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Original Article

To screen for obstructive sleep apnea in patients with type 2 diabetes mellitus and its association with microvascular complications

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ABSTRACT

Objectives: The objectives of this study were to find the association between obstructive sleep apnea (OSA) and microvascualr complications in patients with type 2 diabetes mellitus (T2DM).

Material and Methods: This study was conducted at Bangalore Medical College. One hundred patients fulfilling the inclusion criteria were enrolled for the study. The study group included outpatients and inpatients with T2DM in Victoria Hospital and Bowring and Lady Curzon Hospital. The data were collected according to the pro forma in terms of history, clinical examination, and the necessary investigations (HbA1c and urine microalbumin-creatinine ratio). To screen for OSA, STOP-BANG questionnaire was used. To assess microvascular complications, patients were subjected to fundoscopy, urine microalbumin-creatinine ratio, and Toronto clinical neuropathy scoring system. Based on STOP-BANG score, patients were divided into three groups: Low risk (0–2), intermediate risk (3–4), and high risk (5–8) for OSA. Mean values for the duration of diabetes, HbA1c, urine microalbumin-creatinine ratio, and Toronto neuropathy score were compared in each group using ANOVA variance analysis. To find the association between OSA and diabetic retinopathy, Kruskal–Wallis test was used.

Results: Based on STOP-BANG score, 16% of patients were in the low-risk group, 68% in the intermediate-risk group, and 16% in the high-risk group. There was a significant difference in Toronto neuropathy scores, urine microalbumin-creatinine ratio, and diabetic retinopathy between low-, intermediate-, and high-risk OSA groups indicating higher neuropathy scores, higher values of UMCR, and more advanced diabetic retinopathy among the high-risk group as compared to other two groups. The association between STOP-BANG scores and UMCR, Toronto neuropathy score, and diabetic retinopathy was statistically significant with *P* values of 0.002, 0.029, and 0.03, respectively.

Conclusion: All diabetic patients should be screened for OSA which is simple and inexpensive. Those who fall in intermediate-risk and high-risk categories showed more advanced microvascular complications. They should be subjected to polysomnography and treated for OSA for better glycemic control and to delay the progression of microvascular complications.

Keywords: Obstructive sleep apnea, Type 2 diabetes mellitus, Microvascular complications

INTRODUCTION

Obstructive sleep apnea (OSA) is recurrent episodes of complete (apnea) or partial (hypopnea) or upper airway obstruction that occurs in sleep, leading to a decrease or cessation of airflow, followed by sleep arousals.

In the general population, the prevalence of OSA was estimated to be 2–4%.[1] The prevalence of OSA is especially high among patients with diabetes/hypertension, but majority remain undiagnosed.[2] The prevalence of OSA in type 2 diabetes mellitus (T2DM) is variable in different studies (48–86%).[3-5] The prevalence was 58% in the Sleep Heart Study.[3] In the Sleep Action for Health in Diabetes (Sleep AHEAD) study,[4] the prevalence of OSA among obese subjects with T2DM was 86%.

Studies on the prevalence of OSA among people with diabetes in India are sparse.

In India, more than 62 million individuals are currently diagnosed with type 2 diabetes and it has attained the status of an epidemic.[6] Since intermittent hypoxia has been shown to exert adverse effects on glucose metabolism, OSA increases the risk of developing T2DM and contributes to poor glycemic control in people with existing diabetes.[7] European Sleep Apnea Cohort Study showed that people with diabetes with severe OSA had higher HbA1c levels compared to non-apneic people.[8]

Studies have implicated new evidence of an association between OSA and microvascular complications in diabetes. This study aims to study the correlation between OSA and microvascular complications in T2DM.

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Table 1 : Baseline and clinical characteristics of patients.

Variable	Number of patients (*n*=100)	Number of patients in %
Age (in years)		
31–40	12	12
41–50	24	24
51–60	24	24
61–70	28	28
71–80	12	12
Sex		
Male	54	54
Female	46	46
Duration of diabetes		
<2 years	12	12
2–5 years	28	28
6–10 years	36	36
>10 years	24	24
Hypertension as comorbidity		
Hypertension	44	44
No hypertension	56	56
BMI		
<18	0	0
18–22.9	12	12
23–24.9	22	22
≥25	66	66
HBA1C levels		
<7%	8	8
7–9%	52	52
>9%	40	40
OSA risk groups		
Low risk (0–2)	16	16
Intermediate risk (3–4)	68	68
High risk (5–8)	16	16

OSA: Obstructive sleep apnea

Table 2: Comparison of variables among three groups.

Variable	Number of patients	Mean	Standard deviation
HbA1c			
Low	16	7.76	1.864
Intermediate	68	8.98	2.2095
High	16	11.2	4.2115
Toronto neuropathy score			
Low	16	5	4.2426
Intermediate	68	7.4412	3.1545
High	16	9.5	2.6186
Urine microalbumin-creatinine ratio			
Low	16	125.73	256.47
Intermediate	68	195.59	283.73
High	16	927.12	1186.60

Table 3: Comparison of diabetic retinopathy.

Fundus	Number of patients	Mean rank STOP-BANG score
Normal	44	11.75
Mild to moderate non-proliferative diabetic retinopathy	26	22.33
Severe non-proliferative diabetic retinopathy	20	43.3
Proliferative diabetic retinopathy	10	55.25

Aims and objectives

The aims of this study were as follows:

1) To screen for OSA in patients with T2DM.
2) To study the association between obstructive sleep apnea and microvascular complications in patients with T2DM.

MATERIAL AND METHODS

This cross-sectional study was conducted on patients with T2DM attending outpatient department/admitted in the Department of Medicine of hospitals attached to BMCRI between November 2018 and May 2020. Patients were enrolled in the study based on purposive sampling.

Patients with age more than 18 years, with T2DM according to ADA criteria and who are willing to participate in the study and give informed written consent were included in the study. Patients with active infection, decompensated liver disease, acute stroke acute kidney disease/chronic kidney disease, known connective tissue disease, and pregnant women were excluded from the study.

After obtaining approval from the Institutional Ethics Committee of BMCRI, written informed consent was taken from the patients. Data were collected by semi-structured questionnaire, clinical examination, and investigations. Data of all the patients satisfying the inclusion and exclusion criteria were collected.

One hundred patients who were selected for the study went through the studies prospectively, that is, history, examination, and STOP-BANG questionnaire, followed by evaluation for retinopathy, neuropathy, and nephropathy.

For the study, the following operational standard criteria/definitions were used:

1. Questionnaire regarding basic demographic data, clinical history, and examination
2. Patients were diagnosed to have T2DM based on the ADA criteria
3. Patients were screened for obstructive sleep apnea using STOP-BANG questionnaire [Annexure 1]
4. To assess microvascular complications, patients were subjected to Toronto clinical neuropathy score for

Table 4: Various studies on OSA in T2DM.

Study name	Sample size	Study methodology	Results	Inference
Viswanathan *et al.*[11]	203	Patients with type 2 diabetes mellitus were subjected to comprehensive diabetic evaluation and AHI was used to evaluate OSA.	23.65% of the study subjects had OSA (AHI≥15). People with OSA had higher percentage of diabetic complications such as cardiovascular disease, retinopathy, and neuropathy.	Prevalence of OSA was higher in this study compared to Indian studies
Bhimwal *et al.*[12]	50	This was a cross-sectional hospital-based study in patients, screened at diabetic clinic. Berlin questionnaires and Epworth scores are tools to screen for OSA	OSA was prevalent in the diabetic population (54%); OSA was more in subjects with uncontrolled diabetes (blood sugar>200 mg/dl), smokers, and alcoholics.	This study shows that OSA has a high prevalence in subjects with T2DM
Sharma *et al.*[13]	2150	This was a cross-sectional community-based study. Patients were screened using sleep questionnaire and included into a study by polysomnography study	The prevalence of OSA and OSAS was 13.74% and 3.57%, respectively. Male gender, age, obesity, and waist/hip ratio were the significant risk factors for OSAS.	The risk factors and prevalence demonstrated in this study were similar in India compared to Western studies.
Undi *et al.*[14]	71	This was a cross-sectional study done in an UHC of an urban slum in South India. The data were collected from previously diagnosed T2DM patients attending UHC using a validated structured questionnaire (STOP-BANG and ESS) by interview technique.	66.2% of subjects had high risk of OSA (35.2% had intermediate risk and 31.0% had severe risk of OSA).	Nearly two-third of T2DM patients had high risk of OSA which was not detected earlier during their routine visits to hospitals in urban slum.
Fredheim *et al.*[15]	137	137 extremely obese patients were included. This study was conducted on OSA which was defined by an AHI≥5 events/hour	Among the patients with normal glucose tolerance, 33% had OSA, 67% of the pre-diabetic patients, and 78% of the type 2 diabetic patients had OSA	Type 2 diabetes and pre-diabetes are associated with OSA in extremely obese subjects.
Kosseifi *et al.*[16]	98	A retrospective electronic chart of all veterans referred for sleep studies over a 1-year period was reviewed. Ninety-eight patients with an HbA1c<6.5% were included in the study. The degree of glycemia (HbA1c) and presence of macro- and micro-vascular complications were compared with OSAS variables	The apnea-hypopnea index was significantly related to diabetic microvascular complications, particularly retinopathy. Oxygen desaturation was significantly and inversely related to microalbuminuria, retinopathy, and HbA1c	Sleep apnea is associated with microvascular complications even in well-controlled DM-2 veterans. Screening for OSAS should be considered in patients with DM-2.
Zhang *et al.*[17]	880	This was a multicentric cross-sectional study. Overnight sleep monitoring was used to record respiratory parameters.	Cumulative time of SpO2 below 90% was independently associated with diabetic nephropathy.	Chronic diabetes complications were recorded and found that diabetic nephropathy and retinopathy were more in OSA compared to non-OSA diabetic patients.

AHI: Apnea-hypopnea index, OSA: Obstructive sleep apnea, OSA syndrome: Obstructive sleep apnea syndrome, T2DM: Type 2 diabetes mellitus

diabetic neuropathy [Annexure 2], fundoscopy for diabetic retinopathy, and urine microalbumin-creatinine ratio for diabetic nephropathy.

Based on STOP-BANG score, patients were divided into three groups: Low risk (0–2), intermediate risk (3–4), and high risk (5–8) for OSA.

Statistical analysis was performed using SPSS software. Data were analyzed by descriptive statistics. The student's *t*-test was used for significant difference between the two means. Pearson's correlation was used to analyze the correlation between STOP -BANG score (indicating risk of OSA) and UMCR and Toronto neuropathy score.

The point-biserial correlation was used to analyze the correlation between STOP-BANG score and presence and absence of diabetic retinopathy. Mean values for the duration of diabetes, HbA1c, urine microalbumin-creatinine ratio, and Toronto neuropathy score were compared in each group using ANOVA variance analysis. To find the association between OSA and diabetic retinopathy, Kruskal–Wallis test was used.

RESULTS

The present study was conducted in the Department of Medicine, Bangalore Medical College and Research Institute. A total of 100 cases of diabetes mellitus were taken according to the pro forma detailed in the methodology and the data obtained thereby are presented and analyzed below [Table 1].

It is observed from the above table that the maximum number of patients in our study were in the 61–70 years age group (28%) with mean age of 57 years. The lowest age encountered was 33 years whereas the oldest patient was 85 years in our present study series.

In this study, 54 (54%) patients of the study population were male and 46 (46%) were female. The male-to-female (M: F) ratio is 1.17: 1. From the above [Table 1], it is observed that 28 patients had the disease for 2–5 years, 36 patients had the disease for 6–10 years, 24 patients had the disease for more than 10 years, and 12 patients had the disease for <2 years. The mean duration of disease was 6.514 years with a standard deviation of 4.88.

It is observed from the above [Table 1] that 56 patients were not hypertensive and 44 patients were hypertensive. From the above table, it is seen that majority of the patients were obese according to Asia Pacific Criteria. Twelve patients had normal BMI (18.5–22.9). Twenty-two patients were overweight with a BMI between 23 and 24.9 and 66 patients were obese with a BMI of more than 25. The mean BMI was 26.11 with standard deviation of 2.72. There were 8 (8 %), 52 (52%), and 40 (40%) patients who had HbA1c of <7, 7–9, and >9%, respectively. The mean HbA1c was 9.306% with standard deviation of 2.63 [Table 1].

Based on STOP-BANG score, patients were divided into low, intermediate, and high risk for obstructive sleep apnea. There were 16, 68, and 16 patients in the low-, intermediate-, and high-risk group, respectively.

From the above [Table 2], it is seen that HbA1c is higher in high-risk group indicating poor glycemic status in high-risk group compared to the other two groups and it is statistically significant (P = 0.04). It is seen in the above [Table 2] that the Toronto neuropathy score was higher in high-risk group compared to the other two groups indicating more advanced diabetic neuropathy and it was statistically significant (P = 0.029). The above [Table 2] also shows that urine microalbumin-creatinine ratio is higher in higher risk group compared to intermediate- and low-risk groups, indicating that diabetic nephropathy was more advanced in high-risk group and it was statistically significant (P = 0.002) [Table 3].

As seen in the above table, 44 patients had normal fundus, 26 patients had mild-to-moderate non-proliferative diabetic retinopathy, 20 patients had severe non-proliferative diabetic retinopathy, and 10 patients had proliferative diabetic retinopathy. Kruskal–Wallis test was used to analyze the association between OSA and diabetic retinopathy and it was seen that diabetic retinopathy was more advanced in patients with higher STOP-BANG scores and it was statistically significant (P = 0.03).

DISCUSSION

This tertiary care hospital-based cross-sectional study was undertaken to screen for OSA using STOP-BANG questionnaire in patients with T2DM. We excluded patients with active infection, decompensated liver disease, acute stroke, and acute kidney disease/chronic kidney disease, known connective tissue disease. Other objectives were to study the association between OSA and microvascular complications in patients with T2DM.

In the present study, 64% of the population was above 50 years of age. A study done by Saustika *et al.*, revealed that age is an important risk factor for type 2 diabetes mellitus and cardiovascular diseases.[9] Increase in the prevalence of T2DM in old age may be due to the aging process itself or indirectly through several other age-related risk factors such as central obesity, mitochondrial dysfunction, inflammation, beta-cell dysfunction, insulin resistance, and metabolic syndrome. Incidence of T2DM and obstructive sleep apnea increases with age.

About 92% of study population had HbA1c > 7. According to ADA 2020 guidelines, target HbA1c for T2DM patients is < 7 which has shown to reduce microvascular complications and long-term reduction in macrovascular complications. The majority of our study population had an intermediate and high risk for obstructive sleep apnea. A study by Pamidi *et al.* concluded that diabetic patients with severe OSA had higher HbA1c and were more likely to have poorly controlled T2 DM than non-apneic diabetics.[10]

We divided the study population into OSA risk groups based on STOP BANG score. A score of 0–2, 3–4, and 5–8 indicated low, intermediate, and high risk for OSA, respectively. About 16% of patients were in the low-risk group, 68% in the intermediate-risk group, and 16% in the high-risk group.

There was a significant difference in HbA1c levels between low-, intermediate-, and high-risk OSA groups indicating poorer glycemic control in high-risk group as compared to other two groups and was statistically significant (P = 0.04) [Table 4].

There was also a significant difference in Toronto neuropathy scores, urine microalbumin-creatinine ratio, and diabetic retinopathy between low-, intermediate-, and high-risk OSA groups indicating higher neuropathy scores, higher values of UMCR, and more advanced diabetic retinopathy among high-risk group as compared to other two groups [Table 4].

The association between STOP-BANG scores and UMCR, Toronto neuropathy score, and diabetic retinopathy was statistically significant with *P* values of 0.002, 0.029, and 0.03, respectively. This could be explained by a pro-inflammatory state caused by OSA which impairs glycemic control causing higher prevalence of microvascular complications [Table 4].

Limitations

- Cross-sectional study with small sample size.
- OSA was not confirmed using polysomnography.
- Hypertension was not an exclusion criterion. Hypertension can be independently associated with some microvascular complications.

CONCLUSION

All diabetic patients should be screened for OSA as the STOP-BANG questionnaire is simple and inexpensive.

High risk of OSA is associated with poor glycemic control and more advanced microvascular complications as reported in our study with a strong statistical significance.

Patients in high- and intermediate-risk groups can be subjected to polysomnography and treated for OSA as studies have shown that patients with OSA started on CPAP therapy showed better glycemic control.

In resource-limited settings like India, screening for OSA is useful to identify diabetic patients more likely to develop diabetes-related complications and initiate preventive measures and avoid/delay life-threatening complications.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Doumit J, Prasad B. Sleep apnea in Type 2 diabetes. Diabetes Spectr 2016;29:14-9.
2. Wellman A, Resdline S, Apnea S. In: Kasper D, Fauci A, Hauser S, Longo D, Jameson J, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 20th ed., Vol. 2. New York: McGraw Hill; 2015. p. 1724.
3. Resnick HE, Redline S, Shahar E, Gilpin A, Newman A, Walter R, *et al*. Diabetes and sleep disturbances: Findings from the Sleep Heart Health Study. Diabetes Care 2003;26:702-9.
4. Foster GD, Sanders MH, Millman R, Zammit G, Borradaile KE, Newman AB, *et al*. Obstructive sleep apnea among obese patients with Type 2 diabetes. Diabetes Care 2009;32:1017-9.
5. 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;181:507-13.
6. Einhorn D, Stewart DA, Erman MK, Gordon N, Philis-Tsimikas A, Casal E. Prevalence of sleep apnea in a population of adults with Type 2 diabetes mellitus. Endocr Pract 2007;13:355-62.
7. Joshi SR, Parikh RM. India diabetes capital of the world: Now heading towards hypertension. J Assoc Physicians India 2007;55:323-4.
8. Tasali E, Mokhlesi B, Cauter EV. Obstructive sleep apnea and Type 2 diabetes: interacting epidemics. Chest 2008;133:496-506.
9. Suastika K, Dwipayana P, Siswadi M, Tuty RA. Glucose intolerance by Surekha chakrewarthy. IntechOpen 2012;5:69-73.
10. Pamidi S, Aronsohn RS, Tasali E. Obstructive sleepapnea: Role in the risk and severity of diabetes. Best Pract Res Clin Endocrinol Metab 2010;24:703-15.
11. Viswanathan V, Priyadarshini I, Ramakrishnan N. High prevalence of obstructive sleep apnea among people with Type 2 diabetes mellitus in a tertiary care center. J Assoc Physicians India 2017;65:38-42.
12. Bhimwal R, Jangid R, Bhati RL. To study the prevalence of obstructive sleep apnoea in Type 2 diabetes patients in Western Rajasthan, India. Int J Adv Med 2017;4:894-902.
13. Sharma SK, Kumpawat S, Banga A, Goel A. Prevalence and risk factors of obstructive sleep apnea syndrome in a population of Delhi, India. Chest 2006;130:149-56.
14. Undi M, Rachana R, Badesaab B. A cross-sectional study to assess the burden of OSA among T2DM patients attending urban health centre in an urban slum of South India. Int J Community Med Public Health 2016;3:1927-31.
15. Fredheim JM, Rollheim J, Omland T, Hofsø D, Røislien J, Vegsgaard K, *et al*. Type 2 diabetes and pre-diabetes are associated with obstructive sleep apnea in extremely obese subjects: A cross-sectional study. Cardiovasc Diabetol 2011;10:84.
16. Kosseifi S, Bailey B, Price R, Roy TM, Byrd RP, Peiris AN. The association between obstructive sleep apnea syndrome and microvascular complications in well-controlled diabetic patients. Mil Med 2010;175:913-6.
17. Zhang R, Zhang P, Zhao F, Han X, Ji L. Association of diabetic microvascular complications and parameters of obstructive sleep apnea in patients with Type 2 diabetes. Diabetes Technol Ther 2016;18:415-20.

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ANNEXURE 1

STOP BANG QUESTIONNAIRE

1. Snoring: Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?
   Yes / No
2. Tired: Do you often feel tired, fatigued, or sleepy during daytime?
   Yes / No
3. Observed: Has anyone observed you stop breathing during your sleep?
   Yes / No
4. Blood pressure: Do you have or are you being treated for high blood pressure?
   Yes / No
5. BMI: BMI > 35 kg/m2?
   Yes / No
6. Age: Age >50 yr old?
   Yes / No
7. Neck circumference: Neck circumference >40 cm?
   Yes / No
8. Gender: Gender male?
   Yes / No

High risk of OSA 5-8
Intermediate risk of OSA 3-4
Low risk of OSA 0-2

ANNEXURE 2 TORONTO CLINICAL NEUROPATHY SCORE

Columbia Basin Spinal Rehabilitation Institute

Eric Kurtz, DC, CCSP
1721 W. Kennewick Ave.
Kennewick, WA 99336
509-482-3549
www.PainRelief-Now.com

Toronto Clinical Neuropathy Scoring System

This is a quantitative scoring system for evaluating the severity of peripheral neuropathy - primarily for the feet. Most of the testing is done on or near the toes.
Light touch testing is done with a 10 gm monofilament on the dorsum of the large toe.

Patient Name:_____

Date:	Right	Left
Symptom Scores	Present = 1 Absent = 0	Present = 1 Absent = 0
Pain		
Numbness		
Tingling		
Weakness		
Ataxia		
Upper-Limb Symptoms		
Reflex Scores	Absent = 2 Reduced = 1 Normal = 0	Absent = 2 Reduced = 1 Normal = 0
Knee Reflexes		
Ankle Reflexes		
Sensory Test Scores	Abnormal = 1 Normal = 0	Abnormal = 1 Normal = 0
Pinprick		
Temp		
Light Touch		
Vibration		
Position		
Totals		

Date:	Right	Left
Symptom Scores	Present = 1 Absent = 0	Present = 1 Absent = 0
Pain		
Numbness		
Tingling		
Weakness		
Ataxia		
Upper-Limb Symptoms		
Reflex Scores	Absent = 2 Reduced = 1 Normal = 0	Absent = 2 Reduced = 1 Normal = 0
Knee Reflexes		
Ankle Reflexes		
Sensory Test Scores	Abnormal = 1 Normal = 0	Abnormal = 1 Normal = 0
Pinprick		
Temp		
Light Touch		
Vibration		
Position		
Totals		

Scoring:		
	No neuropathy	0-5 points
	Mild neuropathy	6-8
	Moderate neuropathy	9-11
	Severe neuropathy	12+

Testing based on: "Validation of the Toronto Clinical Scoring System for Diabetic Polyneuropathy."
Diabetes Care. Bril V, Perkins BA. 2002 Nov;25(11):2048-52.