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Evaluation of Obstructive Sleep Apnea in Metabolic Syndrome

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ABSTRACT

Background: There is bidirectional relationship between obstructive sleep apnea and metabolic disease. Sleep apnea results in intermittent hypoxia and sleep fragmentation, which lead to and exacerbate obesity and type 2 diabetes by increasing sympathetic activity, oxidative stress, inflammation and lipolysis. Moreover, metabolic disease can lead to or exacerbate sleep apnea through weight-dependent and physiology-dependent mechanisms.

Objective: The study aimed to explore the association between metabolic syndrome and obstructive sleep apnea (OSA).

Patients and Methods: This study was conducted at Sleep Unit of Chest Department Benha University Hospitals. This study enrolled 100 patients that were divided into two groups: Group A, which included 80 patients with metabolic syndrome as cases and group B that included 20 patients without metabolic syndrome as control group. All patients included in this study were subjected to lipid profile, HbA1c, overnight polysomnography (PSG).

Results: There was highly statistically significant positive correlation between apnea hypopnea index (AHI) and waist circumference, TG, HbA_1C, systolic blood pressure, diastolic blood pressure and sum all night desaturation. There was highly statistically significant negative correlation between AHI and HDL and minimal SPO_2. TG, HDL, Hb A1C and systolic and diastolic blood pressure were significant predictors for increase AHI and increase OSA severity.

Conclusion: OSA was highly prevalent in patients with metabolic syndrome, which is associated with increasing severity of OSA. Also, it is associated with poorer control of diabetes, hypertension, and dyslipidemia, which are all components of metabolic syndrome.

Keywords: Obstructive sleep apnea, Metabolic syndrome, High density lipoprotein–cholesterol, Triglyceride.

INTRODUCTION

The most common type of sleep-disordered breathing (SDB) is obstructive sleep apnea (OSA)[(1)]. OSA is characterized by recurrent collapse of the upper airway during sleep leading to oxygen desaturation with consecutive arousals from sleep [(2)]. The pattern of desaturation and re-oxygenation results in intermittent hypoxia, which is the main reason for metabolic dysfunction in SDB and is associated with the components of metabolic syndrome, which means hypertension, visceral obesity, pathological glucose tolerance, and dyslipidemias [(3)]. The pathological mechanisms of SDB that cause hypertension include baroreflex impairment as well as hypoxia-induced activation of chemoreflex sensors, which increase both the sympathetic tone and peripheral vascular resistance[(4)].

Endothelial dysfunction due to hypoxia and oxidative stress also contribute to cardiovascular disease and hypertension [(5)]. Obesity is strongly associated with OSA in a bidirectional manner: visceral obesity is a risk factor of OSA [(6)] and the accumulation of visceral fat reduces lung volume and thoracic compliance, thus causing more inspiratory effort that leads to pharyngeal occlusion [(7)].

At the same time, OSA leads to weight gain mostly due to endocrine dysregulation and physical inactivity because of daytime sleepiness [(8)]. Endocrine alterations and fragmentation of sleep are also involved in impaired glucose metabolism, leading to pathological glucose tolerance and insulin resistance [(9)]. Thus, SDB increases the risk of developing type 2 DM[(10)]. Dyslipidaemia, which is defined as an increase in triglyceride and a decrease in HDL levels, also contributes to intermittent hypoxia [(11)]. Treatment of SDB includes weight loss as well as therapy with continuous positive airway pressure (CPAP), which lowers blood pressure and improves glucose metabolism as well as the lipid profile [(12)].

The aim of the present study was to explore the association between metabolic syndrome and OSA.

PATIENTS AND METHODS

This study was conducted at Sleep Unit of Chest Department Benha University Hospitals in the period from 9/2020 to 1/2022. The study enrolled 100 patients that were divided into two groups: **Group A** that included 80 patients with metabolic syndrome as cases, and **Group B**, which comprised 20 patients without metabolic syndrome as control group.

Inclusion criteria:

1. For cases, patients of any gender above 30 and below 60 years of age.
2. Assessment of metabolic syndrome. According to the IDF criteria, metabolic syndrome is diagnosed in a patient having [(13)]: (I) Central obesity (waist circumference [WC] ≥ 90 cm in males and ≥ 80 cm in females), and (II) with any two of the following: (a) Serum triglycerides ≥ 150 mg/dL (1.7 mmol/L), or specific treatment for lipid abnormality. (b) Serum HDL cholesterol (HDL-c) < 40 mg/dL (1 mmol/L) in males and < 50 mg/dL (1.3 mmol/L) in females, or specific treatment for lipid abnormality. (c) Blood pressure (BP) in supine position (after 10 min rest): systolic BP ≥ 130 mmHg or diastolic BP

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≥ 85 mmHg, or on the treatment of previously diagnosed hypertension. (d) Fasting blood sugar (FBS) ≥ 100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes mellitus [13].

3. Subjects in the same age group who did not have metabolic syndrome, were included as controls.

Exclusion criteria

1. Patients with chronic respiratory problems.
2. Congestive heart failure.
3. Cerebrovascular accident within the preceding 30 days.
4. Patients on sedatives.
5. Patients on antipsychotics.

Methods:

All patients included in this study were subjected to the following:

- History taking and clinical examination.
- STOP-Bang Questionnaire, Epworth Sleepiness Scale, Berlin Questionnaire.
- ESR.
- Liver function tests.
- Kidney function tests.
- Lipid profile.
- HbA1c.
- Overnight Polysomnography (PSG).

Ethical consent:

An approval of the study was obtained from Benha University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The statistical analysis was conducted using SPSS version 21 software. The collected data were summarized in terms of mean ± SD and range for quantitative data and frequency and percentage for qualitative data. Comparisons between the different study groups were carried out using the Chi-square test (χ^2) and the Fisher Exact Test (FET) to compare proportions as appropriate. After the calculation of each of the test statistics, the corresponding distribution tables were consulted to get the "P" (probability value). Statistical significance was accepted at P value ≤ 0.05. A P ≤ 0.001 was considered highly significant (HS) while a P value > 0.05 was considered non-significant (NS).

RESULTS

The mean BMI was significantly higher in metabolic syndrome group (43.31 ± 9.5) than in control group (32.48 ± 6.81) (p=0.001). The mean age and waist circumference in the metabolic syndrome group were insignificantly higher than that in the control group (P=0.28, P=0.7 respectively).The mean Stop Bang in the metabolic group patients (4.65 ± 1.16), ranging from 2 to 7 was significantly higher than that in the control group (1.8 ± 0.89), ranging from 0 to 3 (P=0.001) **(Table 1)**.

Table (1): Comparison between the studied groups as regards demographic criteria

Variable		Metabolic syndrome group (no.=80)		Non-metabolic syndrome group (no.=20)		Test	P
		No.	%	No.	%		
Sex	**Male**	35	43.8%	10	50%	χ^2 =0.25	0.62
	Female	45	56.3%	10	50%		
		Mean ±SD (Range)		**Mean ±SD (Range)**			
Age (years)		51.14±9.03 (30 - 60)		48.62±9.88 (30 -60)		t=1.1	0.28
BMI (kg/m^2)		43.31±9.5 (31.6-76.2)		32.48±6.81 (20.5-44.6)		t=4.8	0.001
Waist circumference(cm)		111.39 ± 15.11 (89-143)		109.25 ± 23.16 (80-145)		t=0.4	0.7
STOP-Bang score		4.65 ± 1.16 (2 – 7)		1.8 ± 0.89 (0 – 3)		t=10	0.001

Table (2) shows the mean AHI, Hb A_1C and sum of all night desaturation were significantly higher in metabolic syndrome group (33.03 ± 26), (152.26 ± 15.32), (6.25 ± 1.24) and (25.71 ± 17.92) than that in the non-metabolic group patients (11.96 ± 9.5), (113 ± 22.3), (4.98 ± 1.28) and (10.74 ± 9.7) (p=0.001, 0.001, 0.001 and 0.001) respectively. The mean HDL and Min O_2were significantly lower in metabolic syndrome group (39.3 ± 9.1) and (78.6 ± 11.12) than that in the non-metabolic group patients (63.4 ± 14.9) and (84.35 ± 6.92) (p = 0.001 and p = 0.006) respectively. Regarding OSA severity, there was highly statically significant difference between metabolic and non-metabolic groups where majority of metabolic group patients reported severe degree of OSA (46.3%) compared with 5% in the non-metabolic group (p=0.003).

Table (2): Comparison between the studied groups as regard clinical, polysmnography and laboratory finding (N=100)

Variable		Metabolic syndrome group (no.=80)	Non-metabolic syndrome group (no.=20)	Total (N=100)	Test	P
		Mean ±SD	Mean ±SD	Mean ±SD		
AHI (event/hour)		33.03 ± 26	11.96 ± 9.5	28.8 ±25.1	Z=3.3	0.001
TG(mg/dL)		152.26 ± 15.32	113 ± 22.3	144.4 ± 23.1	t=7.4	0.001
HDL (mg/dL)		39.3 ± 5.1	63.4 ± 4.9	44.1 ± 4.2	t=6.9	0.001
Hb A_1C		6.25 ± 1.24	4.98 ± 1.28	5.99 ±1.34	t=4.1	0.001
Minimal spo2 during sleep		78.6 ± 11.12	84.35 ± 6.92	79.8 ± 10.6	t=2.9	0.006
Sum of all night desaturation (%)		25.71 ± 3.92	10.74 ± 2.7	22.7 ± 5.6	t=5.1	0.001
Snore		275.27 ± 6.32	241.9 ± 57.16	268.6 ± 54.32	Z=0.8	0.44
Base SPO_2 (before sleep)		93.53 ± 3.59	94.26 ± 2.56	93.7 ± 3.4	t=0.84	0.4
Bl.P- systole(mmHg)		138.25 ± 13.34	135 ± 17.55	137.6 ± 14.2	t=0.77	0.45
Bl.P-diastole(mmHg)		85.28 ± 9	84 ± 8.21	85 ± 8.8	t=0.57	0.57
OSA severity	**Normal (no. %)**	8 (10%)	6 (30%)	14 (14%)	χ^2 =13.7	0.003
	Mild (no. %)	18 (22.5%)	8 (40%)	26 (26%)		
	Moderate (no, %)	17 (21.2%)	5 (25%)	22 (22%)		
	Severe (no. %)	37 (46.3%)	1 (5%)	38 (38%)		
Central event	**-ve (no., %)**	78 (97.5%)	20 (100%)	98 (98%)	χ^2 =0.5	0.47
	+ve (no., %)	2 (2.5%)	0 (0%)	2 (2%)		

Table (3) shows descriptive characteristics of the study population, stratified according to AHI quartiles. Subjects with moderate and severe OSA were more likely to be older age, male, more obese and to have co-morbidities including dyslipidaemia (higher TG, lower HDL), uncontrolled DM (higher HA_1C) and higher blood pressure. Also, they were more likely to have higher sum desaturation all night. In contrast, they were more likely to have lower min. O_2 and base SPO_2**.**

Table (3): Patient characteristics according to sleep apnea severity

Variable	AHI quartiles				Test	P
	Normal 0- 5 (n=14)	Mild 5.1 – 14.9 (n=26)	Moderate 15 – 29.9 (n=22)	Severe ≥ 30 (n=38)		
Age (years)	44.9±8.8†$	45.3±10.4†$	55.4±5.3	53.7±7.4	F=10.3	0.001
Sex (male)	4 (28.6%)	9 (34.6%)	11 (50%)	21 (55.3%)	χ^2=4.5	0.21
BMI (kg/m^2)	36.5±10.1	39.3±9.5	42.7±12.3	43.2±8.2	F=2	0.11
TG(mg/dL)	128.7±19.9	133.4±27.9	144.6±22.3	157.6±10.9*#	F=10.7	0.001
HDL (mg/dL)	53.1±12.5	50.5±6.3	45.9±4.4	35.4±7*#†	F=11.1	0.001
Hb A_1C	5.1±1.4	5.7±1.1	5.3±0.99	6.9±1.15*#†	F=14.4	0.001
Min O_2 (%)	86.2±8.6	84.7±6.6	81.1±8	73.2±11.5*#†	F=11	0.001
SUM of all night desaturation (%)	4.4±0.9	10.1±4.9	19.5±8.8*#$	40.4±4*#†	F=66.9	0.001
Snore	213.1±236.4	281.7±189.4	249.4±208.3	291.1±249.5	F=0.5	0.69
Base SPO_2	94.6±3.5	95.2±2.2†	91.9±4.2	93.2±3.2	F=4.4	0.006
BL.p- systole (mm Hg)	130±16.2†	132.3±16	142.5±11.3	141.2±11.7	F=4.7	0.004
Bl.p-diastole (mmHg)	80±10.4	83.9±8	85.9±8	87.1±8.7	F=2.6	0.059

* Significant differences compared with normal group. † Significant differences compared with moderate group.
$ Significant differences compared with severe group. # Significant differences compared with mild group.

Table (4) shows that there was highly statistically significant positive correlation between AHI index and TG, Hb A_1C, systolic blood pressure, diastolic blood pressure and sum desaturation all night) (r=-0.419, p = 0.001) (r=-0.502, p = 0.001) (r=0.306, p = 0.006) (r=-0.264, p = 0.018)and (r=-0.873, p = 0.001) respectively. There was highly statistically significant negative correlation between AHI index and HDL and min O_2 (r=-0.469, p=0.001) and (r=-0.554, p=0.001).

Table (4): Correlation between AHI and sociodemographic, clinical and laboratory variables among metabolic syndrome patients (n=80)

AHI / Variables	Pearson's Correlation coefficient (r)	P value
Age (years)	0.22	0.051
BMI (kg/m^2)	0.073	0.517
TG(mg/dL)	0.419	0.001
HDL (mg/dL)	-0.469	0.001
HbA_1c	0.502	0.001
Min O_2 (%)	-0.554	0.001
SUM of all night desaturation (%)	0.873	0.001
Snore	0.084	0.458
Base SPO_2	-0.74	0.515
Bl.P- systole (mmHg)	0.306	0.006
Bl.P-diastole (mmHg)	0.264	0.018

ROC curve analysis of TG and HDL levels. Regarding TG, it is a valuable predictor of occurrence of increasing OSA severity. Area under curve (AUC) was determined as = 0.784, at a cut-off value of 141.5 mg/dL, and with a sensitivity of 89.5% and specificity of 61.3% **(Table 5)**.

Table (5): Receiver operating characteristic curve for cut off value of TG and HDL level to diagnose sever OSA

	TG (mg/dl)	HDL (mg/dl)
Cut off	**141.5**	**32.5**
Sensitivity (%)	**89.5%**	**63.2%**
Specificity (%)	**61.3%**	**11.3%**
AUC*	**0.784 (95% CI = 0.695–0.873)**	**0.183 (95% CI = 0.099 – 0.266)**
P value	**0.001**	**0.001**

DISCUSSION

This study explored the association between metabolic syndrome and OSA. So far, various studies have focused on determining the prevalence of metabolic syndrome in OSA patients and showing that metabolic syndrome is more prevalent in such patients than in the general population. This study, on the other hand attempted to examine the reverse association that is to determine the prevalence of OSA in patients with metabolic syndrome.

This study was conducted on 100 patients, 80% of them were metabolic syndrome patients and 20% were non-metabolic syndrome group and considered as control group. Fifty-five percent of participants were females and 45% were males. The mean age of studied participants was 50.63 ± 9.21 ranged from 30 years to 60 years? These results are in agreement with **Barreiro *et al.*** [14] who studied148 subjects; 104 (73%) were male and 37 (27%) women. The mean age was 54 ± 11 years.

The current study showed that the mean age and waist circumference in the metabolic group patients were insignificantly higher than that in the control group (P=0.28, P=0.7 respectively).The mean Stop-Bang in the metabolic group patients (4.65 ± 1.16), ranging from 2 to 7 was significantly higher than that in the control group (1.8 ± 0.89), ranging from 0 to 3 (P=0.001). According to **Shayestefar *et al.*** [15] based on the findings of the Stop-Bang questionnaire, a low risk of OSA was found in 712 drivers (75.1%) and a high risk of OSA was seen in 236 drivers (24.9%). Moreover, based on the definitions of ATP and IDF, the prevalence of Met S was found to be 392 (41.4%) and 497 (52.4%), respectively.

The current study, showed that the mean AHI, HbA_1c and sum of all night desaturation were significantly higher in metabolic syndrome. The mean HDL and minimal SPO_2 were significantly lower in metabolic syndrome group than that in the non-metabolic group patients. Regarding OSA severity, there was highly statistically significant difference between metabolic and non-metabolic groups where majority of metabolic group patients reported severe degree of OSA (46.3%) compared to 5% in the non-metabolic group (p=0.003). In accordance this result, **Chaudharya *et al.*** [16] found that mean AHI was 62.67 ± 35.22. Mild, moderate and severe category of OSA constituted 7.3%, 15.3% and 77.4% respectively. MS was found in 72.7% (365 out of 502) individuals with OSA. MS was found in 75.8%, 68.4 and 48.7% in severe, moderate and mild OSA patients respectively (p < 0.001). Females OSA patients had significantly high percentage (88.27%) of metabolic syndrome compared to males OSA patients (66.38%) (P< 0.001).

The current study showed descriptive characteristics of the study population, stratified according to AHI quartiles. Subjects with moderate and severe OSA were more likely to be older age, male, more obese and to have co-morbidities including dyslipidaemia (higher TG, lower HDL), uncontrolled DM (higher HbA_1c) and higher blood pressure. Also, they were more likely to have higher sum desaturation

all night. In contrast, they were more likely to have lower minimal SPO_2 and base SPO_2. Also, study by **Kim *et al.*** [13] showed that increase in waist circumference (Hazard ratio 1.99; 95% confidence interval 1.90–2.08) and TG level (HR: 1.32; 95% CI 1.28–1.37) were associated with a marked increase in the risk of OSAS. For the waist circumference component, there was a remarkable difference between men (HR: 2.00 [1.90, 2.10]) and women (HR: 1.68 [1.52, 1.86]). Among those in whom the criterion for Met S (i.e., presence of ≥ 3 of the 5 Met S components) was not met, there was a strong association of OSAS with waist circumference and TG level (HR: 2.22; 95% CI 2.10–2.34). Among patients with three Met S components, the three components associated with the highest risk of OSAS were large waist circumference, high TG level, and low HDL-C level (HR: 2.68; 95% CI 2.52–2.85). Among patients with four Met S components, the risk of OSAS was highest in those with the above combination plus hypertension (HR: 2.82; 95% CI 2.70–2.95**).** The OSAS group participants were more likely to have hypertension and dyslipidemia, and had a higher BMI, larger waist circumference, and higher levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C) and TG. However, the non-OSAS group patients were more likely to have DM, and also had a higher HDL-C level**.** The OSAS group participants were younger, more likely to be male compared to the non-OSAS group**.** The OSAS group showed higher BMI, hypertension, dyslipidemia, higher total cholesterol, higher triglyceride, higher waist circumference, higher LDL cholesterol, and lower HDL cholesterol, indicating association with Met S**.**

The current study, showed that there was highly statistically significant positive correlation between AHI and waist circumference, TG, HbA_1c, systolic blood pressure, diastolic blood pressure and sum desaturation all night. There was highly statistically significant negative correlation between AHI and HDL and minimal SPO_2. The Sleep Heart Health Study reported a significant correlation between OSA severity and TC concentration in younger males and HDL-C and TG concentrations in women [17]**.**

The current study showed that TG, HDL, HbA1c, systolic and diastolic blood pressure were significant predictors for increase AHI and increase OSA severity. Another study revealed that the mean serum TG levels in patients with OSA were significantly higher than in subjects without OSA. Also, as the severity of OSA increased, the mean serum TG levels increased. Similarly, the mean HDL levels in patients with OSA were lower than in subjects without OSA. These levels showed a downward trend with an increase in the severity of OSA, which was statistically significant. **Dubey *et al.*** [18] also noted similar findings, the mean serum TG levels in patients with mild, moderate, and severe OSA were 172.6, 180.86, and 214.91 mg/dL, respectively [18]**.** In another study, the mean serum TG in patients with OSA was 170.31 mg/dL, which was significantly higher than in subjects without OSA [19]**.**

ROC curve analysis of TG and HDL levels. Regarding TG, it is a valuable predictor of occurrence of increasing OSA severity. Area under curve (AUC) was determined as = 0.784, at a cut-off value of 141.5 mg/dL, and with a sensitivity of 89.5% and specificity of 61.3%. According to **Gündüz *et al.*** [21] found that TG and LDL concentrations were better predicted by AHI than by oxygen desaturation index. HDL-C was significantly reduced in the highest AHI quartile (mean _ SE (mg/dL): 48.8 _ 1.49 vs 46.50 _ 1.48; P = 0.002, AHI quartile I vs IV). Morbid obesity was associated with high TC and lower HDL-C values.

CONCLUSION

According to the results of this study, there was a bidirectional relationship between obstructive sleep apnea and metabolic disease. OSA was highly prevalent in patients with metabolic syndrome, which is associated with increasing severity of OSA. OSA was associated with poorer control of diabetes, hypertension, and dyslipidemia, which are all components of metabolic syndrome. Screening by questionnaires and sleep study are recommended for metabolic syndrome patients to assess sleep quality and presence of any sleep disordered breathing. Therefore, the need for screening metabolic syndrome patients for OSA has been reinforced by this study.

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Author contribution: Authors contributed equally in the study.

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