Original Article

Clinical and polysomnographic predictors of severe obstructive sleep apnea in the South Indian population

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Abstract

Background: With the emergence of lifestyle diseases in epidemic proportions, obstructive sleep apnea (OSA) is being increasingly recognized in less developed countries as well. **Aim:** We sought to study the demographic, clinical, and polysomnographic (PSG) predictors of OSA severity in a cohort of South Indian patients. **Materials and Methods:** Consecutive patients with PSG proven OSA [apnea hypopnea index (AHI) ≥5/h] were prospectively recruited. The study period was from January 2012 to December 2012. Demographic data, history of vascular risk factors, substance abuse, sleep quality, snoring, and witnessed apneas were collected using a structured *pro forma*. In addition, PSG variables such as AHI, sleep latency and efficiency, duration of slow wave and rapid eye movement (REM) sleep, and other parameters were collected. Correlations between AHI severity and clinical and PSG parameters were done. **Results:** There were 152 (119 males and 33 females) subjects with a mean age of 53.8 years and body mass index (BMI) of 29.31. Mean AHI was 36.2/h (range: 5.1-110) and 66 subjects had severe OSA. Around 12% had the presenting complaint as insomnia, mainly of sleep maintenance. Of the subjects, 35% had witnessed apneas and 67% had excessive daytime sleepiness (EDS); 40% of patients had ≥2 risk factors. PSG parameters showed short sleep onset latency with a high arousal index. Mean apnea duration was 24.92 s. We found that age >55 years, BMI >25 kg/m^2, witnessed apneas, EDS, hypertension, dyslipidemia, reduced slow wave sleep duration, mean apnea duration >20 s, and desaturation index >10/h correlated well with OSA severity while the arousal index, sleep latency and efficiency, and exposure to smoking and alcohol showed no association. **Conclusions:** Older subjects with witnessed apneas are likely to have more severe OSA. Even though overall sleep architecture was similar between the groups, severe OSA had shorter slow wave sleep, longer apneas, and higher nocturnal hypoxemia.

Key Words

Body mass index (BMI), obstructive sleep apnea (OSA), risk factors

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Introduction

Obstructive sleep apnea (OSA), traditionally thought to be affecting the affluent population in developed countries is increasingly being recognized in developing countries as well.[1,2] With aging of the population, increasing urbanization, and industrialization and emergence of lifestyle diseases, India is experiencing a growing burden of noncommunicable diseases.[3] The four leading chronic diseases in India, in the decreasing order of prevalence are cardiovascular diseases, diabetes mellitus, chronic obstructive pulmonary disease, and cancer.[4]

Many authors have noted a strong association between OSA and cardiovascular risk factors. The mechanisms by which OSA increases the risk of cardiovascular diseases include

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intermittent hypoxia, sleep fragmentation, sleep deprivation (which causes sympathetic activation), dysregulation of the hypothalamus-pituitary axis, increase of reactive oxygen species, and activation of inflammatory pathways, prothrombotic factors, and C-reactive protein.[5,6] However, the reverse association of vascular risk factors with the severity of OSA is not well-understood. Also, the ability of other clinical parameters such as age, body mass index (BMI), symptoms such as excessive daytime sleepiness (EDS), witnessed apneas, and polysomnographic (PSG) parameters to predict the severity of OSA is poorly understood in the South Indian population.

Aim

We sought to study the demographic, clinical, and PSG predictors of OSA severity in a South Indian cohort of patients with OSA of varying severity.

Materials and Methods

Consecutive patients with symptoms suggestive of sleep disordered breathing (snoring, witnessed apneas, and/or EDS) attending the Comprehensive Sleep Disorders Center (CSDC) under the Department of Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvanatapuram, Kerala, India were prospectively recruited for the study. The CSDC runs a sleep clinic, which caters to around 800 patients annually with around 60% being OSA. We also do around 400 overnight PSGs and 150 continuous positive airway pressure (CPAP) titrations annually. The study being noninterventional was approved by the Institutional Ethics Committee for publication. EDS was quantified using vernacular (Malayalam) translation of Epworth Sleepiness Scale (ESS) with score ≥10 considered as abnormal.[7] After informed consent, the demographic and clinical profiles including BMI, neck circumference, and details of their sleep perception were extracted using a structured *pro forma*. BMI was defined as per International Obesity Task Force (IOTF) guidelines as ≥25 kg/m^2 as overweight and ≥30 as obesity.[8] Neck circumference ≥38 cm in males and ≥35 cm in females were considered as abnormal.[9] Details of vascular risk factors — systemic hypertension, type 2 diabetes mellitus, dyslipidemia, history of coronary artery disease, and stroke were also collected. Details of alcohol and tobacco use (current usage = has consumed tobacco/alcohol in the last 3 months past usage = has stopped alcohol/cigarette more than 3 months back) and use of hypnotics were also collected.

The study period was 1 year, from January 2012 to December 2012. All the patients underwent overnight supervised PSG using BIO-LOGIC system (Heinen und Löwenstein, Bad Ems, Germany). The standard PSG recording consisted of four electroencephalograms (EEGs) channels (C3,C4,O1, and O2 referenced to the contralateral ear), two electrooculograms (right and left electro oculogram respectively (ROG) and LOG), chin and *tibialis anterior* electromyography (EMG), electrocardiogram (ECG), and respiratory channels consisting of airflow sensor (nasal thermistor), chest and abdominal belts, pulse oxymeter for oxygen saturation, snore microphone and body plethysmograph for checking the body position. The PSG recording and scoring of sleep stages and respiratory events were done by sleep physicians (SES, PA, and ALR) as per AASM guidelines.[10] "Obstructive sleep apnea" was defined as the cessation of airflow for a duration of 10 s or more with continuing respiratory effort as evidenced by thoracic and abdominal excursions and "hypopnea" was defined as reduction in respiratory effort by 30% lasting for 10 s or more, associated with a decline in oxygen saturation by 4%. Number of apneas/hypopneas per hour of sleep was scored (apnea hypopnea index or AHI) to calculate the severity of OSA, which was classified into mild (AHI 5–15/h), moderate (15-30), and severe (>30/h). The patients were divided into two groups — those with mild to moderate OSA (AHI <30/h) and the group with severe OSA (AHI ≥30/h).

In addition, other PSG parameters measured were sleep latency (time from lights off to onset of sleep, that is, three consecutive epochs of stage I nonrapid eye movement (NREM) or 1 epoch of any other sleep stage),sleep efficiency (fraction of time in bed when the patient is sleeping), arousal index (number of arousals per hour of sleep) and fraction of total sleep time spend in Stage III NREM, and rapid eye movement (REM) sleep and apnea duration. Severity of nocturnal hypoxemia was measured using two parameters — desaturation index, which is the number of desaturations (>4% drop of SaO2 from the baseline) per hour of sleep and fraction of total sleep time with SaO2 <90%.

Statistical analysis

Analysis was done using SPSS version 16 software (SPSS Inc., Illinois, Chicago, USA). Variables were expressed in means and percentages. The subjects were divided into two groups — those with mild to moderate OSA versus those with severe OSA. Fisher's exact test and chi-square test were used to test the association between variables and OSA severity. Those parameters, which became significant on univariate analysis were subjected to multivariate analysis by logistic regression modeling and values less than 0.05 were considered as statistically significant.

Results

Our study cohort was predominantly male and middle-aged with the majority being overweight with a high neck circumference. Excessive daytime sleepiness followed by nocturnal arousals with respiratory difficulty was the most common complaint at presentation. Snoring was found in all the patients. Baseline characteristics including risk factor profile is given in Table 1. Ours being a predominantly neurocardiac center, we did not have many patients with concomitant obstructive airway disease in the study population. Table 2 gives the PSG data of our study population. We did not include patients with a primary diagnosis of central sleep apnea syndrome in the present study.

Univariate analysis of clinical parameters showed that apart from clinical symptoms, hypertension and dyslipidemia were found more in patients with severe OSA. However, diabetes, exposure to cigarette or alcohol (current or past), or the presence of two or more risk factors did not increase the risk of having severe OSA. We could not study the impact of gender as the majority of our subjects were males. Among the PSG parameters, shortening of slow wave sleep duration, longer apneas, and more nocturnal desaturation were associated with

severe OSA while REM duration and nocturnal arousals were comparable between the two groups.

Multivariate analysis [Table 3] showed that among the clinical parameters, age >55 years and history of witnessed apneas were independently associated with severe OSA. BMI and excessive daytime sleepiness did not have a statistically significant association with the severity of OSA in our population. Among the PSG parameters, longer apnea duration and more severe nocturnal hypoxemia as evidenced by higher desaturation index and nocturnal desaturation occupying >10% of total sleep time correlated independently with OSA severity.

Table 1: Baseline characteristics — clinical

Clinical parameters	*N* = 152 subjects
Age	53.81±12.01 (26-85 years)
Gender	119 M:33 F
BMI	29.31±5.01 kg/m^2
Collar size >38 cm in men and >35 cm in women	71.7%
Insomnia as presenting complaint	11.8%
Witnessed apneas	34.9%
Arousals with respiratory difficulty	39.5%
Wakes up refreshed after sleep	36.8%
Excessive daytime sleepiness	67.1%
Systemic hypertension	55.3%
Diabetes mellitus	43%
Dyslipidemia	36.8%
≥2 risk factors	40.4%
Coronary artery disease	15.2%
History of smoking	36.2%
History of alcohol intake	44.7%

BMI = Body mass index

Table 2: Baseline characteristics — PSG

Polysomnographic parameters	*N* = 152 subjects	Percentage
Apnea hypopnea index	36.2 (5.1-110)	
Sleep latency >30 min	10	6.6
Sleep efficiency <80%	49	32.2
Arousal index >10/h	144	94.7
Slow wave sleep as % of TST		21.4
REM sleep as % of TST		14.63
Desaturation index	21.67/h	
Mean apnea duration	24.92 s	
Cumulative fraction of sleep with saturation <90%		13.35

TST = Total sleep time, REM = Rapid eye movement

Table 3: Multivariate analysis

Parameters	*P* value	Adjusted odds ratio
Age 55 years	.046	3.108
BMI ≥25 kg/m^2	.647	1.319
Witnessed apneas	.006	5.086
EDS	.324	1.835
Hypertension	.302	1.817
Dyslipidemia	.152	2.238
Mean apnea duration >20 s	.031	4.599
Nocturnal desaturation >10% of TST	.013	5.003
Desaturation index >10	.001	8.145

BMI = Body mass index, EDS = Ehlers-Danlos syndrome, TST = Total sleep time

Discussion

A few authors from India have studied the impact of demographic profile and excessive daytime sleepiness on OSA severity. However, the effect of vascular risk factors and PSG parameters on OSA severity is poorly understood. With increasing prevalence of noncommunicable diseases in the middle-aged population, their impact on OSA severity needs to be known. This is especially important so as to sensitize the primary physicians about OSA as a modifiable risk factor for cardiovascular diseases,[11] more so in those with other vascular risk factors.

The impact of age and gender on OSA severity has been well-described. Large community-based studies have identified the high prevalence of sleep-disordered breathing (SDB) in the middle-aged population.[12-15] The mean age of our study cohort is comparable to the literature in the West.[12,15,16] We found that age >55 years was an independent predictor of OSA severity. The effect of age on OSA severity has yielded mixed results across studies. Bixler *et al*.[14] found an increasing OSA severity with age while British authors found a less robust effect of age on OSA severity.[17] Asian studies from China have shown contradictory results with Ip *et al*.[18,19] showing an increase in OSA severity with age and others[20] finding a decrease in severity with increasing age. Indian authors have found an increase in the prevalence of OSA with aging but have not looked into the severity of the illness.[21] Almost all the authors across the world have found a male predominance in OSA, ranging from 2.3:1[12] to 7:1,[21] which was independent of BMI.[19]

Our study cohort was overweight and the BMI did not significantly differ between the two groups. A majority of authors in the West and Asia have found a statistically significant association between BMI and OSA severity. However, in the sleep heart health study cohort, a less robust association between BMI and OSA severity was found.[16] Previous studies from India also have shown mixed results in the association between BMI and OSA severity. In a study on urban men, there was a linear relationship between BMI and increasing OSA severity[22] while a hospital-based case-control study found a higher BMI among cases but could not correlate it with OSA severity.[23]

Among the clinical symptoms, EDS was the most common, seen in around 2/3rd of the patients followed by arousals with respiratory difficulty and witnessed apneas. However, in multivariate analysis, only witnessed apneas had a consistent association with the severity of OSA. Johns proposed the Epworth Sleepiness Scale (ESS), an objective measure of daytime sleepiness as a tool to differentiate a primary snorer from OSAS, way back in 1993.[24] The association between ESS and AHI severity has yielded conflicting results in the literature with some showing a good correlation[25,26] and others not so.[27,28] Some Indian authors have found that ESS as a screening tool has a good discriminatory power in detecting OSA[22,23] but they did not look into the effect on OSA severity. Another

study from Delhi, India could not find an association between OSA severity and EDS.[29] An association of breathing pauses with OSA severity has been found in community-based studies as well. Young *et al*.[16] found that those with breathing pauses were three to four times more likely to have AHI >15, more so in middle age.

Among the risk factors, the presence of hypertension and dyslipidemia were found to be significant in univariate analysis but they failed to show significance on final results. Simon *et al*.[30] in a cohort of 190 subjects tried to see whether any of the cardiovascular diseases correlated with the severity of OSA. They found that patients with any risk factor were noticed to have more severe OSA with an odds ratio 3.24. They also had poor sleep efficiency and more nocturnal desaturations without concomitant increase in EDS. In a Cincinnati, Ohio, USA veterans study of 596 subjects,[31] the presence of hypertension, T2DM, and congestive heart failure had a positive correlation with OSA severity. It is well-known that OSA can predispose to the development of high blood pressure (BP)[32] and metabolic syndrome[33] but the reverse association is less studied. The reason behind why any of the cardiovascular diseases failed to show a positive correlation in our study could be due to a smaller number of patients in each arm. Also, BMI in our patients was comparable between OSAs of varying severity, which is a reflection of a widely prevalent metabolic syndrome in the Asian and Indian populations.

Overall sleep characteristics including latency, efficiency, and arousal index were comparable between OSA of varying severity. While REM sleep duration was comparable, there was a greater reduction of slow wave sleep in patients with severe OSA in univariate analysis. A few authors have looked into the changes in sleep architecture with increasing OSA severity. Bianchi *et al*.[34] found that when compared to controls and those with medical comorbidities, OSA patients have a faster decay rate of NREM and REM sleep, manifesting as shorter sleep bouts and more arousals but failed to find an association with OSA severity. Shorter slow wave sleep correlated with more EDS in OSA of comparable severity in one study.[35] Since the number of subjects without EDS was less in our study cohort, we could not find its association with slow wave sleep shortening.

Longer apneas are seen more often in clinical practice in patients with severe OSA, which was observed in our study as well. However, this parameter has been least studied among the PSG variables across the literature. The fact that apnea lengthens as night progresses has been reported much earlier.[36] Recently, Sasai *et al*. reported a prolongation of apnea late at night in subjects with severe OSA.[37] We did not look into variation in apnea duration with progression of the night. Recently, Finnish authors have reported that AHI severity and apnea duration dichotomize beyond a certain level, as the number of apneas cannot increase concomitant with the lengthening of apneas.[38] However, they used ambulatory level 1 PSG where only respiratory parameters were monitored and hence, sleep stages and the effect of REM were not known. This observation of longer apneas >20 s as an independent predictor of OSA severity is useful in clinical practice, especially for technologists doing split-night studies where the time for assessing OSA severity is less.

Our study showed a positive correlation of OSA severity with nocturnal hypoxemia. This observation has been reported by other authors as well. Sasai *et al*. found more desaturations late at night in severe OSA subjects.[37] Some have reported that extent of nocturnal hypoxemia is a direct determinant of OSA severity and can lead to the development of daytime desaturations as well.[39] Nocturnal hypoxemia can lead to increased BP and increase the risk of cerebrovascular and cardiovascular events. This is also reported to be a major cause of EDS in the OSA population.

Our study of 152 subjects with OSA of varying severity is not without limitations. We did not have data on neck circumference and waist hip ratio in all subjects and could not assess their impact on OSA severity, especially since the majority of our study subjects were of comparable BMI. Looking into these surrogate markers of obesity may be especially relevant in Indian subjects who are of a smaller built than western subjects with more of central obesity. We collected data only on the presence or absence of risk factors and did not look into their duration or control status. Whether the long duration of risk factors and their poor control has an impact of OSA severity needs to be studied. Also, we did not perform cephalometry or Mallampati scoring in our subjects. All the PSGs were manually scored by the sleep physicians; there could be interobserver differences in the staging of sleep and marking the duration of apneas but these are only minor lacunae, which is unlikely to have an impact on the final results.

Conclusions

OSA predominantly affects middle-aged men who are overweight with many having high neck circumference. Increasing age >55 years and witnessed apneas are indicative of increasing OSA severity while BMI and EDS are comparable across OSA of increasing severity. The presence or absence of any of the cardiovascular risk factors did not have an impact on OSA severity. Severe OSA patients had longer apneas and more severe nocturnal desaturation, compared to mild to moderate disease despite having similar sleep architectures and fragmentations.

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Conflicts of interest
There are no conflicts of interest.

References

1. Vijayan VK, Patial K. Prevalence of obstructive sleep apnoea syndrome in Delhi, India. Chest 2006;130:92S.
2. Sharma SK, Kumpawat S, Banga A, Goel A. Prevalence and risk factors of obstructive sleep apnea syndrome in a population in Delhi, India. Chest 2006;130:149-56.
3. Upadhyah RP. An overview of the burden of non-communicable diseases in India. Iran J Public Health 2012;41:1-8.
4. Taylor DW. The Burden of Non-Communicable Diseases in India. Hamilton, ON: The Cameron Institute; 2010; p. 13.
5. Galletti F, Barbato A, Versiero M, Iacone R, Russo O, Barba G, *et al*. Circulating leptin levels predict the development of metabolic syndrome in middle-aged men: An 8-year follow-up study. J Hypertens 2007;25:1671-7.

6. Minoguchi K, Yokoe T, Tazaki T, Minoguchi H, Tanaka A, Oda N, *et al*. Increased carotid intima-media thickness and serum inflammatory markers in obstructive sleep apnea. Am J Respir Crit Care Med 2005;172:625-30.
7. Johns MW. A new method for measuring daytime sleepiness: The Epworth sleepiness scale. Sleep 1991;14:540-5.
8. WHO Expert Consultation. Appropriate-body mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363:157-63.
9. Yang GR, Yuan SY, Fu HJ, Wan G, Zhu LX, Bu XL, *et al*.; Beijing Community Diabetes Study Group. Neck circumference positively related with central obesity, overweight, and metabolic syndrome in Chinese subjects with type 2 diabetes: Beijing Community Diabetes Study 4. Diabetes Care 2010;33:2465-7.
10. Iber C, Ancoli-Israel S, Chesson AL, Quan SF. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications. 1st ed. Westchester: American Academy of Sleep Medicine; 2007.
11. Goldstein LB, Bushnell CD, Adams RJ, Appel LJ, Braun LT, Chaturvedi S, *et al*.; American Heart Association Stroke Council; Council on Cardiovascular Nursing;Council on Epidemiology and Prevention; Council for High Blood Pressure Research; Council on Peripheral Vascular Disease, and Interdisciplinary Council on Quality of Care and Outcomes Research. Guidelines for the primary prevention of stroke: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2011;42:517-84.
12. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993;328:1230-5.
13. Gislason T, Almqvist M, Eriksson G, Taube A, Boman G. Prevalence of sleep apnea syndrome among Swedish men — An epidemiological study. J Clin Epidemiol 1988;41:571-6.
14. Bixler EO, Vgontzas AN, Lin HM, Ten Have T, Rein J, Vela-Bueno A, *et al*. Prevalence of sleep-disordered breathing in women: Effects of gender. Am J Respir Crit Care Med 2001;163:608-13.
15. Durán J, Esnaola S, Rubio R, Iztueta A. Obstructive sleep apnea-hypopnea and related clinical features in a population-based sample of subjects aged 30 to 70 yr. Am J Respir Crit Care Med 2001;163:685-9.
16. Young T, Shahar E, Nieto FJ, Redline S, Newman AB, Gottlieb DJ, *et al*.; Sleep Heart Health Study Research Group. Predictors of sleep-disordered breathing in community-dwelling adults: The Sleep Heart Health Study. Arch Intern Med 2002;162:893-900.
17. Stradling JR, Crosby JH. Predictors and prevalence of obstructive sleep apnoea and snoring in 1001 middle aged men. Thorax 1991;46:85-90.
18. Ip MS, Lam B, Lauder IJ, Tsang KW, Chung KF, Mok YW, *et al*. A community study of sleep-disordered breathing in middle-aged Chinese men in Hong Kong. Chest 2001;119:62-9.
19. Ip MS, Lam B, Tang LC, Lauder IJ, Ip TY, Lam WK. A community study of sleep-disordered breathing in middle-aged Chinese women in Hong Kong: Prevalence and gender differences. Chest 2004;125:127-34.
20. Bixler EO, Vgontzas AN, Ten Have T, Tyson K, Kales A. Effects of age on sleep apnea in men: I. Prevalence and severity. Am J Respir Crit Care Med 1998;157:144-8.
21. Sharma SK, Reddy EV, Sharma A, Kadhiravan T, Mishra HK, Sreenivas V, *et al*. Prevalence and risk factors of syndrome Z in urban Indians. Sleep Med 2010;11:562-8.
22. Udwadia ZF, Doshi AV, Lonkar SG, Singh CI. Prevalence of sleep-disordered breathing and sleep apnea in middle-aged urban Indian men. Am J Respir Crit Care Med 2004;169:168-73.
23. Pradeep Kumar VG, Bhatia M, Tripathi M, Srivastava AK, Jain S. Obstructive sleep apnoea: A case-control study. Neurol India 2003;51:497-9.
24. Johns MW. Daytime sleepiness, snoring, and obstructive sleep apnea. The Epworth Sleepiness Scale. Chest 1993;103:30-6.
25. Roure N, Gomez S, Mediano O, Duran J, Peña Mde L, Capote F, *et al*. Daytime sleepiness and polysomnography in obstructive sleep apnea patients. Sleep Med 2008;9:727-31.
26. Hesselbacher S, Subramanian S, Allen J, Surani S, Surani S. Body mass index, gender, and ethnic variations alter the clinical implications of the Epworth Sleepiness Scale in patients with suspected obstructive sleep apnea. Open Respir Med J 2012;6:20-7.
27. Sauter C, Asenbaum S, Popovic R, Bauer H, Lamm C, Klösch G, *et al*. Excessive daytime sleepiness in patients suffering from different levels of obstructive sleep apnoea syndrome. J Sleep Res 2000;9:293-301.
28. Mediano O, Barceló A, de la Peña M, Gozal D, Agustí A, Barbé F. Daytime sleepiness and polysomnographic variables in sleep apnoea patients. Eur Respir J 2007;30:110-3.
29. Reddy EV, Kadhiravan T, Mishra HK, Sreenivas V, Handa KK, Sinha S, *et al*. Prevalence and risk factors of obstructive sleep apnea among middle-aged urban Indians: A community-based study. Sleep Med 2009;10:913-8.
30. Simon R, Chirakalwasan N, Teerapraipruk B, Hirunwiwatkul P, Jaimchariyatam N, Desudchit T, *et al*. Severity of obstructive sleep apnea in patients with and without cardiovascular-related diseases. Respir Care 2012;57:1476-82.
31. Samson P, Casey KR, Knepler J, Panos RJ. Clinical characteristics, comorbidities, and response to treatment of veterans with obstructive sleep apnea, Cincinnati Veterans Affairs Medical Center, 2005-2007. Prev Chronic Dis 2012;9:E46.
32. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 2000;342:1378-84.
33. Tasali E, Mokhlesi B, Van Cauter E. Obstructive sleep apnea and type 2 diabetes: Interacting epidemics. Chest 2008;133:496-506.
34. Bianchi MT, Cash SS, Mietus J, Peng CK, Thomas R. Obstructive sleep apnea alters sleep stage transition dynamics. PLoS One 2010;5:e11356.
35. Oksenberg A, Arons E, Nasser K, Shneor O, Radwan H, Silverberg DS. Severe obstructive sleep apnea: Sleepy versus nonsleepy patients. Laryngoscope 2010;120:643-8.
36. Charbonneau M, Marin JM, Olha A, Kimoff RJ, Levy RD, Cosio MG. Changes in obstructive sleep apnea characteristics through the night. Chest 1994;106:1695-701.
37. Sasai T, Inoue Y, Matsuo A, Matsuura M, Matsushima E. Changes in respiratory disorder parameters during the night in patients with obstructive sleep apnoea. Respirology 2011;16:116-23.
38. Muraja-Murro A, Nurkkala J, Tiihonen P, Hukkanen T, Tuomilehto H, Kokkarinen J, *et al*. Total duration of apnea and hypopnea events and average desaturation show significant variation in patients with a similar apnea-hypopnea index. J Med Eng Technol 2012;36:393-8.
39. Fanfulla F, Grassi M, Taurino AE, D'Artavilla Lupo N, Trentin R. The relationship of daytime hypoxemia and nocturnal hypoxia in obstructive sleep apnea syndrome. Sleep 2008;31:249-55.