Sleep Apnea Prevalence and Severity among Patients with Type II Diabetes Mellitus

Amr Abul-hasan[a], Suzan Salama[b], Hoda Makhlouf[b], Mohammed Zein El-deen[c], Shazly Baghdady[a]

[a]Chest Diseases Department, Faculty of Medicine, Aswan University, Aswan, Egypt.
[b]Chest Diseases Department, Faculty of Medicine, Assiut University, Assiut, Egypt.
[c]Internal Medicine Department, Faculty of Medicine, Assiut University, Assiut, Egypt.

Abstract

Background: The relationship between sleep disorders and diabetes is bidirectional; sleep disorders can raise the risk of developing insulin resistance, while diabetes would worsen sleep quality.

Objectives: Assessment of the prevalence and severity of sleep apnea among patients with type II diabetes mellitus.

Patients and Methods: a prospective cross-sectional study was carried out on 45 cases with type II diabetes mellitus that were either admitted in Aswan University hospital or sought medical advice in the out-patient clinics during the period from 2017 to 2019. For every patient, the demographic and clinical data were collected, blood glucose levels and HBA1c were measured and full night attended polysomnography was done.

Results: 77.78% of the diabetic cases had sleep apnea syndrome. The most common pattern was obstructive sleep apnea (82.86%). Apnea hypopnea index, obstructive sleep apnea and mixed sleep apnea were considerably higher among cases who had clinical picture of neuropathy compared to those without clinical picture of neuropathy. There was a moderate positive correlation between HbA1c with both AHI (P =0.005, r= 0.464) and obstructive sleep apnea (P value 0.016, r= 0.405). Furthermore, there was a mild positive correlation between HbA1c and percentage of time spent with oxygen saturation <90% (TST< 90%) (P =0.022, r =0.385).

Conclusion: The prevalence of sleep apnea and its severity is high among patients with type II diabetes mellitus.

Keywords: Sleep apnea, Diabetes mellitus, Sleep disorders.

Introduction

Type II diabetes mellitus (T2DM) is a metabolic disease characterized by decreased insulin sensitivity and increased insulin resistance, Beta cell malfunction, and raised hepatic glucose production(**Ota et al., 2019**).

Diabetes mellitus has grown to be a main public health concern with incidence rates rising globally at an alarming rate. The global prevalence of the disease in adults over 18 years old is expected to double, from 4.3% in 2010 to a predictable 8.5% in 2030 (**Bani-issa et al., 2018**).About 400 million peoples living with diabetes mellitus worldwide with an approximate 46.3% of them are being undiagnosed. This number projected to increase by the year of 2035 by 55% with the Middle East been 2ndregion with the highest expected increase worldwide(**Alshehri et al., 2018**).

Sleep disordered breathing (SDB) is a spectrum of disorders consisting of upper airway resistance syndrome, snoring, and sleep apnea. Sleep apnea can be obstructive, central or mixed (**Foldvary-Schaefer and Waters, 2017**).Obstructive sleep apnea (OSA) is the most common type of sleep disordered breathing and one of the most important disorders recognized in the last 50 years. Obstructive sleep apnea is characterized by upper airway instability during sleep, which leads to recurrent upper airway obstruction causing either complete or partial cessation of airflow (**Holt et al., 2019**).

The relationship between sleep disorders and diabetes is dual-sided, chronic sleep disturbances would raise the risk of developing insulin resistance, while diabetes would worsen the quality of sleep (**Mok et al., 2017**). A positive association between obstructive sleep apnea severity and diabetes mellitus was confirmed during the follow up period over 12 years (**Nagayoshi et al., 2016**).This study was performed to assess the prevalence and severity of sleep apnea among patients with type II diabetes mellitus and to assessthe relation between the severity of sleep apnea and the long-term control of type II diabetes mellitus.

Patients and Methods

This study is a prospective cross-sectional study. It was performed in Aswan University Hospital (including Chest Diseases and Internal Medicine Departments), during the period from2017 to 2019. The patients included in this study if they ≥ 18 years old and had type II diabetes diagnosedbased on the fasting glucose values, 2-hour post-load glucose values and level of HbA1c ≥6.5% (**Kerner et al., 2014**).

The patients either admitted to Aswan University hospital or sought medical advice in the outpatient clinic (chest and internal medicine clinics).The patients with associated pulmonary diseases such as chronic obstructive pulmonary diseases (COPD), asthma, interstitial lung disease, and bronchiectasis were excluded from the study. The study was approved by the Faculty of Medicine Ethics Committee, Aswan University (IRB number: aswu/42/12/15) and an informed written consent was obtained from all the patients.

All the patients subjected to the following:

-Full history taking including history suggestive of sleep disordered breathing, diabetes mellitus and neurological disorders.

-Complete clinical examination including hemodynamic data and neurological examination.

-Anthropometric measures: BMI, neck circumference.

-Chest X-ray.

-Pulmonary function tests.

-Blood glucose level and HBA1c measurement.

-Full night attended polysomnography (PSG) was done in the sleep unit of chest department of Aswan University hospital using Polysomnography (Nihon Kohden`s Polysmith, California, USA) with a full 10-20 montage, 8 bipolar inputs, 6 DC channels, bedside impedance checking, designated channels for electrooculogram (EOG), chin, and 3 electroencephalogram (EEG) channels with a dedicated reference. The PSG amplifier has a built-in pressure transducer and SpO_2. The PSG data collected included: apnea hypopnea index (AHI), desaturation index (DI), average oxygen level, minimum oxygen level, time spent below 90% (TST<90). AHI is calculated as the

number of apnea and hypopnea events per hour of sleep. Sleep apnea is diagnosed if AHI score ≥ 5 with sleep apnea symptoms or if AHI ≥ 15 without sleep related symptoms. The severity is defined as mild for AHI score ≥5 - <15/hr, moderate for AHI score ≥15 and ≤30/hr, and severe for AHI score >30/hr **(Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep, 2009).**

Statistical analysis

Statistical analysis was done by SPSS, version 25 (IBM Inc., Armonk, New York, USA). Non-parametric tests were utilized in the current study. The correlation between different parameters was done using Pearson test. P≤ 0.05 deliberated statistically important.

Results

The study enrolled 45 cases. Female patients were 30 cases (66.7%) were females, while 15 cases (33.3%) were males. The mean age was 57.33 ± 12.10. The rest of demographic data and anthropometric measures were shown in Table (1).

Table (2) illustrates sleep disordered breathing among patients with type II diabetes mellitus, where

sleep apnea was diagnosed in 35 cases (77.78%). Regarding the type of sleep apnea, patients who had obstructive sleep apnea syndrome were 29 (82.86%), while patients who had central sleep apnea were 6 (17.14%). Moreover, according to the severity of sleep apnea, the patients who had mild sleep apnea were 2 (5.7%), moderate sleep apnea were 7 (20%), while patients who had severe sleep apnea were 26 (74.29 %).

The patients included in the study were categorized according to the clinical picture of neuropathy (history of numbness of both hands and feet, stock and gloves hypoesthesia and diminished deep reflexes on examination) into two groups; a group of patients with clinical picture of neuropathy and a group of patients without clinical picture of neuropathy. Cases with clinical picture of neuropathy had significantly higher AHI (P = 0.031), obstructive sleep apnea (P= 0.045) and mixed sleep apnea (P = 0.013) in comparison to those without clinical picture of neuropathy, as illustrated in Table (3).

There was a moderate positive correlation between HbA1c with both AHI (P =0.005, r= 0.464) and obstructive sleep apnea (P value 0.016,

r= 0.405). Furthermore, there was a mild positive correlation between HbA1c and percentage of time spent with oxygen saturation <90% (TST<90%) (P =0.022, r =0.385).

Table 1. Demographic data and anthropometric measures of the patients included in the study (N= 45):

Variables	DM (45)	
	No.	%
Gender:		
Male	15	33.3%
Female	30	66.7%
Smoking status:		
Non-smoker	33	73.3%
Smoker	12	26.7%
	Mean ± SD	
Age (years)	57.33 ± 12.10	
BMI (kg/m^2)	38.82 ± 10.37	
Neck circumference (cm)	41.64 ± 5.46	
MAP	102.74 ± 14.79	

Data expressed as mean ± SD and number (%). BMI: body mass index, MAP: mean arterial pressure.

Table 2. The frequency and severity of sleep apnea among the study population (N= 45).

Final diagnosis	DM (N= 45)	
	N	%
Sleep apnea	35	77.78
Obstructive sleep apnea syndrome	29	82.86
Central sleep apnea	6	17.14
Mild	2	5.71
Moderate	7	20
Severe	26	74.29

Data expressed as number (%).DM: diabetes mellitus.

Table 3. Comparison of respiratory events between patients with clinical picture of neuropathy and those without clinical picture of neuropathy (N= 45).

Variables	Clinical picture of neuropathy		P-value
	Yes (17)	No (28)	
AHI (event/hr)			
Mean ± SD	52.82 ± 33.01	36.07 ± 41.98	**0.031***
Obstructive sleep apnea			
Mean ± SD	82.86 ± 96.11	51.16 ± 107.88	**0.045***
Central sleep apnea			
Mean ± SD	12.92 ± 21.84	11.00 ± 1.41	0.125
Mixed sleep apnea			
Mean ± SD	18.88 ± 22.02	2.00 ± 1.41	**0.013***
Hypopnea:			
Mean ± SD	133.18 ± 91.86	124.88 ± 129.01	0.314

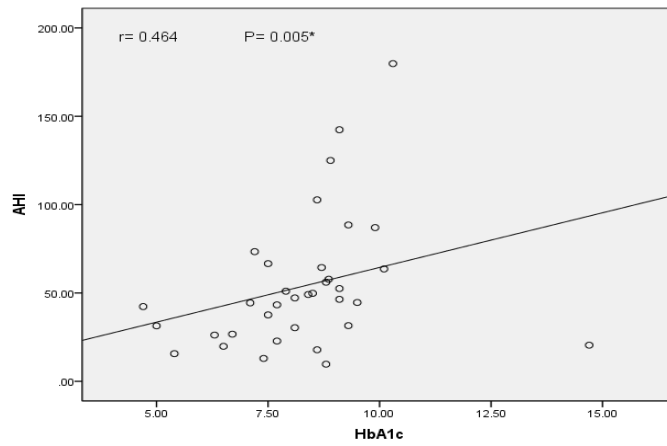Data expressed as mean ± SD. AHI: Apnea hypopnea index.

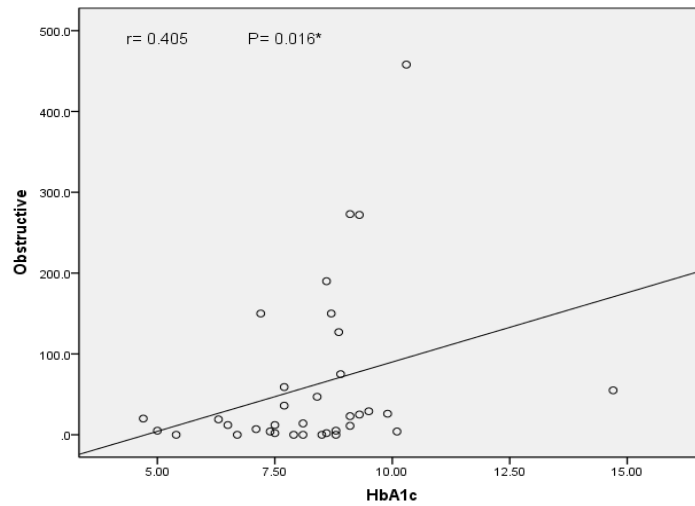**Fig.1. Positive correlation between HbA1c and AHI**

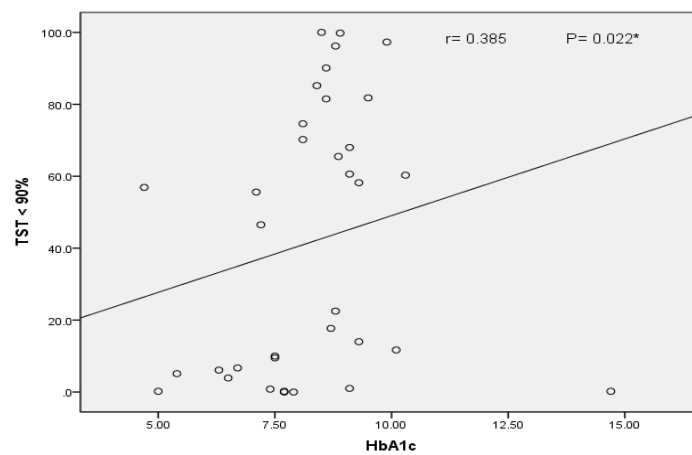**Fig.2. Positive correlation between HbA1c and obstructive apnea**

Fig.3. Positive correlation between HbA1c and TST<90%

Discussion

The current study demonstrated that 77.78% of patients with diabetes mellitus had sleep apnea and the most common pattern of sleep apnea was obstructive sleep apnea syndrome. Similarly, **Zhang et al. (2016)** found that 60% of cases with type II diabetes mellitus had sleep apnea, based on a transportable sleep monitoring device. Moreover, **Rajan et al. (2015)**concluded that patients with type II diabetes mellitus had a suggestively high prevalence of obstructive sleep apnea syndrome (23–86%).

A retrospective, population-based study of cases with type II diabetes mellitus in the primary care setting discovered that 18% of the study population had obstructive sleep apnea, diagnosed based on polysomnography (**Lee et al., 2019**).Furthermore, previous studies showed that the prevalence of obstructive sleep apnea was high among people with type II diabetes mellitus; it was53.2% (**Alshehri et al., 2018**)and 58-86% (**Siwasaranond et al., 2018**).The current study observed that the majority of sleep apnea cases among the study population were

moderate-to-severe in grading. **Amin et al. (2017)** similarly summarized that the prevalence of moderate-to-severe obstructive sleep apnea in cases with diabetes mellitus was 23.8%–70%.

The current study also noticed that AHI was higher in the group of patients who had clinical picture of neuropathy compared with those without clinical picture of neuropathy (P value= 0.031). A previous study showed substantial increase in sleep apnea syndromes in diabetic peripheral neuropathy cases compared to diabetic neuropathy free patients and healthy control (P value< 0.0001) (**Bahnasy et al., 2018**).On the other hand, **Meng et al. (2016)**found no relation between neuropathy in diabetic cases and the presence of sleep complaints. This diverse result may be due to their dependence on a subjective sleep quality questionnaire without using of objective polysomnography.

The present study summarized that obstructive and mixed apnea were more common than other respiratory events among patients who had clinical picture of peripheral neuropathy. **Nagayoshi et al. (2016)** observed that obstructive sleep apnea is the main

sleep respiratory disorder in their studied diabetic peripheral neuropathy cases. **Lecube et al. (2015)** found that type II diabetes mellitus cases with diabetic peripheral neuropathy were more likely to have not only central sleep apnea, but also obstructive sleep apnea, than those without it.

In this study, there was a mild positive correlation between HbA1c and TST< 90% (P =0.022, r =0.385). These results were consistent with **Lecube et al. (2015)**who revealed that patients with type II diabetes mellitus showed two-fold increase in the percentage of time spent with oxygen saturation <90% (P value <0.001).Furthermore, **Doumit et al. (2016)** reported that patients with type II diabetes mellitus had higher rates of oxygen desaturation events than subjects without diabetes mellitus.

Conclusion

The prevalence of sleep apnea is high among patients with type II diabetes mellitus. The most common pattern of sleep apnea among patients who have type II diabetes mellitus is obstructive sleep apnea syndrome. AHI, obstructive sleep apnea and mixed sleep apnea are significantly higher in the patients who have clinical picture

of neuropathy compared to those without clinical picture of neuropathy. HbA1c has a positive correlation with AHI, obstructive sleep apnea and the percentage of time spent with oxygen saturation <90%.

Abbreviations

AHI: Apnea hypopnea index; COPD: Chronic obstructive pulmonary diseases; DI: Desaturation index; DM: Diabetes mellitus; EEG: Electroencephalogram; EOG: Electrooculogram; HbA1c: Haemoglobin A1C; OSA: Obstructive sleep apnea; SDB: Sleep disordered breathing; PSG:Polysomnography; TST<90: time spent below 90%.

References

Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine, 2009. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. Journal of clinical sleep medicine, *5*(3), pp.263-276.

Alshehri, M.A., Alharthi, S.R., Alsuwat, A.A. and Alswat, K.A., 2018. Clinical characteristics of type 2 diabetics who are at high risk for

obstructive sleep apnea. Medical Archives, *72*(4), p.249.

Amin, A., Ali, A., Altaf, Q.A., Piya, M.K., Barnett, A.H., Raymond, N.T. and Tahrani, A.A., 2017. Prevalence and associations of obstructive sleep apnea in South Asians and White Europeans with type 2 diabetes: a cross-sectional study. *Journal of* clinical sleep medicine, 13(4), pp.583-589.

Bahnasy, W.S., El-Heneedy, Y.A.E., El-Seidy, E.A.S., Labib, N.A.A. and Ibrahim, I.S.E., 2018. Sleep disturbances in diabetic peripheral neuropathy patients: a clinical and polysomnographic study. The Egyptian journal of neurology, psychiatry and neurosurgery, *54*(1), pp.1-7.

Bani-issa, W., Al-Shujairi, A.M. and Patrick, L., 2018. Association between quality of sleep and health-related quality of life in persons with diabetes mellitus type 2. Journal of clinical nursing, *27*(7-8), pp.1653-1661.

Doumit, J. and Prasad, B., 2016. Sleep apnea in type 2 diabetes. Diabetes Spectrum, 29(1), pp.14-19.

Foldvary-Schaefer, N.R. and Waters, T.E., 2017. Sleep-disordered breathing. CONTINUUM: Lifelong Learning in Neurology, *23*(4), pp.1093-1116.

Holt NR, Downey G, Naughton MT, 2019. Perioperative considerations in the management of obstructive sleep apnoea. Medical Journal of Australia. 211(7):326-32.

Kerner W, Brückel J, 2014. Definition, classification and diagnosis of diabetes mellitus. Exp Clin Endocrinol Diabetes.122(7):384-6.

Lecube A, Sampol G, Hernández C, Romero O, Ciudin A, Simó R, 2015. Characterization of sleep breathing pattern in patients with type 2 diabetes: Sweet Sleep Study. PLoS One. 11;10(3):e0119073.

Lee, C.P., Kushida, C.A. and Abisheganaden, J.A., 2019. Epidemiological and pathophysiological evidence supporting links between obstructive sleep apnoea and type 2 diabetes mellitus. Singapore medical journal, 60(2), p.54.

Meng, L.L., Liu, Y., Geng, R.N., Tang, Y.Z. and Li, D.Q., 2016.

Association of diabetic vascular complications with poor sleep complaints. Diabetology & metabolic syndrome, *8*(1), pp.1-7.

Mok, Y., Tan, C.W., Wong, H.S., How, C.H., Tan, K.L.A. and Hsu, P.P., 2017. Obstructive sleep apnoea and Type 2 diabetes mellitus: are they connected?. Singapore medical journal, *58*(4), p.179.

Nagayoshi, M., Punjabi, N.M., Selvin, E., Pankow, J.S., Shahar, E., Iso, H., Folsom, A.R. and Lutsey, P.L., 2016. Obstructive sleep apnea and incident type 2 diabetes. Sleep medicine, *25*, pp.156-161.

Ota, H., Fujita, Y., Yamauchi, M., Muro, S., Kimura, H. and Takasawa, S., 2019. Relationship between intermittent hypoxia and type 2 diabetes in sleep apnea syndrome. International journal of molecular sciences, *20*(19), p.4756.

Peña-Zarza, J.A., De la Peña, M., Yañez, A., Bauça, J.M., Morell-Garcia, D., Caimari, M., Barceló, A. and Figuerola, J., 2018. Glycated hemoglobin and sleep apnea syndrome in children: beyond the apnea–hypopnea index. Sleep and Breathing, *22*(1), pp.205-210.

Rajan P, Greenberg H, 2015. Obstructive sleep apnea as a risk factor for type 2 diabetes mellitus. Nature and Science of Sleep. 7:113.

RusuA, Bala CG, Craciun AE, Roman G, 2017. HbA1c levels are associated with severity of hypoxemia and not with apnea hypopnea index in patients with type 2 diabetes: Results from a cross-sectional study: 2 HbA1c. Journal of diabetes. 9(6):555-61.

Siwasaranond, N., Nimitphong, H., Manodpitipong, A., Saetung, S., Chirakalwasan, N., Thakkinstian, A. and Reutrakul, S., 2018. The relationship between diabetes-related complications and obstructive sleep apnea in type 2 diabetes. Journal of diabetes research, 2018.

Zhang, R., Zhang, P., Zhao, F., Han, X. and Ji, L., 2016. Association of diabetic microvascular complications and parameters of obstructive sleep apnea in patients with type 2 diabetes. Diabetes technology & therapeutics, 18(7), pp.415-420.