Pak. J. Chest Med. 2022;28(02)

Original Article

journal homepage: https:/www.pjcm.net/

Pakistan Journal of Chest Medicine

Official journal of Pakistan Chest Society

Chronic Obstructive Sleep Apnea: A Predictor of Abnormal Glucose Metabolism

Tayyaba Anis Chaudhry[1], Aysha Mushtaq[2]✉, Ayesha Zafar[3], Rubab Rameez[4], Tooba Jamal[5], Fatima Iqbal[6]

[1]Department of Physiology, Watim Medical and Dental College, Rawat, Rawalpindi – Pakistan [2]Department of Physiology, Islamic International Medical College, Rawalpindi – Pakistan [3]Department of Physiology, Dental College HITEC- IMS, Taxila – Pakistan [4]Department of Physiology, Islamabad Medical and Dental College, Barakahu, Islamabad- Pakistan [5]Department of Physiology, Shifa College of Medicine, Islamabad – Pakistan [6]Department of Physiology, Fauji Foundation Medical College, Islamabad – Pakistan

Corresponding Author:
Aysha Mushtaq
Department of Physiology,
Islamic International Medical College, Rawalpindi –Pakistan
E-mail: aysha.armughan@gmail.com

Article History:

Received:	Apr 22, 2022
Revised:	May 12, 2022
Accepted:	May 20, 2022
Available Online:	Jun 02, 2022

Author Contributions:
TAC AM conceived idea, AM drafted the study, AZ collected data, RR did statistical analysis and interpretation of data, TJ FI critical reviewed manuscript. All approved final version to be published.

Declaration of conflicting interests:
The authors declare that there is no conflict of interest.

How to cite this article:
Chaudhry TA, Mushtaq A, Zafar A, Rameez R, Jamal T, Iqbal F. Chronic Obstructive Sleep Apnea: A Predictor of Abnormal Glucose Metabolism. Pak J Chest Med. 2022;28(02):162-166.

ABSTRACT

Background: Metabolic syndrome (MS), a widely used term referring to the combination of hypertension, obesity, dyslipidemia, and insulin resistance impacts millions of individuals globally.

Objectives: The present study aimed to assess the chronic obstructive sleep apnea as apredictor of abnormal glucose metabolism.

Methodology: This cross-sectional study was conducted on 120 cases (60 cases of chronic obstructive sleep apnea (OSA) and 60 matched controls) in the Department of Physiology Pakistan Railway Hospital, Rawalpindi from April 2021 to March 2022. Patients who exhibited nocturnal symptoms such as snoring and shortness of breath were enrolled. Detailed information about their sleep patterns, medical background, and body mass index (BMI) was collected. A fasting blood sample was collected from all participants. Blood sugar levels were compared between the two groups, and the comparison was also conducted based on the severity of apnea, categorizing patients into mild, moderate, and severe apnea groups.

Results: The overall mean age of cases and control was 48.5 ± 2.64 years and 47.04 ± 2.82 years respectively. Out of 60 OSA cases, the incidence of mild, moderate, and severe OSA was 25% (n=15), 35% (n=21), and 40% (n=24) respectively. The overall mean Epworth sleep scale (ESS) among cases and control was 11.96 ± 3.8 and 4.48±1.78 respectively. The average fasting blood sugar (FBS) level was 111.82 ± 20.67 mg/dl in the cases group and 96.98 ± 28.82 mg/dl in the controls group, indicating a significant difference between the two groups (p=0.005). The frequency of individuals with abnormal glucose metabolism was significantly higher in the OSA (Obstructive Sleep Apnea) group (p=0.001).

Conclusion: The present study found that obstructive sleep apnea is linked to a greater disruption in glucose metabolism. Additionally, this disruption in glucose metabolism is associatedwith the severity of obstructive sleep apnea (OSA).

Keywords: Chronic Obstructive Sleep Apnea; Glucose Metabolism; Predictors

Introduction

Obstructive sleep apnea (OSA) is a condition on the rise,marked by recurring blockages in the upper airwayleading to intermittent periods of low oxygen levelsand fragmented sleep due to frequent awakenings. Lately,, there has been significant attention on the connection between OSA and metabolic issues. Specifically, OSA has been linked independently to insulin resistance, indicating that it might play a crucial role in the onset of type 2 diabetes and the constellation of conditions known as the metabolic syndrome (MS), which includes obesity, insulin resistance, hypertension, and dyslipidemia.[1,2] Numerous epidemiological studies have revealed that individuals who sleep less than 6.5 hours per night are at a higher risk of gaining weight over time.[3] OSA and sleep duration both significantly affect the insulin resistance irrespective of BMI.[4] Dyslipidemia, hypertension, abnormal metabolism, obesity, and hyperglycemia were associated with metabolic syndrome.[5] Obesity is directly related to the metabolic syndrome and obesity is considered as a risk factor for both metabolic syndrome and OSA. In contrast, metabolic syndrome and OSA are associated with each other irrespective of obesity.[6] Obstructive sleep apnea (OSA) is a condition characterized by recurrent upper airway blockages during sleep, lasting at least 10 seconds and accompanied by decreased blood oxygen levels and excessive daytime sleepiness (EDS).[7] In OSA, repeated episodes of apnea and hypopnea, along with decreased oxygen and increased carbon dioxide levels in the blood, have significant detrimental effects on various organ systems, particularly concerning metabolic and neurocognitive health. This condition leads to high morbidity and mortality rates in patients with OSA.[8,9] In Pakistan, research studies on obstructive sleep apnea (OSA) are scarce, and the majority of them rely on questionnaires.[10] However, in a previous studies, a high prevalence of metabolic syndrome and disruptions in lipid metabolism within the OSA population in our region was highlighted.[11] Therefore, the present study aimed to assess the obstructive sleep apnea as a predictor for abnormal glucose metabolism.

Objectives

The present study aimed to assess the chronic obstructive sleep apnea as a predictor of abnormal glucose metabolism.

Methodology

This cross-sectional study was carried out on 120 cases(60 cases of chronic obstructive sleep apnea (OSA) and 60 matched controls) in the Department of Physiology, Pakistan Railway Hospital, Rawalpindi from April 2021 to March 2022. Patients who exhibited nocturnal symptoms such as snoring and shortness of breath were enrolled. Detailed information about their sleep patterns, medical background, and body mass index (BMI) was collected. A fasting blood sample was collected from all participants. Blood sugar levels were compared between the two groups, and the comparison was also conducted based on the severity of apnea, categorizing patients into mild, moderate, and severe apnea groups.

Potential candidates for the study were individuals referred to the sleep lab for polysomnography (PSG) due to symptoms such as excessive daytime sleepiness, snoring, and witnessed apnea. A thorough physical examination was conducted, and the Epworth Sleepiness Scale (ESS) score was calculated to confirm the presence of excessive daytime sleepiness (EDS). An ESS score higher than 9 indicated the likelihood of sleep apnea. Fasting blood sugar (FBS) levels were determined using a spectrophotometric method, and some participants provided their FBS readings obtained from a glucometer. Abnormal glucose metabolism was considered in cases where FBS level of ≥100 mg/dl or individual was already using hypoglycemicmedications.

Results

The overall mean age of cases and control was 48.5±2.64 years and 47.04±2.82 years respectively. Out of 60 OSA cases, the incidence of mild, moderate, and severe OSA was 25% (n=15), 35% (n=21), and 40% (n=24) respectively. The overall mean Epworth sleep scale (ESS) among cases and control was 11.96±3.8 and 4.48±1.78 respectively. The average fasting blood sugar (FBS) level was 111.82±20.67 mg/dl in the cases group and 96.98±28.82 mg/dl in the controls group, indicating a significant difference between the two groups (p=0.005). The frequency of individuals with abnormal glucose metabolism was notably higher in the OSA (Obstructive Sleep Apnea) group (p=0.001). The abnormal glucose metabolism was significantly associated with apnea severity: the incidence of abnormal glucose metabolism in mild, moderate, severe, and control cases was 53.3% (n=8), 76.2% (n=16), 62.5% (n=15), and 30% (n=18) respectively. The average Apnoea-Hypopnoea Index (AHI) for the OSA group was 31.89±20.8, whereas it was recorded as zero for the control group since they did not experience any sleep disturbances. The severity of OSA is illustrated in Figure 1. Demographic details and baseline characteristics are shown in Table 1. Incidence of abnormal glucose metabolism among mild, moderate, severe, and control cases are depicted in Figure 2. Table 2 compare the normal and abnormal fasting blood glucose levels.

Table 1. Demographic details and baseline characteristics

Parameters	OSA Cases (N = 60)	Control (N = 60)	P-value
Age (years)	48.5 ± 2.64	47.04 ± 2.82	0.129
Weight (Kg)	88.6 ± 5.84	81.58 ± 4.98	0.069
Height (m)	1.68 ± 0.43	1.64 ± 0.39	0.392
BMI (Kg/m^2)	30.28 ± 2.13	28.94 ± 4.32	0.078
Fasting blood glucose level (mg/dl)	11.96 ± 3.8	4.48 ± 1.78	0.089

Discussion

The present study mainly focused on the chronic obstructive sleep apnea as a predictor for abnormal glucose metabolism and found that the frequency of individuals with abnormal glucose metabolism was notably higher in the OSA (Obstructive Sleep Apnea) significantly associated with apnea severity. We observed a positive linear relationship between the frequency of hyperglycemia and the severity of obstructive sleep apnea (OSA). The mean fasting blood sugar (FBS) value and the proportion of individuals with elevated FBS were significantly higher in the OSA group. The percentage of patients with elevated FBS or those on hypoglycemic medication was directly linked to the severity of OSA. These findings suggest that in OSA patients, factors other than obesity are contributing to the disturbed glucose metabolism, indicating a more complex interplay of mechanisms in the pathophysiology of this condition. Still, the pathophysiological mechanism between abnormal glucose metabolism and OSA is yet too determined. However, several potential mechanisms have been proposed for this association.[12] OSA patients often exhibit an increased production of reactive oxygen species (ROS) and elevated sympathetic tone which suggested mechanisms for this connection.[13]

Studies have also shown that the beta cells of the pancreas, responsible for insulin production, are highly sensitive to hypoxia. Moderate to severe apnea places excessive functional demands on these pancreatic beta cells, leading to exhaustion and impairment in their ability to secrete insulin over time.[14] Additionally, inadequate sleep can reduce glucose tolerance due to decreased brain glucose utilization.[15] Furthermore, Intermittent Hypoxia (IH) experienced in apnea is considered a significant link between OSA and altered glucose metabolism. IH can negatively impact glucose metabolism by increasing sympathetic nervous system activity, promoting systemic inflammation, altering counter-regulatory hormones, and directly causing damage to pancreatic beta cells.[16] These factors collectively contribute to the disturbance in glucose metabolism observed in individuals with OSA.

Insulin resistance are caused by sleep loss and chronic intermittent hypoxia associated with OSA.[17,18] Glucose metabolism variation associated with OSA are potentially caused by elevated sympathetic tone, reactive oxygen species generation, and pro-inflammatory state.[19,20] These factors collectively contribute to the disturbances observed in glucose metabolism in individuals affected by OSA.

An earlier study reported that metabolic syndrome and OSA are more dominant in middle-aged adults. The incidence of OSA in men and females varies from 9-14% and 4-7% respectively with advancement of age.[21]

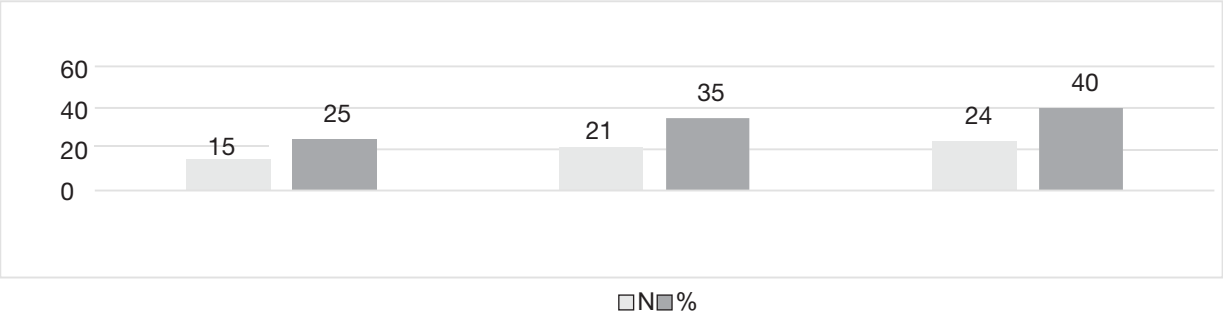

Figure 1. Severity of OSA (N=60)

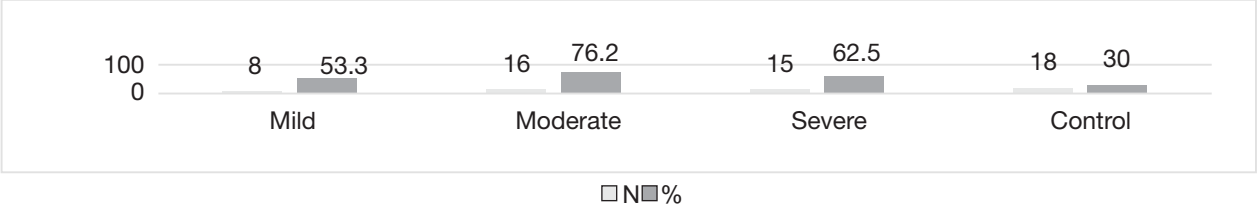

Figure 2. Incidence of abnormal glucose metabolism in mild, moderate, severe, and control cases (N=120)

Another study conducted on 2074 patients of polysomnography (PSG) associated with sleep- disordered breathing was independently related with metabolic syndrome.[22]

Gamaldo et al. showed in their study that obstructive sleep apnea (OSA) during REM (rapid eye movement) sleep is independently linked to a higher prevalence and incidence of hypertension. They observed a strong association between increasing quartiles of REM AHI (Apnoea-Hypopnoea Index during REM sleep) and hypertension, indicating a dose- response relationship between REM AHI and the likelihood of developing hypertension.[23]

Conclusion

The present study found that obstructive sleep apnea is linked to a greater disruption in glucose metabolism. Additionally, this disruption in glucose metabolism is associated with the severity of obstructive sleep apnea (OSA).

Table 2. compare the normal and abnormal fasting bloodglucose levels

	Mild OSA (N = 15)	Moderate OSA (N = 21)	Severe OSA (N = 24)
Normal FBS	7 (46.7%)	5 (23.8%)	9 (37.5%)
High FBS	8 (53.3%)	16 (76.2%)	15 (62.5%)
Total	15 (100.0%)	21 (100%)	24 (100%)

References

1. Vargas CA, Guzmán-Guzmán IP, Caamaño-Navarrete F, Jerez-Mayorga D, Chirosa-Ríos LJ, Delgado-Floody P. Syndrome metabolic markers, fitness and body fat is associated with sleep quality in women with severe/morbid obesity. Int J Environ Res Public Health. 2021;18(17):9294.
2. Qamar A, Haque Z, Baig MS, Owais M, Iffat W, Qamar Obstructive sleep apnoea: A predictor of abnormal glucose metabolism. Pak J Physiol. 2018;14(4):5-8.
3. Newbold R, Benedetti A, Kimoff RJ, Meltzer S, Garfield N, Dasgupta K, et al. Maternal sleep-disordered breathing in pregnancy and increased nocturnal glucose levels in women with gestational diabetes mellitus. Chest. 2021;159(1):356-65.
4. Javaheri S, Barbe F, Campos-Rodriguez F, Dempsey JA, Khayat R, Javaheri S, et al. Sleep Apnea: Types, Mechanisms, and Clinical Cardio-vascular Conseq-uences. J Am Coll Cardiol. 2017; 69:841–58.
5. Azarbarzin A, Sands SA, Stone KL, Taranto-Montemurro L, Messineo L, Terrill PI, et al. The hypoxic burden of sleep apnoea predicts cardiovascular diseaserelated mortality: the Osteoporotic Fractures in Men Study and the Sleep Heart Health Study. Eur Heart J. 2018;40:1149–57.
6. Senaratna CV, Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, et al. Prevalence of obstructive sleep apnea in the general population: a systematic review. Sleep Med Rev. 2017; 34:70–81.
7. Shivashankar R, Kondal D, Ali MK, Gupta R, Pradeepa R, Mohan V, et al. Associations of sleep duration and disturbances with hypertension in metropolitan cities of Delhi, Chennai, and Karachi in South Asia: cross-sectional analysis of the CARRS study. Sleep. 2017;40(9):zsx119.
8. Matsiki D, Deligianni X, Vlachogianni-Daskalopoulou E, Hadjileontiadis LJ. Wavelet-based analysis of nocturnal snoring in apneic patients undergoing polysomnography. In 2007 29th Annual International Conference of the IEEE Engineering in Medicine and Biology Society. 2007;1912-1915.

9. Di Mauro P, Cocuzza S, Maniaci A, Ferlito S, Rasà D, Anzivino R, Vicini C, Iannella G, La Mantia I. The effect of adenotonsillectomy on children's behavior and cognitive performance with obstructive sleep apnea syndrome: State of the art. Children. 2021;8(10):921.
10. Ren R, Covassin N, Zhang Y, Lei F, Yang L, Zhou J, Tan L, Li T, Li Y, Shi J, Lu L. Interaction between slow wave sleep and obstructive sleep apnea in prevalent hypertension. Hypertension. 2020;75(2): 516-23.
11. Zhang J, Zhuang Y, Wan NS, Tang X, Zhou W, Si L, et al. Slow-wave sleep is associated with incident hypertension in patients with obstructive sleep apnea: a cross-sectional study. J Int Med Res. 2020;48(9):0300060520954682.
12. Ahmad M. Makati D. Akbar S. Review of and Updates on Hypertension in Obstructive Sleep Apnea. Int J Hypertens. 2017; 1848375.
13. Jin ZN, Wei YX. Meta-analysis of effects of obstructive sleep apnea on the renin-angiotensin-aldosterone system. Journal of geriatric cardiology. J Geriatr Cardiol. 2016;13: 333–43.
14. Qamar A, Baig MS, Saifullah N. Obstructive sleep apnea and metabolic syndrome; causal association or coexistence? Med Forum. 2017;28(4):188–92.
15. Ormazabal V, Nair S, Elfeky O, Aguayo C, Salomon C, Zuñiga FA. Association between insulin resistance and the development of cardiovascular disease. Cardiovasc. Diabetol. 2018;17: 122.
16. Sun LM, Chiu HW, Chuang CY, Liu L. A prediction model based on an artificial intelligence system for moderate to severe obstructive sleep apnea. Sleep Breath. 2011;15:317-23.
17. Qamar A, Ali SI, Ghuman F, Owais M, Ahmed R. Effect of Obstructive sleep apnoea on lipid metabolism: Across sectional study from a tertiary care hospital of Pakistan. Pak J Physiol. 2017;13(4):7–10.
18. Isaac BT, Clarke SE, Islam MS, Samuel JT. Screening for obstructive sleep apnoea using the STOPBANG questionnaire and the Epworth sleepiness score in patients admitted on the unselected acute medical take in a UK hospital. Clin Med. 2017;17(6):499.
19. Ruel G, Martin SA, Lévesque JF, Wittert GA, Adams RJ, Appleton SL, et al. Association between multimorbidity and undiagnosed obstru-ctive sleep apnea severity and their impact on quality of life in men over 40 years old. Glob Health Epid Genom. 2018;3:e10.
20. Chiang CL, Chen YT, Wang KL, Su VY, Wu LA, Perng DW, et al. Comorbidities and risk of mortality in patients with sleep apnea. Ann Med. 2017; 49: 377–83.
21. Archontogeorgis K, Voulgaris A, Nena E, Strempela M, Karailidou P, Tzouvelekis A, et al. Cardiovascular risk assessment in a cohort of newly diagnosed patients with obstructive sleep apnea syndrome. Cardiol Res Pract. 2018; 6572785.
22. Chuang HH, Huang CG, Chuang LP, Huang YS, Chen NH, Li HY, et al. Relationships among and predictive values of obesity, inflammation markers, and disease severity in pediatric patients with obstructive sleep apnea before and after adenoton-sillectomy. J Clin Med. 2020; 9: 579.
23. Gamaldo C, Buenaver L, Chernyshev O, Derose S, Mehra R, Vana K, et al. OSA Assessment Tools Task Force of the American Academy of Sleep Medicine. Evaluation of clinical tools to screen and assess for obstructive sleep apnea. J of Clin Sleep Med. 2018;14(7):1239-44.