Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

Obstructive Sleep Apnea (OSA) in Patients with Type 2 Diabetes: A Prospective Study.

Khaja Ahmed Khan Imtiyaz[1], Sara Iqbal[2], Fahad Aleem[3]

[1]Consultant, Department of Internal Medicine, Gleneagles Global Hospital, Hyderabad- India.
[2]Junior Resident, Department of Pediatrics, Deccan College of Medical Sciences, Hyderabad- India.
[3]Assistant Professor, Department of Pulmonology, MNR Medical College and Hospital, Sangareddy- India.

Received: August 2018
Accepted: August 2018

ABSTRACT

Background: The incidence of obstructive sleep apnea (OSA) is more in type II diabetis patients as compared to healthy individuals. One of the links between OSA and type 2 diabetes is obesity and increased Body mass index is found to be associated with increased risk of metabolic syndrome, diabetes and OSA. OSA is found to have an adverse effect on overall glycemic control in type 2 diabetes and diabetics who have OSA have found to have relatively higher levels of HbA1c indicating poor long-term glycemic controls. As the diagnosis of OSA is usually delayed due to non-specific symptomatology any patient having disturbed sleep and daytime somnolence must be investigated for OSA. It is important from the perspective of treating physician to diagnose OSA in diabetics so as to optimally manage long term glycemic control. We conducted this study to find out the incidence of OSA in type 2 diabetics and its effect on long term glycemic control. **Methods:** This was a prospective observational study conducted in a tertiary care hospital in which 50 diagnosed cases of type 2 diabetes and suspected to be having Obstructive sleep apnea and came for evaluation were included on the basis of a predefined inclusion and exclusion criteria. Detailed history was taken and thorough clinical examination was done. OSA was diagnosed on the basis of polysomnography. The diagnosis of OSA was done on the basis of polysomnography OSA was defined as apnea-hypopnea index (AHI) > 5 per hour sleep. The incidence of OSA in diabetics and its effect on long term glycemic control was studied. Data was analyzed using SSPE 17.0 software. P value less than 0.05 was taken as significant for statistical purposes. **Results:** Out of 50 studied cases there were 32 (64%) were males and 18 (36%) were females with a M:F ratio of 1:0.56. Mean age of the studied cases was found to be 46.16+/- 8.53 years. 32 patients were obese (BMI =/> 30) and 10 patients were overweight (BMI=\> 25 but < 30). Common co-morbidities seen were hypertension (36%), hypertriglyceridemia (68%) and low HDL levels (44%). 24 (48%) patients were found to be having obstructive sleep apnea on the basis of polysomnography and history of associated symptoms. Raised BMI and Fasting blood sugar levels were found to be higher in patients with OSD (P<0.0001). There was a statistically significant difference in glycosylated Hemoglobin levels in patients with and without OSA. Patients with OSA were found to have higher HbA1c levels indicating poor glycemic control. **Conclusion:** Patients with Type 2 Diabetes are more at risk of developing OSA which is usually diagnosed late due to non-specific symptomatology. OSA is associated with poor long-term glycemic control in these patients. It is important from the perspective of treating physician to diagnose and treat OSA in diabetics for optimum management.

Keywords: Type 2 Diabetes, Obstructive Sleep Apnea, HbA1c, Long term glycemic control.

INTRODUCTION

Obstructive sleep apnea (OSA) is defined as a sleep disorder in which there is cessation or significant decrease in airflow in the presence of breathing efforts.[1] A classical feature of OSA is collapse of upper airway during sleep. This periodic cessation of sleep is associated with decreased SPO2 levels and a fairly disturbed sleep causing daytime somnolence. Before the significant sleep disturbance occurs and the patient seek consultation there is a long period of subtle signs consisting of snoring and episodes choking sensations due to which patient suddenly wakeup from sleep. In some cases, patient is brought for consultation because the sleep apnea is witnessed by relatives. These features may be associated with daytime somnolence leading to clinical features such as daytime fatigue, intellectual problems personality changes, depression and confusion during daytime.[2] OSA remains an underdiagnosed condition because of non-specific symptomatology and in many patients the only complaint is either snoring or disturbed sleep. A high index of suspicion is necessary on the part of treating physician for a prompt diagnosis and appropriate treatment. A detailed history with a special emphasis on episodes of disturbed sleep, daytime somnolence and sudden waking episodes should be enquired into.[3] A thorough clinical examination particularly determination of BMI, examination of mouth, nose

Name & Address of Corresponding Author
Dr. Fahad Aleem
Assistant Professor,
Department of Pulmonology,
MNR Medical College and Hospital,
Sangareddy, India.

and airways and cardiovascular and respiratory system examination must be carried out in all patients suspected to be having OSA because in many cases OSA is associated with various cardiovascular morbidities.[4] The diagnosis of OSA is usually confirmed by polysomnography which may show episodes of apnea during sleep. apnoea-hypopnea index (AHI) of ≥ 5/hr, together with the presence of snoring, nocturnal gasping or choking events, excessive daytime somnolence, daytime confusion and hypertension. A AHI ≥ 15/hr in a patient even if no accompanying signs or symptoms are present is diagnostic of OSA.[5]

The risk factors for OSA include obesity, central fat distribution, diabetes mellitus, hypothyroidism, postmenopausal status, chromosomal abnormalities (Downs syndrome), structural defects (macroglossia, neoplastic growth etc), alcoholism and use of sedatives.[6] The association of OSA and diabetes mellitus is interesting since both of them have a common risk factor in the form of obesity and the triad of obesity, diabetes and OSA has been the subject of immense interest amongst researchers.[7] Many epidemiological studies have shown that there is an increased incidence of OSA in patients with diabetes and conversely insulin resistance and frank diabetes is more common in patients with OSA.[8] The crucial link may be presence of hypoxemia causing insulin resistance. Not only there is an association between diabetes mellitus and OSA but also OSA worsen glycemic control in patients with diabetes and levels of glycosylated hemoglobin (HbA1c) were found to be uniformly higher in patients with diabetes having OSA in comparison with those having diabetes without OSA.[9] It is important from the perspective of treating physician to understand that the presence and severity of untreated OSA may cause worsening glycemic control in type 2 diabetic patients and poorly controlled diabetes in itself is a risk factors for insulin resistance and diabetes. A high index of suspicion is necessary in these patients and any diabetic patient having complaints like snoring and daytime somnolence should be investigated for presence of OSA.[10] These findings may have important clinical implications in the management of diabetes as appropriate management of OSA is essential in optimum management of diabetes.

MATERIALS AND METHODS

This was a prospective observational study conducted in a tertiary care hospital situated in a metropolitan city. 50 diagnosed cases of type 2 diabetes and suspected to be having Obstructive sleep apnea and came for evaluation were included in this study on the basis of a predefined inclusion and exclusion criteria. Informed consent was obtained from all the patients. Demographic details of patients were noted. A detailed history was taken in all the patients. Duration of diabetes, history of snoring, sleeping difficulty or disturbed sleep and history of episodes of choking was noted. Close family members were interviewed to assess pattern of sleep of the patients. Clinical examination was done in all the cases. Body mass index of all the patients was noted. Blood pressure, fasting and post-prandial blood sugar levels, lipid profile, 2D Echo and HbA1c was done in all the cases. The diagnosis of OSA was done on the basis of polysomnography OSA was defined as apnea- hypopnea index (AHI) > 5 per hour sleep. Apneas were defined as 90% or greater reduction in the airflow signal lasting 10 seconds or longer. Hypopneas were defined as a 30% or greater reduction in the airflow signal lasting at least 10 seconds and associated with a desaturation of 3% or greater. OSA were divided into mild (AHI ≥ 5 - <15), moderate (AHI ≥ 15 and ≤ 30) and severe (AHI > 30/hr) on the basis of AHI. The correlation between OSA and glycemic control was determined by HBA1c levels. The statistical analysis was done using SSPE 17.0 software. P value less than 0.05 was taken as significant for statistical purposes.

Inclusion Criteria

1. All diagnosed cases of type 2 diabetes who were referred for evaluation of obstructive sleep apnea.
2. Age of the patients should be more than 12 years.
3. Those who have given informed consent.

Exclusion Criteria

1. Age less than 12 years
2. Those who refused consent.
3. Critically ill patients.
4. Patients with co-morbid conditions which are likely to affect glycemic control.

RESULTS

The study consisted of 50 diagnosed cases of diabetes mellitus out of which 32 (64%) were males and 18 (36%) were females with a M:F ratio of 1:0.56.

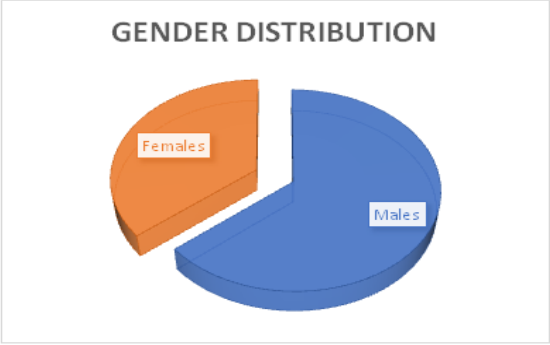

Figure 1: Gender Distribution of the studied cases.

The analysis of the age groups of the studied patients showed that there was 1 (2 %) patients in age group between 12 – 30 years, 11 (22 %) patients in age

group between 31 – 40 years and 20 (40 %) patients in age group between 41-50 years. 18 (36 %) patients were above 50 years of age. There was only 1 patient in adolescent age group. Mean age of the study group was 46.16+/- 8.53 years.

Table 1: Age groups of the studied cases.

Age groups	No. of Patients	Percentage
12 - 30 years	1	02.00%
31 - 40 years	11	22.00%
41 – 50 years	20	40.00%
> 50 years	18	36.00%
Total	50	100.00%
Mean Age ± SD =46.16+/- 8.53 years.		

Overweight and obesity was found to be one of the striking features of the studied cases. 42 (84%) patients were either overweight or obese. Only 8 (16%) patients had a normal BMI. The analysis of BMI of the studied cases showed that amongst 50 studied cases 32 patients were obese (BMI =/> 30) and 10 patients were overweight (BMI=\> 25 but < 30). Rest of the patients had BMI less than 25. The mean waist circumference and the mean neck circumference of the study population were 119.93 ± 12.36 cm and 17.34 ± 2.12 inches respectively.

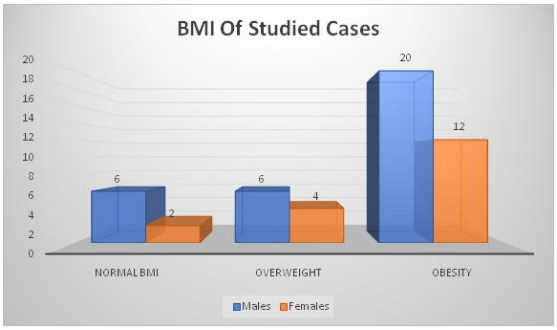

Figure 2: Body mass index of the studied cases.

The analysis of presence of co-morbid conditions showed that 42 (84%) patients were either overweight or obese. Hypertension was present in 18 (36%) patients. 34 (68%) patients had hypertriglyceridemia and 22 (44%) were found to be having low HDL levels. Hypothyroidism, history of sedative intake and alcoholism was present in 2 (4%), 3 (6%) and 5 (10%) respectively.

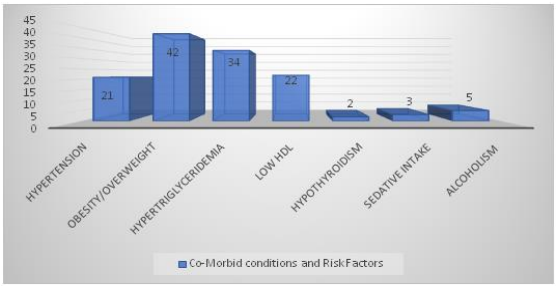

Figure 3: Co-Morbid conditions in the studied cases.

Out of the 50 studied cases with diabetes mellitus who were evaluated for OSA 24 (48%) patients were found to be having obstructive sleep apnea on the basis of polysomnography and history of associated symptoms. Out of 24 patients with OSA 12 patients had mild OSA while moderate and severe OSA was seen in 8 and 4 patients respectively.

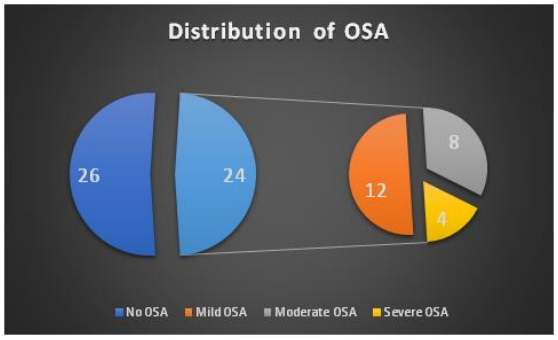

Figure 4: Distribution and severity of OSA in studied cases.

The analysis of variables like Mean Age, BMI, Systolic blood pressure and fasting blood sugar levels showed that there was a statistically significant difference in OSA and non OSA groups in Body mass index, systolic blood pressures and fasting blood sugar levels. The patients in OSA group were found to have a statistically significant higher BMI, systolic blood pressures and fasting blood sugar levels indicating that there was a positive correlation between poor glycemic control and incidence of OSA.

Table 2: BMI, Systolic blood pressure and Fasting Blood Glucose levels in studied cases.

Variable	OSA	NO OSA	P value
BMI (kg/m2)	30.24±2.14	26.60±1.98	<0.0001 (Significant)
Systolic BP (mm Hg)	128.96±12.23	122.78 ±14.12	<0.08(Not Significant)
Fasting Blood Sugar (mg/dl)	168.45±38.66	102.37±12.46	< 0.0001 (Significant)

In an attempt to whether incidence of OSA adversely affect the long-term glycemic control glycosylated hemoglobin levels of all the patients were done. It was found that glycosylated hemoglobin levels increased with increasing severity of OSA.

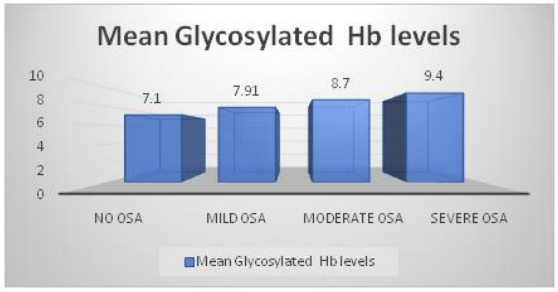

Figure 5: Mean Glycosylated Hb Levels in studied cases.

The comparison of mean glycosylated hemoglobin levels in diabetic patients with and without OSA showed that there was a statistically significant

difference in glycosylated Hemoglobin levels in these 2 groups indicating that presence of OSA adversely affect the glycemic control of diabetic patients with OSA.

Table 3: Mean Glycosylated hemoglobin levels in diabetic patients with and without OSA.

Mean Glycosylated Hb levels in diabetic patients without OSA	**7.10 +/- 0.16**	**P< 0.0001. Statistically Significant**
Mean Glycosylated Hb levels in diabetic patients with OSA	8.67 +/- 0.74.	

DISCUSSION

Obesity is the common factor associated with Obstructive sleep apnea and diabetes. It has been of immense interest for chest physicians and endocrinologists to find out whether there exists a connection between diabetes and obstructive sleep apnea independent of obesity. Various studies have found that the obstructive sleep apnea predisposes an individual for development of metabolic syndrome and diabetes and presence of diabetes predisposes an individual for development of obstructive sleep apnea.[11]

The mechanism of development of insulin resistance in patients with obstructive sleep apnea has also been investigated by many researchers. The probable mechanism by which obstructive sleep apnea causes insulin resistance is hypoxic injury to beta cells of pancreas and alterations in central pathways for glycemic control.[12] Sharma S K et al in their study involving 86 patients with obstructive sleep apnea found that out of 86 patients, metabolic syndrome was present in 75 patients.[13] When OSA in these patients was treated by CPAP, the patients showed significant mean decreases in systolic blood pressure, diastolic blood pressure, serum total cholesterol, non-high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides and glycated hemoglobin. There was also reversal of metabolic syndrome in 11 patients. The findings of this study was significant since it showed that management of OSD have a positive impact on glycemic control. Similar association between diabetes and OSA has also been reported Aronsohn R. S.et al.[14]

The correlation of obesity, diabetes and OSA is well established. Increase BMI is a significant risk factor for development of metabolic syndrome, diabetes and obstructive sleep apnea. In our study patients with OSA were found to have an increased BMI than patients who were not having OSA on polysomnography. The difference in BMI was found to be statistically significant. Wall et al conducted a large study to quantify the association between BMI and a recorded diagnosis of OSA in primary care for people aged 50 years.[15] The authors found that patients with a BMI recorded of 40+ kg/m2 were 27.39 times (95% CI 24.64 to 30.46) more likely to have OSA (p<0.0001). There was a lower prevalence of OSA with increasing age and levels of deprivation. Similar positive association between increased BMI and OSA has been reported by authors like Schwartz AR et al and Jehan S et al.[16,17]

In our study there was a direct relation between glycosylated hemoglobin level and patients with OSA. In patients with OSA there was a higher level of HbA1C than in patients without OSA. The difference was found to be statistically highly significant indicating that OSA adversely affect long term glycemic control. Many randomized controlled trials have come up with the conclusion that OSA is associated with increased HbA1c levels in diabetic as well as nondiabetic patients indicating that OSA is associated with increased insulin resistance and may predispose individuals for development of metabolic syndrome as well as diabetes. Papanas N et al in their study of 31 male patients diagnosed with OSAS by full polysomnography a significant correlation of fasting glucose and glycosylated hemoglobin (HbA1c) levels with arousal index.[18] Moreover, HbA1c levels were correlated with apnea hypopnea index, a widely accepted marker of the severity of OSAS, and with percentage of sleep time with saturation of hemoglobin with oxygen as measured by pulse oximetry. The authors such as Shpirer I et al and Malik J A et al,[19,20] reported that proper management of OSA (by CPAP) have a positive impact on glycemic control in patients with type 2 diabetes.

CONCLUSION

Obstructive sleep apnea is common in Type 2 Diabetes Mellitus patients. Diagnosis and management of OSA is crucial for proper management of diabetes. This is important from the point of management for primary care and chest physicians because failure to identify and treat OSA in these patients is associated with increased HbA1c level suggesting poor long-term glycemic control.

REFERENCES

1. Patil SP, Schneider H, Schwartz AR, Smith PL. Adult Obstructive Sleep Apnea: Pathophysiology and Diagnosis. Chest. 2007;132(1):325.
2. Seneviratne U, Puvanendran K. Excessive daytime sleepiness in obstructivesleep apnea: prevalence, severity, and predictors. Sleep Med. 2004 Jul;5(4):339-43.
3. Spicuzza L, Caruso D, Di Maria G. Obstructive sleep apnoea syndrome and its management. Therapeutic Advances in Chronic Disease. 2015;6(5):273-285.
4. Gozal D, Kheirandish-Gozal L. Cardiovascular Morbidity in Obstructive Sleep Apnea: Oxidative Stress, Inflammation, and Much More. American Journal of Respiratory and Critical Care Medicine. 2008;177(4):369-375.

5. Foroughi M, Razavi H, Malekmohammad M, Adimi Naghan P, Jamaati H. Diagnosis of Obstructive Sleep Apnea Syndrome in Adults: A Brief Review of Existing Data for Practice in Iran. Tanaffos. 2016;15(2):70-74.
6. Al Lawati NM, Patel SR, Ayas NT. Epidemiology, risk factors, and consequences of obstructive sleep apnea and short sleep duration. Prog Cardiovasc Dis. 2009 Jan-Feb;51(4):285-93.
7. Pamidi S, Tasali E. Obstructive Sleep Apnea and Type 2 Diabetes: Is There a Link? Frontiers in Neurology. 2012;3:126.
8. Chasens ER, Weaver TE, Umlauf MG. Insulin resistance and obstructive sleep apnea: is increased sympathetic stimulation the link? Biol Res Nurs. 2003 Oct;5(2):87-96.
9. Reichmuth KJ, Austin D, Skatrud JB, Young T. Association of Sleep Apnea and Type II Diabetes: A Population-based Study. American Journal of Respiratory and Critical Care Medicine. 2005;172(12):1590-1595.
10. Punjabi NM, Shahar E, Redline S, Gottlieb DJ, Givelber R, Resnick HE. Sleep-disordered breathing, glucose intolerance, and insulin resistance: the Sleep Heart Health Study. Am J Epidemiol2004;160:521–530.
11. Gerber PA, Rutter GA. The Role of Oxidative Stress and Hypoxia in Pancreatic Beta-Cell Dysfunction in Diabetes Mellitus. Antioxidants & Redox Signaling. 2017;26(10):501-518. doi:10.1089/ars.2016.6755.
12. Pallayova M, Lazurova I, Donic V. Hypoxic damage to pancreatic beta cells--the hidden link between sleep apnea and diabetes. Med Hypotheses. 2011 Nov;77(5):930-4.
13. Sharma SK, Agrawal S, Damodaran D, Sreenivas V, Kadhiravan T, Lakshmy R, JagiaP, Kumar A. CPAP for the metabolic syndrome in patients with obstructive sleep apnea. N Engl J Med. 2011 Dec 15;365(24):2277-86.
14. Aronsohn RS, Whitmore H, Van Cauter E, Tasali E. Impact of untreated obstructive sleep apnea on glucose control in type 2 diabetes. Am J Respir Crit Care Med. 2010 Mar 1;181(5):507-13.
15. Wall H, Smith C, Hubbard R. Body mass index and obstructive sleep apnoea inthe UK: a cross-sectional study of the over-50s. Prim Care Respir J. 2012 Dec;21(4):371-6.
16. Schwartz AR, Patil SP, Laffan AM, Polotsky V, Schneider H, Smith PL. Obesity and obstructive sleep apnea: pathogenic mechanisms and therapeutic approaches. Proc Am Thorac Soc. 2008 Feb 15;5(2):185-92.
17. Jehan S, Zizi F, Pandi-Perumal SR, et al. Obstructive Sleep Apnea and Obesity: Implications for Public Health. Sleep medicine and disorders : international journal. 2017;1(4):00019.
18. Papanas N, Steiropoulos P, Nena E, Tzouvelekis A, Maltezos E, Trakada G,Bouros D. HbA1c is associated with severity of obstructive sleep apnea hypopnea syndrome in nondiabetic men. Vasc Health Risk Manag. 2009;5:751-6.
19. Shpirer I, Rapoport MJ, Stav D, Elizur A. Normal and elevated HbA1C levels correlate with severity of hypoxemia in patients with obstructive sleep apnea and decrease following CPAP treatment. Sleep Breath. 2012 Jun;16(2):461-6.
20. Malik JA, Masoodi SR, Shoib S. Obstructive sleep apnea in Type 2 diabetes and impact of continuous positive airway pressure therapy on glycemic control. Indian J Endocrinol Metab. 2017 Jan-Feb;21(1):106-112.

How to cite this article: Imtiyaz KAK, Iqbal S, Aleem F. Obstructive Sleep Apnea (OSA) in Patients with Type 2 Diabetes: A Prospective Study. Ann. Int. Med. Den. Res. 2018; 4(5):ME27-ME31.

Source of Support: Nil, **Conflict of Interest:** None declared