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ACCURACY OF STOP BANG QUESTIONNAIRE IN UNCONTROLLED TYPE 2 DIABETES MELLITUS AND CPAP TREATMENT EFFECTS.

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ABSTRACT **Background:** The co-existence of obstructive sleep apnea and type 2 diabetes mellitus is well documented. Early diagnosis and treatment of both of these diseases is a must, given the long term irreversible sequalae. **Methods:** STOPBANG questionnaire SBQ was used to screen for OSA and was validated usin in lab Polysomnogram (PSG) to diagnose OSA in patients with uncontrolled T2D (HbA1C >8). Interval glycemic effects of CPAP treatment was evaluated. **Results:** PSG confirmed OSA in 99 (83.2%) of the 119 participants. SBQ predicted the risk and severity of OSA with good specificity at scores of above 6.5. The positive predictive value (PPV) at scores above 6 for SBQ was 81% with an accuracy of 68% for a diagnosis of moderate to severe OSA validated with AHI on PSG. HbA1c improved in all the groups, more so in the CPAP arm ($p < 0.001$). **Conclusion:** SBQ is a very reliable OSA screening tool in our patient population particularly in those with moderate to severe disease. CPAP, along with conventional diabetic treatments, improves glycemic control over a short-term follow-up.

KEYWORDS : STOPBANG questionnaire (SBQ), Obstructive Sleep Apnea (OSA), Polysomnogram (PSG), Type 2 Diabetes Mellitus (T2D), Apnea Hypopnea Index (AHI), Continuous positive airway pressure (CPAP)

INTRODUCTION

Obstructive sleep apnea (OSA) occurs due to recurrent upper airway collapse causes sleep fragmentation and arterial hypoxemia along with dynamic intrathoracic pressure changes, resulting in blood pressure and pulse alteration as well as increased sympathetic activity [1,2].

The diabetic epidemic in Asia contributes to 60% of global burden [3]. Incidence of T2D in Kerala is almost 20% [4] twice the Indian national average and this number seems to be worsening with progressively improving socio economic status [5].It is estimated that the prevalence of obesity among Indian men will be 10% and for Indian women will be 14% by 2040 [6]. Combination of untreated sleep apnea and uncontrolled diabetes with the overlap of obesity, are predicted to be reaching epidemic proportions in India. The full spectrum of cardiovascular diseases ensues from these risk factors and almost 90% of these are preventable.[7]. Inadequate public awareness of sleep disordered breathing coupled with limited resources for testing, high out of pocket expense for CPAP and need for long term treatment compliance, are major hurdles. OSA is known to cause glycemic variability irrespective of presence of diabetes [8]. Untreated OSA is presumed to be one of the major contributors of poor glycemic control [9]. Therefore, it is clinically important to screen OSA in diabetic patients.

Sleep studies are the gold standard for screening and diagnosing OSA. SBQ has been proven to be a reliable tool worldwide, but has not been rigorously evaluated in the Indian population, where there are several confounding factors especially perception of snoring during sleep can be considered good, etc. In India the access to a sleep lab carries long wait times and the ever increasing out of pocket costs deters effective implementation of standard of care. This warrants the need for simpler, cost-effective solutions.

This study aimed at an early diagnosis of OSA using a well-established simple screening tool - the STOP-BANG questionnaire (SBQ) in the Indian population by comparing its diagnostic ability with the gold-standard technique – the polysomnogram in the high risk uncontrolled T2D population. We also wanted to evaluate effects of CPAP on the glycemic control over a short term follow up.

METHODS

i. Study protocol: Patients with uncontrolled T2D defined by HbA1C > 8, attending the Endocrine outpatient clinic and suspected to have OSA based on history and physical exam were included in this study. The patients were excluded if they had a diagnosis of OSA or were currently on CPAP or any alternate treatment or were unable to or refused to undergo a formal Level 1 in lab PSG or had a need to be admitted in the hospital for more than 1 week or received steroids during the study period. PSG with or without CPAP trial was done on all the patients who agreed to participate in our study. All patients diagnosed with OSA were offered CPAP treatment. All the patients were advised sleep hygiene, life stye modification and exercise. Patients were advised to follow up in the outpatient clinic in 3 months. If they were unable to handle the CPAP further troubleshooting was done mostly through phone calls or in person. Irrespective of being on CPAP or not the patients were reviewed at follow up in the outpatient clinic setting with an HbA1C. The patients were included only if their 3 month check with HbA1c was obtained. CPAP compliance was measured subjectively. An Institutional Ethics Committee approval was taken prior to the start of the study.

ii. Technical information:

Data collection: A written informed consent was obtained from each participant. All participants were interviewed using a semi-structured questionnaire to collect their demographic details and clinical history related to the duration and treatment of diabetes.

Anthropometric measurements: Standard measurement guidelines were followed to measure the waist, hip, and neck circumferences.

STOP-BANG Questionnaire (SBQ): All the participants were screened for OSA using the SBQ. Appendix 1 – SBQ.

Polysomnography: All subjects who were screened by SBQ were subjected to overnight in lab level 1 PSG. Respiratory events were scored according to the American Academy of Sleep Medicine (AASM) criteria. Apnea was defined as complete cessation of airflow for 10 s or more; hypopnea was defined as either a >50% reduction in airflow for 10 s or more or a <50% but discernible reduction in airflow accompanied either by a >3% decrease in oxyhemoglobin saturation or an arousal. The Apnea Hypopnea Index (AHI) score was classified as follows: Normal: AHI < 5; Mild-sleep apnea: 5≤AHI<15; Moderate sleep apnea: 15≤AHI<30; and Severe sleep apnea: AHI ≥ 30.

Quasi-experimental study with CPAP intervention: Patients who opted for CPAP were classified as the experimental group (n = 82) and those who opted out of CPAP were classified as control group (n = 17). The HbA1c and blood glucose levels were measured before and 3 months after CPAP and compared.

iii. Statistics: Data entry and analysis was done using SPSS version 21.0. Student's independent t-test was used to test the mean differences between two samples and paired t-test was used to determine differences between the mean HbA1c levels before and after CPAP. Pearson's correlation test was used to assess the correlation between STOP-BANG and AHI scores. A p-value of 0.05 was considered statistically significant.

RESULTS:

150 patients were referred for this study out of which 31 were excluded: 4 had a previous diagnosis of OSA and they refused to get a repeat PSG or retry CPAP. 22 patients refused to undergo a PSG. 2 patients were lost to follow up. 1 patient died due to unrelated causes

and 2 patients were admitted in the hospital during the study period with 1 of them receiving steroids for asthma exacerbation.119 patients fulfilled all the inclusion criteria. The mean age was 59.7 ± 10.2 years with predominance of male (73%, n = 87). The average BMI in our study population was 31.53 kg/m2. [Table 1]. 99 (83.2%) were confirmed to have OSA while 20 patients did not have sleep apnea. 91.8% of the smokers tested positive for OSA in our study (p=0.01). Symptoms of headache, day-time sleep, and witnessed apneas noted on history had statistically significant correlation with the final diagnosis of OSA [Table 1]. Majority of those with OSA (88.4%) were on oral hypoglycemic drugs plus insulin therapy. 95% of the patients on insulin therapy had sleep apnea out of which 88.8% had moderate to severe OSA.

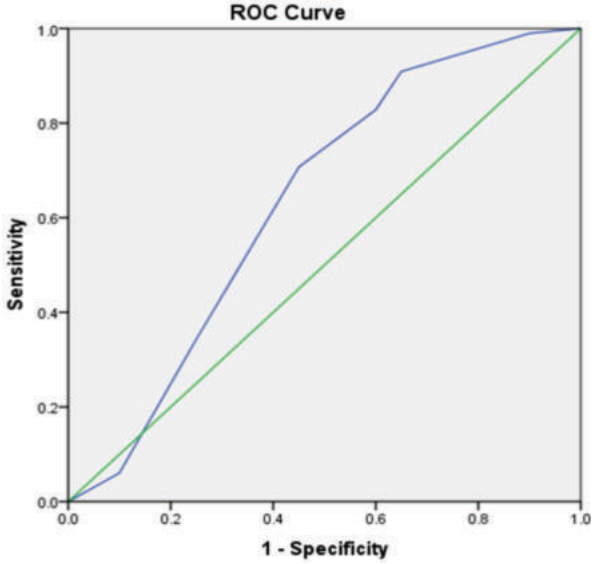
Table 1: Socio-demographic And Clinical Characteristics Of The Study Participants (n=119)

Clinical variables	NON-OSA	OSA	p-value*
Age (in years)	56.95 ± 9.6	60.34 ± 10.2	0.175
Gender (M: F)	1:1	2.2:7.7	<0.001
ESS	13.25 ± 2.6	13.1 ± 4.5	0.887
STOPBANG score	4.95 ± 1.9	5.84 ± 1.4	0.01
BMI (Kg/m2)	28.5 ± 1.3	32.1 ± 3.9	<0.001
Neck circumference (cm)	14.8 ± 1.9	15.8 ± 1.9	0.029
Systolic BP	126.4 ± 17.8	135.9 ± 14.7	0.012
Diastolic BP	75.5 ± 11.4	82.7 ± 10.3	0.006
Anti-diabetic medication			
Oral hypoglycemic (OHA) only	10 (17.5)	47 (82.5)	0.04
Insulin only	0 (0)	8 (100)	
OHA plus insulin	5 (11.6)	38 (88.4)	
Addictions			
Smoker	5 (8.2)	56 (91.8)	0.01
Alcoholic	4 (10.8)	33 (89.2)	0.24
Co-morbid conditions			
Hypertension	11 (14.1)	67 (85.9)	0.27
CAD	4 (9.3)	39 (90.7)	0.10
Dyslipidemia	7 (12.7)	48 (87.3)	0.27

* Student unpaired t-test

Figure 1: Correlation of AHI from PSG and SBQ

	STOP BANG SCORE >3				Total	STOP BANG SCORE <3		Total	Grand TOTAL
AHI	<4.9	5-14.9	15-29.9	>30		<4.9	15-29.9		
NO OSA	18				18	2		2	20
YES OSA		12	37	49	98		1	1	99
Grand TOTAL	18	12	37	49	116	2	1	3	119



Area under the ROC curve =0.634 (95% CI: 0.48, 0.78)

Figure 2: Efficacy of STOPBANG Score In Predicting Risk Of OSA Against Sleep Test

Score of 3 or more on the SBQ correlated with moderate -severe OSA (AHI >15) as noted in [Figure 1]. 6 of the 8 patients with a SBQ score of 8 had moderate to severe sleep apnea. 1 had very poorly controlled DM with fasting sugar of 358 and HbA1c of 10.8 which could have caused the high SBQ. There were 7 other patients with SBQ > 6 who were not diagnosed as OSA. Only 50% of these patients complained of daytime tiredness or restless sleep. Higher SBQ scores exhibited 75% agreement with severe OSA as measured by the AHI. The specificity was acceptable at 76% at scores above 6.5. Area under the ROC curve =0.634 (95% CI: 0.48-0.78) [Figure 2]. A lower SBQ score exhibited 66.7% agreement with AHI scores to define patients without OSA. There was a significant positive correlation (r^2 = 0.409; p < 0.001) between the SBQ score and AHI severity among the study participants [Figure 3]. Patients with a SBQ score of 6 or more had a Positive Predictive Value (PPV) of 81% and were noted to have at least moderate to severe OSA with an accuracy of 68% [Table 2]. Mean HbA1c of the study population improved from 8.80 to 8.17 irrespective of treatment. Our results also indicated a statistically significant (p < 0.001) improvement in the HbA1c values after 3 months of being on CPAP (mean HbA1c reduction = 0.7%). The improvement in HbA1c in the CPAP treated group was statistically significant which was not the case in the control arm. [Table 3].

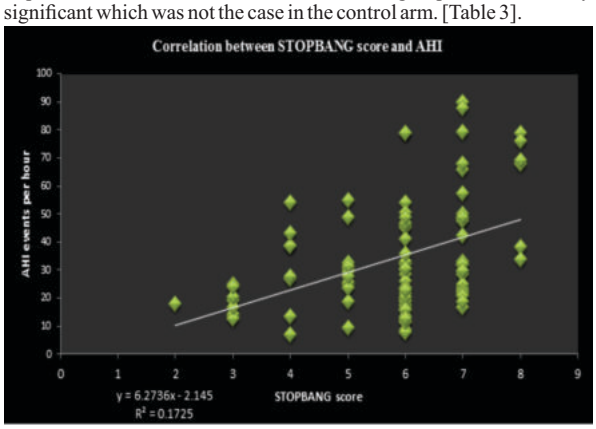


Figure 3: Correlation between STOPBANG score and AHI events per hour among patients with OSA (n=99)

		AHI, no. of events/h
STOP BANG	Pearson Correlation (r)	0.409**
	p-value	<0.001
	N	119

Table 2: STOPBang Score (SBQ) compared to a diagnosis of sleep apnea (AHI >5)

	AHI>15	AHI<15
STOPBANG >/=6	64	15
STOPBANG </=5	23	17

PPV = 81% (95%CI 74% to 86%) with an Accuracy of 68 % (95% CI 59% to 76%) Positive LR =1.57

Prevalence of OSA in T2D ~ 73% (17)

Table 3: Differences in HbA1c levels among OSA with and without CPAP over 3 months

	With CPAP (n=82)	Without CPAP (n=17)	p-value*
HbA1c at entry	9.05 ± 1.7	9.01 ± 1.4	0.93
HbA1C after 3 months	8.35 ± 1.1	8.7 ± 1.2	0.24
t-test value	9.58	2.43	
p-value**	<0.001	0.027	

*Student Independent unpaired t-test ** Student independent paired t-test

DISCUSSION

Type 2 diabetes mellitus (T2D) the silent epidemic of the current generation is often found to coexist with OSA as they share and are mutual risk factors as well [9,10]. Beta cell dysfunction and insulin resistance is mediated through multiple neurohumoral and inflammatory mechanisms which makes OSA a risk factor for T2D. In its turn T2D also has been found to be an independent risk factor for development of OSA[6]. Uncontrolled OSA has been linked with poor glycemic control in T2D [9]. But CPAP treatment for OSA in rigorous

RCTs has not consistently improved glycemic control in TD2 [13,14]

To our knowledge SBQ has not been rigorously evaluated in the Indian population in direct comparison with a formal in lab PSG, especially in the uncontrolled diabetics. This population was chosen as there is a suspected high prevalence of OSA ~73% and the impact of untreated disease in this group can be catastrophic [16]. Effect of CPAP along with other antidiabetic treatment for glycemic control even though plausible, has not been consistently proven [13,14,17].

Shaw et al did not show adequate glycemic improvement with CPAP in a fairly large RCT. But these patients had very well controlled diabetes based on HbA1c measure and patients on insulin were excluded [13]. In contrast CPAP has been shown to be effective in the treatment of OSA and reduction of HbA1c levels in diabetics with poorly controlled T2D, as noted by Martinez et al in their RCT[14]

We found SBQ score to be an excellent tool to diagnosis patients with moderate to severe sleep apnea at scores higher than 6.5. We found that the probability and severity of OSA increased with an increasing SBQ score. The sensitivity of the former was highest using a diagnostic cut-off value of 3 (85.6%), with a specificity of 60%. The relative lower specificity at this cut off precludes using SBQ as a diagnostic tool at these scores. Positive predictive value (PPV) for SBQ was over 80% in our study with an accuracy of 68% for detecting moderate to severe sleep apnea at scores more than 6. This finding has been consistently found in multiple studies in literature [18]. The consistent performance of SBQ score in picking up moderate to severe OSA, makes this a very reliable tool that should be used in every T2D patient even at the time of initial diagnosis. Patients with a diagnosis of OSA were more likely to be on insulin treatment consistent with the finding of possible insulin resistance. Hence when insulin is considered in T2D, a SBQ questionnaire should be done and if more than 6, prompt measure to diagnose and treat moderate to severe sleep apnea should be considered.

We also observed a significant reduction in HbA1c values 3 months after CPAP in the OSA group ($p < 0.001$). Martinez et al. [14] noted a significant reduction in HbA1c levels ($p = 0.02$) at 6 months after CPAP without significant changes at the 3 month follow-up; however, they recruited the diabetics with baseline HbA1c levels of $7.6 \pm 1.3\%$, which was much lower compared to the baseline levels considered in our study ($9.05 \pm 1.7\%$). The poorer controlled T2D may have been responsible for this difference. Shaw et al [13] showed that PAP therapy did not improve glycemic control in patients with relatively well-controlled type 2 diabetes and OSA. They used autoCPAP as compared to fixed CPAP used in the study by Martinez et al. In our study, fixed CPAP was used and the measurement done at 3 months showed statistically significant improvement in HbA1C. Some studies have found fixed CPAP to be more effective than AutoCPAP in stabilizing cardiac parameters by lowering sympathetic activity. The exact mechanism in unclear but it is possible that with autoCPAP there is more sleep fragmentation and arousals [19]. Our study had patients with poorer glycemic control and more severe OSA as compared to the study by Shaw et as well as Martinez et al. While the later study noted a mean baseline HbA1c and ODI of 7.3% and 23 events per hour, our study had a mean baseline HbA1c and ODI of 8.74% and 42.45 events per hour respectively.

We also noted, the group with OSA who did not consent for PAP therapy, also exhibited a drop in HbA1c albeit lower than that with the CPAP treatment. In this study PAP compliance was assessed verbally during follow-up visits or telephonic conversations. Although we could reliably identify adults with the newly-diagnosed OSA who were using PAP regularly and correct any immediate problems, their adherence and hours of use could not be tracked. Hence, presuming that the glycemic control in the CPAP group was entirely due to PAP therapy would be an erroneous conclusion. But given that the change in HbA1C was more in the CPAP treated group probably alludes to a role of CPAP treatment.

Patient education can change behavior favorably which in turn helps disease management. A plausible explanation to the HbA1c decline in both groups is that the additional diagnosis of OSA in an individual already suffering from a chronic illness could have contributed to lifestyle changes altering the disease dynamics. Thus, diagnosing OSA up front using a simple screening tool such as STOPBANG and educating the patients about this disease, may influence better compliance with lifestyle modification and antidiabetic medication consumption, thereby improving glycemic control. Nevertheless, OSA diagnosis in uncontrolled T2D patients needs to be managed as would be managed in those without diabetes, irrespective of the effects of CPAP on glycemic control.

The strengths of the study included a good sample size, usage of a gold standard i.e in lab formal polysomnogram to measure and confirm the diagnosis of OSA thereby increasing the reliability of the results. Follow up biochemical parameters allowed objective measures of effects of CPAP and other antidiabetic treatment on the overall patient management.

The limitations of the study included differences in dietary habits, customs, and cultural practices and anti-diabetic treatment modalities between the experimental and control group. SBQ has subjective questions which can be positive in T2D patients with as well as without OSA and hence conclusively relying on this scale maybe clinically difficult. While the lower numbers in the control arm can be considered as a limitation, holding of standard of care treatment in those with OSA would not have been ethical. Once again using a sham trial can be considered but may go against standard of care management. The CPAP compliance was assessed verbally and hence objective number of hours of use could not be determined.

In conclusion, the STOP-Bang questionnaire showed good sensitivity and a high positive predictive value for OSA screening and severity assessment among patients with uncontrolled diabetes mellitus. Screening for OSA using the STOP-Bang questionnaire should be considered in all diabetic patients at the time of diagnosis and patients should be educated about their diagnosis which may have benefits even if CPAP treatment is not pursued. Further larger studies with long term follow up to elucidate role of CPAP along with other diabetic treatment are needed probably with the use of sham CPAP to answer the question of glycemic control.

CONCLUSION

The study confirmed good correlation between SBQ and AHI scores obtained from a formal PSG in patient with uncontrolled T2D, especially in those with moderate to severe OSA. Hence, STOP-BANG questionnaire can be used as a reliable screening tool for detecting and grading the severity of OSA in this group. Furthermore, CPAP in addition to conventional T2D treatment led to significant decrease in HbA1c among patients during a short term follow up.

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