects with OSA[25,26,33,35]. Increased insulin resistance was shown by elevated fasting plasma insulin and Homeostatic model assessment (HOMA) index in most of the studies [25,26,33,35]. However, in the Winconsin Sleep Cohort, a four-year follow up of 1387 participants failed to find increased incidence of diabetes mellitus in those with OSA defined by AHI >15[36].

In this study, FBG has been done to assess insulin resistance or impaired glucose metabolism. The number of subjects with impaired FBG was higher in the group with OSA as compared to controls (55.55% vs. 20.68%). After adjusting for age, BMI, and smoking status, FBG was significantly higher in subjects with OSA (P=0.004). Thus, the result of our study is consistent with most of the studies showing impaired glucose metabolism in patients with OSA.

In regards to waist circumference (WC), previous studies, again, have shown conflicting results. A few studies have found statistically significant difference in WC in subjects with OSA as compared to controls[25,33,] while other did not found so[26,34]. In our study, WC was higher in subjects with OSA but the difference lost statistical significance (P=0.567) after adjustment for body mass index (BMI) which was significantly higher in subjects with OSA as compared with controls (27.93 vs. 24.38; P=0.0001).

Parish et al.[32] in their retrospective study of 228 subjects (174 OSA vs. 54 controls) found no difference in the prevalence of dyslipidaemia in the two groups when a AHI cut off of =5 and also =10 was taken to define OSA. In their study TG and HDL levels were not assessed separately. Some other studies have found high TG levels in subjects with OSA as compared to controls[25,26,33] while others have not[34,35]. HDL was found low in subjects with OSA found no such difference[25,26,33-35].

In this study, TG levels were significantly higher in subjects with OSA but the difference became insignificant (CI -18.62, 3.24; P=0.166) after adjusting for age, BMI, and smoking status. HDL levels were lower in subjects with OSA (CI 0.28, 6.04; P=0.031). The difference in HDL levels remained significant after adjusting for age, BMI and smoking status.

To summarize, this study is probably the first study on this subject done in a South Indian population. The study groups (OSA vs. controls) were comparable in terms of age, sex distribution, smoking, and alcohol status. On comparison, the subjects with OSA had significantly higher systolic and diastolic blood pressure, fasting blood glucose and Epworth sleepiness scores. Serum triglycerides and waist circumferences were also higher in subjects with OSA but the difference became non-significant on adjustment for age, smoking status and, BMI. Serum HDL levels were significantly lower in subjects with OSA. This finding favours the concept that subjects with OSA have higher incidence of hypertension, impaired glucose metabolism and dyslipidaemia irrespective of obesity, thus favouring OSA as the underlying cause of MS.

Several epidemiological and observational studies[37,38] have demonstrated a strong, independent, etiologically significant continuum of cardiovascular risk across all levels of systolic and diastolic blood pressure. Likewise, several epidemiological studies have identified a low plasma HDL cholesterol concentration as a strong independent predictor of coronary heart disease in the general population[39,40]. In contrast, the trend towards higher triglyceride concentrations in subjects with OSA may not provide any additional information over HDL cholesterol about their long-term cardiovascular risk[39,40]. Furthermore, the metabolic syndrome is associated with a threefold increase in the risk of coronary heart disease and stroke and a significant increase in cardiovascular mortality[41,42]. The trend we demonstrated towards greater fasting blood glucose in subjects with OSA after adjusting for obesity and other known covariates may also contribute to the increased cardiovascular mortality associated with this group.

Overall, this study demonstrated that OSA is an important risk factor for the metabolic syndrome and therefore, for cardiovascular disorders. It is important to recognize patients suffering from OSA because treatment with CPAP and other modalities are effective in treating OSA and have beneficial effects on the metabolic syndrome as well[43].

The strengths of this study were: (1) Selection bias was eliminated as consecutive subjects were recruited. (2) The study groups were comparable in terms of age, sex distribution, smoking status, and alcohol intake status. (3) Though BMI was higher in the OSA group, this bias was eliminated after multivariate analysis. (4) The control group had undergone complete overnight polysomnography. The limitations of this study were: (1) Serum insulin levels, which can give a better idea of

insulin resistance, were not measured. (2) The number of subjects in the control arm were less.

Further studies are needed in this field with a larger sample size. Fasting serum insulin levels along with fasting blood glucose should be assayed in all the subjects. Other areas worthy of research include (1) Assess endothelial dysfunction and its relation to OSA. (2) Correlate the lowest level of oxyhaemoglobin during sleep study with metabolic syndrome. (3) Assess the effect of CPAP therapy on the components of MS, and (4) A long term follow up (5-10 years) for cardiovascular and cerebrovascular events in the study group patients.

Based on the analysis we found that the presence of OSA was independently associated with a nearly 3 ½ fold increased risk of having the metabolic syndrome (Table 10).

With recruited patients who attended the sleep clinic of the hospital, there could be a referral bias leading to a higher prevalence of MS in the study group. The prevalence of MS in community-based studies in India has been estimated to be around 43% and that of syndrome Z 4.5%[44]. The prevalence of sleep disordered breathing (SDB) in community has been estimated to be around 19.5% and that of OSAS (SDB with daytime hypersomnolence) as 7.5%[45].

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