



The Association between Obstructive Sleep Apnea and Glycated Haemoglobin A1c (HbA1c) Level in Diabetes Mellitus Type II Patient



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ABSTRACT

Background: Obstructive sleep apnea (OSA) is a chronic condition characterized by repetitive episodes of upper airway collapse, apnea, and arousal during sleep. OSA and type 2 diabetes mellitus (T2DM) are common comorbid conditions. Haemoglobin A1c (HbA1c) is an approximation of an individual's average blood glucose level for the prior two to three months, and therefore is considered to be a major index for monitoring glycaemic control in diabetic patients

Objective: This study aimed to examine the association between OSA and HbA1c levels in T2DM patients.

Methods: This was a cross-sectional study. The study assesses the association between OSA and HbA1c levels in 75 T2DM patients. OSA in the patient was assessed with Epworth Sleepiness Scale (ESS) questionnaire. HbA1c values were obtained from the patient's records. Data presented in mean \pm SD, max, and min. Correlations analyses using Pearson correlation coefficient with $p < 0.05$ were considered statistically significant.

Results: A total of 75 T2DM has a mean BMI were 25.26 ± 48.31 kg/m² with mean HbA1c levels of about $7.1 \pm 0.19\%$. The mean ESS score was 5 ± 0.429 . The very weak correlation between OSA and BMI was statistically significant, $r = 0.213$; $p = 0.047$. Meanwhile, a very weak correlation between OSA and HbA1c levels was not statistically significant, $r = 0.137$; $p = 0.242$

Conclusion: Among adults with T2DM, the correlation between OSA with HbA1c was not statistically significant

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1. Introduction

Obstructive sleep apnea syndrome (OSA), a common disorder, affecting approximately 34% of adult men and 17% of adult women in the general population, is being increasingly recognized as an important cause of morbidity and mortality.¹⁻⁴

OSA is characterized by sleep-disordered breathing, whereby collapse of the upper airway during sleep leads to airflow obstruction, recurrent hypoxemia and reoxygenation, sympathetic overactivity, and microarousals from sleep. Patients with OSA experience excess daytime sleepiness, impaired cognitive function, and reduced quality of life. Of more relevance from a physical health perspective, however,

is the relationship between sleep-disordered breathing and cardiometabolic comorbidities.^{1,5,6}

OSA and type 2 diabetes mellitus (T2DM) are common comorbid conditions. Indeed, the prevalence of OSA is estimated to be between 18% and 36% in subjects with type 2 DM. Vice versa, the prevalence of T2DM is approximately 30% in OSA patients.¹ Epidemiologic and clinical studies have shown that OSA promotes adverse alterations in glucose metabolism and that the prevalence of impaired glucose tolerance (IGT) or diabetes mellitus (DM) increases according to the severity of OSA in patients with OSA.⁴

Glycosylated Hemoglobin A1c (HbA1c) is an approximation of an individual's average blood glucose level for the prior two to three months, which is confirmed by a multicenter study including type 1

diabetic patients, T2DM patients, and non-diabetic subjects and therefore is considered to be a major index for monitoring glycemic control in diabetic patients.⁴ The present study aimed to examine the association between OSA and HbA1c level in T2DM patient.

2. Methods

This study is cross-sectional with the observational analytic method. The inclusion criteria of this study were medication-controlled T2DM patients with the latest HbA1c value during the previous 3 months, women or men around 30 – 55 years old, with normal body temperature (36.5°C). Patients with anemia, asthma, COPD, TB, under sedatives and alcohol were excluded from the study. The study protocol was approved by the Ethics Committee Faculty of Medicine Diponegoro National Hospital Semarang No. 25/EC/KEPK/FK-UNDIP/III/2020. Informed consent was obtained from the patients before enrollment.

A detailed history of complaints including snoring, witnessed apneas, nocturia, disturbed nocturnal sleep, morning headaches and subjective daytime sleepiness was assessed by Epworth Sleepiness Scale (ESS) questionnaire. Height, weight, BMI, blood pressure, and ENT anatomical examination were measured in all patients. HbA1c values were obtained from the patient's records if assessed during the previous 3 months.

Descriptive data are presented in table form while statistical analysis for normally distributed data

Table 1. Characteristics of T2DM patients

Subject Characteristics	Average ± SD	Median (min-max)
Age (Year)	54 ± 0.693	(36-60)
Height (cm)	156 ± 0.99	(140-181)
Weight (kg)	62.6 ± 1.42	(41.3-89.5)
BMI (kg/m ²)*	25.26 ± 48.31	24.46(18-35.6)
Systolic Pressure (mmHg)*	150.68 ± 22.07	(110-220)
Diastolic Pressure(mmHg)	90 ± 2.29	(60-195)
Temperature (°C)	36. ± 0.39	(34.3-36.9)
ESS	5 ± 0.429	(0-15)
HbA1c (%)	7.1 ± 0.19	(4.3-10.8)

*Normal distribution data with $p > 0.05$ using Kolmogorov-Smirnov. SD: Standard Deviation, min: lowest value, max: highest value

using Kolmogorov-Smirnov is presented as min, max, and mean ± SD. Correlations between two variables were analyzed using the Pearson correlation coefficient. Statistical analyses were performed using SPSS version 18.0 statistical software (SPSS Inc., Chicago, IL, USA). A p-value of < 0.05 was considered statistically significant.

3. Results

A total of suitable 75 patients with controlled T2DM were obtained in this study. Subjects in this study consisted of 27 men (36%) and 48 women (64%) patients.

About 3 (4.0%) subjects of this study were underweight, 23 (30,67%) normal, 17 (22,67%) overweight and 32 (42,67%) obese. 72 (96%) of the subjects were taking T2DM medication regularly meanwhile 3 (4%) of them were noncompliant. Among the subjects, 43 (57,33%) had a good controlled DMT2 (HbA1c $< 7.5\%$), 15 (20%) had moderate controlled (HbA1c $\geq 7.5\%$), and 17 (22,67%) had a poor controlled DMT2 (HbA1c $> 9\%$). 65 (86,67%) patients on this study had an ESS score 0-10 and 10 (13,33%) patients were had ESS score ≥ 11 .

A very weak correlation between OSA and BMI was statistically significant, with r 0.21 and P value of 0.047. Meanwhile, a very weak correlation between OSA and HbA1c levels was not statistically significant, with r 0.137 and P value 0.242, as presented in Table 2

Table 2. Correlation between ESS, HbA1c, and BMI

Parameter	ESS	
	R	p*
BMI	0.231	0.047
HbA1c	0.137	0.242

*Significant correlation if $p < 0.05$

4. Discussions

Obstructive sleep apnoea (OSA) is a common chronic disorder characterized by repetitive episodes of the complete or partial collapse of the upper airway (mainly the oropharyngeal tract) during sleep, with a consequent cessation/reduction of the airflow. The clinical features of OSA include tiredness after awake, less concentration, and daytime sleepiness. One of the most commonly associated comorbidities of OSA is metabolic syndrome.^{1,5,6} The prevalence of OSA is even more in obese and DM patients.^{6,7}

Equally important, HbA1c is being increasingly appreciated as a risk marker for the development of DM in the general population.¹

The present study examined the correlation of OSA with HbA1c levels in T2DM patients. Our results suggest that the mean age of the present study population was 54 ± 0.693 years. The study of the correlation of apnea-hypopnea index (AHI) severity with fasting blood sugars and HbA1c values in patients with metabolic syndrome by Meenakshi, N et al also showed a similar result with the mean age of 63 participants with metabolic syndrome showed a mean age of 50.9 ± 12.98 years.⁶ The Regional Office for the Western Pacific Region of WHO (WPRO) as cited in Somprasit C et al and Murakami Y et al study proposed a specific classification in 2004 for obesity in Asian populations. The definitions of underweight, normal, overweight, and obesity were defined as BMI in <18.5 , $18.5-22.9$, $23-24.9$, and >25 kg/m², respectively. The mean BMI in this study subjects was 25.26 ± 48.31 kg/m² (range 4.3-10.8), indicating most of the subjects were obese. Murakami et al in their study showed that The prevalence of diabetes across the BMI groups in Asia was underweight: 2%, normal weight at 2%, high-normal at 3%, overweight at 5%, and obese at 10%.⁹ Obesity and abdominal obesity are established risk factors for OSA while abdominal obesity is known to play an important role in the development of insulin resistance and metabolic syndrome.^{9,10}

In this study, we found the subject's mean systolic and diastolic pressures were 150.68 ± 22.07 mmHg and 90 ± 2.29 mmHg. Lam et al showed an independent association between OSA and elevated diastolic blood pressure in their cohort study. There is a consensus of evidence to support that OSA has an adverse effect on elevation of blood pressure and OSA patients have an increased risk of hypertension, independent of obesity and age.⁹

Excessive daytime sleepiness (EDS) as scored by the Epworth Sleepiness Scale, measures an individual's perceived sleepiness. Higher levels of EDS are associated with an increased risk of falling asleep at work or driving and are associated with decreased life satisfaction. In a large sleep study, 76% of individuals with severe OSA exhibited EDS, and 56% of individuals with mild or moderate OSA exhibited EDS.¹¹⁻¹³ ESS score 0-10 indicates the least daytime sleepiness; ESS score ≥ 11 indicates excessive daytime sleepiness. The

mean ESS in this study was 5 ± 0.36 and showed a low risk of sleepiness in the daytime. Our study showed that the majority of T2DM subjects do not complain of sleepiness. Lam et al in his study also showed a similar result with mean ESS in 73 patients with OSA and 89 patients without OSA were 6 (range 3-8) and 6 (3-10) respectively. The importance of sleepiness as an indicator of the adverse cardiometabolic syndrome in OSA is controversial.^{6,10,13} Some studies suggested that the presence of sleepiness in OSA indicated the propensity to develop hypertension or insulin resistance, as well as their response to OSA treatment. The absence of excessive daytime sleepiness would pose the problem of recognition as well as compliance with CPAP treatment.¹¹⁻¹³

HbA1c severity levels based on the latest DM Guideline on PERKENI were grouped based on the patient's response to hyperglycemic medication. A good DM controlled, moderate DM controlled, and poor DM controlled with HbA1c $< 7\%$, HbA1c $\geq 7.5\%$, and HbA1c $> 9\%$, respectively. The mean HbA1c levels among the study population, was $7.1 \pm 0.19\%$, showing that the study populations have good DM control. This HbA1c levels finding were similar to the HbA1c baseline level in Priou et al study assessing glucose control in patients with untreated versus treated diabetes and Meenakshi et al study about Apnea Hypopnea Index Severity with Fasting Blood Sugars and HbA1c values.^{6,11} HbA1c values reflect the 2- to 3-month average endogenous exposure to glucose, including postprandial spikes in the blood glucose level, and present low intraindividual variability, particularly in persons without diabetes. HbA1c is superior to fasting blood glucose for assessment of the long disease in nondiabetic middle-aged adults, especially at values above 6.0%. Furthermore, HbA1c is similarly associated with the risk of diabetes as is fasting blood glucose.^{12,13} The utility of HbA1c as a predictor of T2DM in subjects with OSA is plausible, given the association between these two conditions.¹

In this study, we found a very weak correlation between OSA and BMI was statistically significant with $r = 0.231$ and $p = 0.047$. Studies that have controlled for obesity, have shown an important association between T2DM and OSA. The Sleep AHEAD study recruited 306 obese subjects with diabetes and found an OSA prevalence of 86%, where BMI and waist circumference were identified as

significant predictors of OSA.^{12,9,10,14} The novel association of HbA1c with the severity of OSA appears interesting, and may have important implications in clinical practice. Essentially, not only is HbA1c the major target for the prevention of complications in T2DM but it also represents a significant risk marker for cardiovascular disease in the general population.¹ In this present study, we found a very weak correlation between OSA and HbA1c levels was not statistically significant with $r = 0.137$ and $p = 0.242$. Lam et al. found no significant association between measures of OSA severity and HbA1c levels in 165 diabetic patients.¹⁰ Meenakshi et al in their study also showed that apnea-hypopnea index (AHI) severity did not correlate with HbA1c values in patients with metabolic syndrome.⁶ Previous studies evaluating the association between OSA and glycated hemoglobin (HbA1c) in patients with diabetes also yielded conflicting results.^{10,15-16} In contrast, Aronsohn et al. found an independent association between the severity of OSA and HbA1c in diabetic patients.¹⁷ Priou et al also reported the similar result as they tested the 2,139 patients to assess the independent association between obstructive sleep apnea severity and glycated hemoglobin in adults without diabetes and found increasing OSA severity is independently associated with impaired glucose metabolism, as assessed by higher HbA1c values.¹² Tamrani et al and Kurosawa et al also found the association between OSA severity and severity of OSAS among nondiabetic men is associated with increased HbA1c levels in non-diabetic patient indicating that controlling HbA1c levels may clinically important target in OSA management.^{1,7} The exact reasons for the conflicting results are unclear but, several factors may have contributed to these conflicting results, including differences in sample sizes, ethnic risk factors for both OSA, and whether patients were recruited from diabetes clinics or sleep units.^{5,10,11,15}

The limitations of the present report include the small number of patients and the cross-sectional design. As most of the subjects did not complain of daytime sleepiness and ESS is not so useful in screening for OSA (sensitivity 47%, specificity 62%) other standard examinations for assessing OSA should be considered such as AHI and polysomnography (PSG).^{13,17,18}

5. Conclusion

In conclusion, among adults with T2DM, the correlation between OSA with HbA1c was not statistically significant. However, further prospective research is required to confirm our findings

Ethical Approval

The study protocol was approved by the Ethics Committee Faculty of Medicine Diponegoro National Hospital Semarang No. 25/EC/KEPK/FK-UNDIP/III/2022.

Conflicts of Interest

The authors declare that there was no conflict of interest.

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Author Contributions

Conceptualization, AMKD and PH; methodology, AMKD, PH and DER; software, EKSL; validation, AMKD, PH, and DER; formal analysis, EKSL; investigation, AMKD; resources, AMKD; data curation, AMKD; writing—original draft preparation, AMKD; writing—review and editing, AMK; funding acquisition, AMKD.

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