

Original Article

Sleep Disordered Breathing in Patient with Type 2 Diabetes Mellitus and its Association with Diabetic Retinopathy: Single Center Study

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ABSTRACT

Introduction: Sleep-disordered breathing comprises of obstructive sleep apnea, central sleep apnea, and periodic breathing. There is a link between obesity diabetes and sleep apnea with its association with retinopathy. Therefore this study was done to find out the association of sleep-disordered breathing in uncontrolled diabetes mellitus and association with retinopathy.

Materials and Methods: This study was done from 2015 September to 2018 September in Sleep center, Nepal. Patients diagnosed with Type 2 diabetes mellitus were included. Diabetes mellitus was diagnosed as blood sugar fasting ≥ 126 mg/dl, or blood sugar postprandial ≥ 200 mg/dl and glycosylated hemoglobin above 6.5%. Obstructive sleep apnea risk was determined using the STOP-BANG questionnaire. Relationships between the risk of Obstructive sleep apnea and clinical variables along with its association with diabetic retinopathy were evaluated using bivariate analyses and covariate-adjusted logistic regression models.

Results: A total of 150 diabetic patients were analyzed. Among them 30 (20.0%) patients had mild Obstructive sleep apnea, 14 (9.3%) patients had moderate Obstructive sleep apnea and 15 (10.0%) patients had severe sleep apnea. Among patients with diabetes mellitus on multivariate regression analysis Obstructive sleep apnea was associated with diabetes mellitus OR 2.05, 95% CI (1.69- 8.83) and diabetic retinopathy OR 1.20 (0.67-5.89).

Conclusions: This study concludes that those individuals having diabetes may be suffering from obstructive sleep apnea and association with retinopathy these individuals can be considered for the screening of sleep-disordered breathing by polysomnography.

Keywords: Apnea; Diabetes, Glycosylated; Haemoglobin, Obstructive sleep apnea; Polysomnography; Retinopathy

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INTRODUCTION

Sleep-disordered breathing (SDB) comprises obstructive sleep apnea (OSA), central sleep apnea & upper airway resistance syndrome. Identification and management of modifiable risk factors such as obesity, hypertension and dyslipidemia are important to reduce complications associated with type 2 diabetes mellitus. Sleep-related breathing disorders, including obstructive sleep apnea (OSA), may be another comorbidity that deserves attention in the overall approach to the care of patients with type 2 diabetes mellitus. The prevalence of obstructive sleep apnea may also increase with age.^{1,2} In the Sleep Heart Health Study, the prevalence of obstructive sleep apnea was two to eight times higher among participants ages 60 years and older compared to those ages 25–60 years.³

Obesity is common to diabetes and obstructive sleep apnea; however, upper body obesity is more characteristic of individuals with obstructive sleep apnea.⁴ Type 2 diabetes is a major cause of morbidity and mortality linked to microvascular and macrovascular complications and is considered as a coronary artery disease risk equivalent for myocardial infarction.⁵ Recent studies indicate that obstructive sleep apnea is associated with atherosclerosis and initiation and progression of cardiovascular disease.^{6–8} Obstructive sleep apnea is also associated with other risks for cardiovascular disease, including hypertension,^{9–11} obesity,¹² and dyslipidemia¹³ and may interact synergistically with these risk factor to increase morbidity and mortality related to cardiovascular events.^{13,14}

Investigators also have observed an association between obstructive sleep apnea, insulin resistance, and impaired glucose tolerance. A number of studies have shown that OSA may be associated with increased risk of diabetic retinopathy independent of glucose control.^{15–19} Proposed mechanisms that may influence retinal damage include increases in blood pressure and sympathetic activation, oxygen desaturation causing retinal hypoxia with production of vascular growth factors and autonomic dysregulation.²⁰ There were no studies regarding sleep disordered breathing in type 2 diabetes mellitus and association with target organ damage as retinopathy in developing countries like Nepal till date. Therefore aim of this study was to find sleep disordered breathing in Type 2 diabetes mellitus and its association with retinopathy.

MATERIALS AND METHODS

This is a hospital based cross-sectional study of patients with type 2 diabetes mellitus attending Swacon International hospital who were enrolled from September 2015 to September 2018(3 yrs). The ethical committee of the concerned institute approved the study. Patients referred from different centers in Kathmandu who had diabetes mellitus were included. Written consents were taken from all the participants.

Patients with uncontrolled diabetes mellitus with complain of sleep-disordered breathing were included in the study. Subjects were recruited using STOP BANG questionnaire. All the patients were evaluated by ophthalmologist. Fundoscopy was done for evaluation of diabetic retinopathy. Diabetes Mellitus was diagnosed as having fasting blood sugar ≥ 126 mg/dl or blood

sugar post prandial ≥ 200 mg/dl, or glycosylated hemoglobin (HbA1C) above 6.5 percent. Demographic data including age, sex, Body Mass Index (BMI), history of diabetes duration, smoking history and medication for diabetes were collected in structured Proforma after informed consent. Subjects who met inclusion criteria underwent overnight level II polysomnographic test using ALICE 5 done in sleep lab. Polysomnography reporting was done by certified sleep physician.

Statistical Analysis

Analysis was performed using a statistical software package (SPSS 22 for windows). Nominal variables were compared using Chi-square test or Fisher's exact test. Step wise multivariate logistic regression was performed with potential candidate variables as covariates. All the statistical tests performed were two tailed; $p < 0.05$ was considered statistically significant.

RESULTS

A total of 150 patients with diabetes mellitus were included. Among them, 110 (73.3%) were males and 40 (26.6%) were females. Mean age of patient was 62.5 ± 5.9 years. Among the studied population, 65 (43.3%) patients had BMI ≥ 30 with a mean of 33.5 ± 5.9 . Hypertension was present in 120 (80.0%) patients along with diabetes mellitus. Fasting blood glucose of these patients ranged from 145 mg/dL to 200 mg/dL. Similarly postprandial blood glucose ranged from 220mg/dL to 300 mg/dL with HbA1c of 8.5 ± 2.5 . Among these patients 120 (80.0%) had HbA1c level ≥ 8.0 (poor control).

All the patients underwent overnight polysomnography. Among them 59 (39.33%) had OSA (Table 1). Apnoea-Hypopnoea Index (AHI) was 5-15/hr in 30 (20.0%) patients and was categorized as mild OSA (Table 1) followed by 15 (10%) patients had Severe OSA. On logistic regression analysis not adjusted for age, sex, BMI, or smoking, OSA was associated with diabetes mellitus (OR 2.05, 95% CI (1.69-8.83) $P=0.02$) and diabetic retinopathy OR1.20 (0.67-5.89) (Table 2). Among patient having OSA, 30 (20%) had diabetic retinopathy and 10 (6.66%) had macular oedema.

Table 1: Obstructive sleep apnea in diabetic patients (n=59)

Grade of OSA	Number of patients (%)
Mild OSA (AHI 5-15/hr)	30 (20%)
Moderate OSA (AHI 15-30/hr)	14 (9.3%)
Severe OSA (AHI >30/hr)	15 (10%)

Table 2: Correlation of variables with OSA and diabetes mellitus using logistic regression analysis

Factor	OR(95% CI)	P Value
Age	1.03 (0.97-1.10)	0.38
Male	0.97 (0.4-2.35)	0.95
Body Mass Index (>35kg/m ²)	1.06 (1.00-1.16)	0.04
Diabetes mellitus	2.05 (1.69-8.83)	0.02

Factor	OR(95% CI)	P Value
Smoking	1.82 (0.73-4.61)	0.03
Hypertension	2.75(1.45-8.35)	0.003
Diabetic retinopathy with macular oedema	1.20 (0.67-5.89)	0.02

DISCUSSION

Sleep-disordered breathing was more common among patients with diabetes mellitus. The result confirms the finding from Botros et al. who had found that OSA increased the risk of type 2 diabetes in a cohort of 544 patients referred for evaluation of SDB after adjusting for age, gender, ethnicity, blood glucose, BMI and weight change.²¹ In a cross-sectional analysis, in the European Sleep Apnea Cohort study, the prevalence of type 2 diabetes and poorer glycaemic control was observed to be associated with increasing severity of OSA assessed by the oxygen desaturation index (ODI).²² In this study, 120 (80.0%) patients had poor glycaemic control.

Vgontzas et al. evaluated obese males with symptomatic sleep apnea with age and BMI matched controls and found that mean fasting blood glucose and insulin levels were higher in OSA than in obese controls suggesting that SDB is an independent risk factor for hyperinsulinaemia.²³ This finding was consistent with our study showing BMI of >35kg/m² has OR1.06 (1.00-1.16) for SDB.

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There was presence of diabetic retinopathy in 30 (20.0%) patients and 10 (6.6%) patients had macular edema in our study. This is similar to study done by West et al. who showed that in males with type 2 diabetes, the presence of OSA is associated with diabetic retinopathy.²⁴ Mason et al. found a high prevalence of SDB in patients with type 2 diabetes and diabetic macular edema, although no relationship was observed between the severity of SDB as defined by ODI and macular oedema.²⁰ OSA patients have an increased risk of hypertension, independent of obesity and age.^{25,26} which is similar in our study that severe OSA associated with hypertension of OR 2.75(1.45-8.35). Furthermore, untreated patients with proven OSA have been found to have an increased risk of hypertension.²⁷

Limitation of this study was that HbA1c reading was taken for uncontrolled blood sugar. Cardiovascular disease, dyslipidemia was not considered as confounding factors. Dosage, duration and compliance of medication were not recorded. These patients also had several factors, such as, obesity, hypertension, and smoking behaviour which might be the confounding factors for sleep-disordered breathing.

CONCLUSIONS

This study concludes that patients of type 2 diabetes mellitus had increased risk of having sleep disordered breathing and association with diabetic retinopathy. Therefore, these individuals should be considered to undergo screening with polysomnography for sleep disordered breathing.

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