

Original Article:**Sleep disordered breathing in patients with epilepsy****B. Vengamma,¹J. Vijayabhaskara Rao,¹Alladi Mohan²***Departments of ¹Neurology, ²Medicine, Sri Venkateswara Institute of Medical Sciences, Tirupati***ABSTRACT**

Background: Sleep has long been known to affect epilepsy. Little has been documented regarding the epidemiology of sleep disordered breathing (SDB) in patients with epilepsy from India.

Methods: Between April 2009 and September 2011, in the first stage of the study, 452 consecutive patients with epilepsy (cases) and 500 age- and gender-matched normal control subjects were screened using Epworth's Sleepiness Scale (ESS). Of these, 98 (23%) had an ESS score of 10 or more, suggestive of excessive day time sleepiness (EDS). Of these, 30 patients (mean age was 35.8±13.1; 26 males) were taken up for the second stage of the study, underwent detailed evaluation and overnight in-hospital polysomnography (PSG) in the sleep laboratory.

Results: Their mean age was 35.8 ±13.1; 26 males); Of these, 13 (43.3%)(all males) had evidence of OSAS on PSG: 9 had mild OSAS [apnoea-hypopnoea index (AHI) 5-15]; 3 had moderate OSAS (AHI 15-30) and one patient had severe OSAS (AHI >30). On univariate analysis, a higher proportion of patients with nocturnal seizures had OSAS compared with those with diurnal seizures and combined periodicity (7/8 vs 6/16; p=0.009). Patients with uncontrolled seizures had a higher prevalence of OSAS (p=0.045).

Conclusions: Our observations suggest that EDS is an important symptom being six times more common in patients with epilepsy compared to healthy control subjects. Furthermore, PSG study indicated that 43.3% of epilepsy patients with EDS have OSAS. Thus, SDB appears to be an underdiagnosed disease in patients with epilepsy from India.

Key words: *Epilepsy, Sleep disordered breathing, Obstructive sleep apnoea*

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INTRODUCTION

Epilepsy is a common condition that affects up to 1%-5% of the population.¹ Sleep has long been known to affect epilepsy and nearly 21% of patients had seizures solely during sleep.² There is a reciprocal relationship between sleep and epilepsy.³ Sleep affects epilepsy and epilepsy, in turn, affects sleep. Patients with epilepsy are particularly sensitive to the adverse effects of sleep disruption. Sleep disturbances are common in epilepsy causing impairment of daytime functioning and quality of life and impairment of seizures control.^{4,5} Furthermore, primary sleep disorders such as obstructive sleep apnoea (OSA) may worsen epilepsy and

treatment of these sleep disorders has been shown to lead to improved seizure control. Both sleep disordered breathing (SDB) and epilepsy; however, are common, treatable conditions.

Sparse data are available regarding the prevalence of SDB from developing countries like India. Sleep-related breathing disorders are increasingly recognized as an important cause of morbidity. Attention to sleep in patient with epilepsy has important implications for diagnosis, seizure control, and quality of life. Sleep disorders in patients with epilepsy have rarely been investigated systematically. Even less is known regarding the epidemiology

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of SDB in patients with epilepsy and the relationship between the two entities from India. Keeping these facts in mind, the present study was designed to assess the prevalence of SDB in patients with epilepsy at a tertiary care teaching centre in south India.

MATERIAL AND METHODS

During the period April 2009 to September 2010, consecutive patients diagnosed to have and treated for various forms of epilepsy at the neurology and medicine out-patients departments, epilepsy clinic, acute neurological care unit (ANCU), medical intensive care unit (MICU) and medicine and neurology wards of the Sri Venkateswara Institute of Medical Sciences, Tirupati were screened for inclusion in the study. Patients diagnosed to have various form of epilepsy⁶ who were willing to participate in the study were included. Pregnant women, patients with life threatening co-morbid conditions and those not willing to participate in the study were excluded.

The study was approved by the Institutional Ethics Committee.

Written informed consent was obtained from all patients for participating in the study. The study was carried out in two stages.

First stage

In the first stage, 452 consecutive patients with epilepsy who had given consent to participate in the study; and age and gender matched 500 normal control subjects were screened for excessive day time sleepiness (EDS) using Epworth's Sleepiness Scale (ESS).⁷ Excessive day time sleepiness (EDS) was defined as an ESS score greater than 10. Of the epilepsy patients in whom ESS was 10 or greater, 30 were randomly selected for undergoing detailed evaluation and PSG.

Second stage

Thirty subjects underwent a detailed evaluation that included clinical history focused on sleep-

related symptoms such as self-reported snoring, history of snoring from the relative, history of choking during sleep, associated conditions, and co-morbidities. Severity of snoring and choking was graded via one-on-one interview by an investigator blinded to the PSG data on a four-point frequency scale: never [0]; less than 1/week [1]; 1-2/week [2]; 3 to 4/week [3]; and 5 to 7/week [4]. All subjects were subjected to a detailed ear, nose and throat examination to rule out significant upper airway obstruction, such as, enlarged adenoids, pharyngeal tonsils and lingual tonsils significant deviated nasal septum with/without spur and macroglossia, blood pressure measurement and anthropometry.

Body weight (to the nearest 0.5 kg) and height (H, measured to the nearest 1 cm) was recorded in all subjects while wearing only light clothes and no shoes. Body-mass index (BMI) was calculated as body weight (in kilograms)/height (in metres)². Neck circumference (in cm) was measured at the level of cricothyroid membrane. Neck length (NL, cm) was measured from the occipital tubercle to the vertebra prominens. Percent predicted neck circumference (PPNC) was calculated from the measured neck circumference (NC) and the height (H, cm) using the following formula:⁸⁻¹¹

$$PPNC = (1000 \times NC) / (0.55 \times H + 310).$$

H to NL ratio was calculated by dividing the H (cm) by NL (cm).⁸⁻¹¹ Waist circumference (WC) (cm) was measured midway between the lower rib margin and the anterior superior iliac spine. Hip circumference (in cm) was measured at the maximum circumference of the buttocks while the subject was standing with feet placed together. Mean of three readings of each circumference was taken for the calculation of waist-hip ratio (WHR). Mid-arm circumference (MAC) was measured using a non-stretchable tape midway between the acromian process of the scapula and the olecranon process. Mean of three readings was recorded.

Central obesity was defined as WC \geq 90 cm for men and \geq 80cm for women.¹² *Abdominal obesity* was defined as a WHR >0.90 in men and >0.80 in women.¹³ Obesity was classified as per the International Obesity Task Force Guidelines for Asians.¹⁴

In all the patients, the following laboratory investigations were carried out: complete haemogram, fasting and post-prandial blood glucose and glycosylated haemoglobin (HbA1c) estimation, thyroid profile, serum chemistry including fasting lipid profile, chest radiograph and electrocardiography. Metabolic syndrome was diagnosed as per International Diabetes Federation definition.¹²

Electroencephalography (EEG) was done in all patients using GalileoNT Systems (EBNeuro, Firenze, Italy), 32 channel EEG machine. Computed tomography (CT) (Siemens Somatom Emotion Spiral CT Scanner) and/or magnetic resonance imaging (MRI) of the brain (Siemens Symphony Maestro Class, 1.5 Tesla MRI Scanner) was done in all patients. The lung volumes and their subdivisions were measured using a constant volume variable pressure body plethysmograph (P.K. Morgan Chatham, Kent, UK) as described previously.^{15,16}

Polysomnography

Patients with epilepsy were called for sleep study to the sleep laboratory at 8 pm, on the day of their appointment. They were hooked to Sleepscan Vision (Biologic Systems Corp, Illinois, USA) by standard gold cups after cleansing the area of attachment by spirit followed by Omniprep. The patient was advised to sleep at around 21:00 hours. The recording sleep study was started after ensuring that the impedance of recording electrodes were set to zero. Various parameters that will be monitored included EEG, electro oculogram (EOG), electro cardiogram (ECG), chin and leg electromyogram (EMG), nasal airflow, tracheal breath sounds, thoracic wall and abdominal movements, transcutaneous oxygen saturation,

body position, and continuous positive air way pressure titration when required.

The data were recorded overnight until the subject woke up naturally from his sleep in the morning or till 7 am, which was the “lights on” time. The data stored in the system were retrieved later. The sleep data recorded and automatically scored by the computer were manually scored for sleep stages, apneas, and hypopnoeas. An experienced laboratory technician, who was blinded to any clinical data, scored all the polysomnograms. Apnea was defined as cessation of oronasal airflow for greater than 10 seconds. Obstructive sleep apnea was scored when airflow was absent but respiratory efforts were present. Hypopnoea was defined as a discernible reduction in respiratory airflow of 50% - 90% for greater than 10 seconds accompanied by a decrease of 4% or more in oxyhemoglobin saturation during sleep. AHI was calculated using the following formula¹⁷:

$$\text{AHI} = (\text{total number of obstructive apneas} + \text{total no. of hypopnoeas}) / \text{total sleep time (hours)}.$$

As per the American Academy of Sleep Medicine¹⁷ obstructive sleep apnea syndrome was defined as AHI greater than or equal to 5 accompanied by EDS. The severity of OSAS was classified as mild (AHI of 5 - 15); moderate (AHI 16 - 30); and severe OSA (AHI > 30).

Statistical analysis

Data were recorded on a predesigned proforma and managed using Microsoft Excel 2007 (Microsoft Corp, Redmond, WA). All the entries were double-checked for any possible error. Descriptive statistics for the categorical variables was performed by computing the frequencies (percentages) in each category. For the quantitative variables, approximate normality of the distribution was assessed.

Variables following normal distribution were summarized by mean and standard deviation.

Continuous variables that were normally distributed were compared using unpaired students' t-test. Categorical variables were compared using chi-square test. Correlation between ESS, AHI and other anthropometric variables was studied using Pearson's correlation coefficient.

Statistical softwares PASW Statistics 18, Release 18.0.0, (IBM SPSS Statistics, Somers NY, USA); and MedCalc Version 11.3.0 for Windows 2000/XP/Vista/7 (MedCalc Software bvba, Belgium) were used for statistical analysis.

RESULTS

First stage of the study

Between April 2009 and September 2011, 452 consecutive patients with epilepsy (cases) who had given consent to participate in the study and age and gender matched 500 normal control subjects were screened for EDS using ESS. Of these, 426 patients satisfied the inclusion criteria and screened with ESS for EDS (Figure 1). Their mean age was 37.5 ± 10.9 years; there were 295 males. Mean age of onset of seizures was 25.1 ± 11.5 years and the mean

duration of seizures was 136 ± 63.7 months. Majority of the patients had GTCS (49%), followed by CPS with (25%) and without (18%) secondary generalization.

Healthy control subjects (n=500) who consented to participate in the study were also screened with ESS for EDS (Figure 1). Their mean age was 37.3 ± 10.7 years; there were 369 males. The health control and the epilepsy group were age ($p=0.389$) and gender ($\chi^2=2.1294$) $p=0.1445$.

Of the 500 healthy control subjects who were screened, 18 (3.6%) were found to have EDS (ESS score ≥ 10). In comparison with healthy controls, patients with epilepsy had an almost 6-times higher prevalence of EDS ($p<0.001$) (Table 1).

Second stage of the study

Of the 426 patients studied in the first stage of the study, 98 (23%) had an ESS score of 10 or more, suggestive of EDS. Their mean age was 36.4 ± 13.2 years; there were 84 males. Mean age of onset of seizures was 24.7 ± 12.7 years and the mean duration of seizures was 153.7 ± 93.3 months.

Majority of the patients had GTCS (52%), followed by CPS with (25%) and without

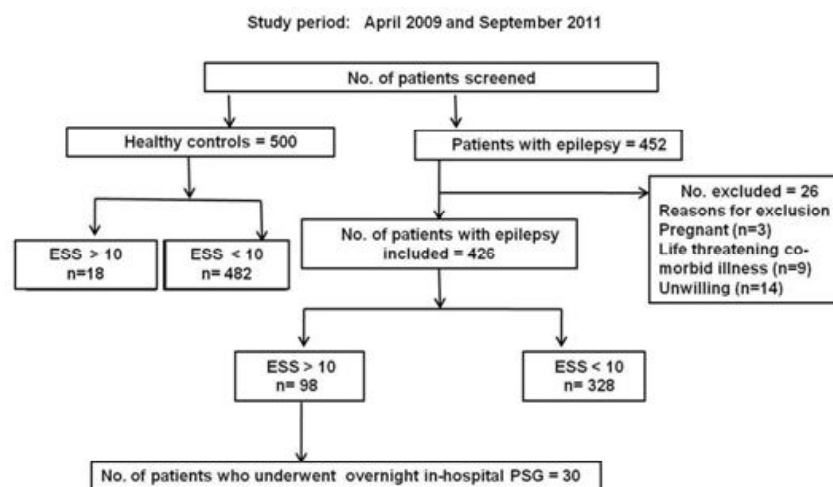


Figure 1: Study plan
ESS=Epworth's sleepiness scale; PSG=polysonnography

Table 1: Prevalence of EDS

	Patients with epilepsy (cases) (n=426) No. (%)	Healthy control subjects (n=500) No. (%)	Chi-square	p-value
Patients with EDS	98 (23%)	18 (3.6%)	77.2817	p<0.0001

EDS=excessive daytime sleepiness

(14%) secondary generalization. Of these, 30 patients were taken up for the second stage of the study and underwent detailed evaluation and overnight in-hospital PSG in the sleep laboratory.

The baseline demographic characteristics of patients with epilepsy included in the study are shown in the Table 2. Majority of patients were in their third decade of life; males (n=26) outnumbered females (n=4). Their mean age was 35.8 ± 13.1 .

Median symptom duration of epilepsy was 72 [interquartile range (IQR) 72 to 180] months. All patients (n=30) manifested EDS (ESS score >10); 70% complained of snoring; (n=10) 33.3% had uncontrolled seizures. Median age of onset of seizures was 22 years (IQR 10.5 - 37). GTCS was the most common seizure type (n=16; 53.3%) followed by CPS with (n=7; 23%) and without secondary generalization (n=4; 13%), among others.

Majority of patients had idiopathic epilepsy (n=22; 73%). Of the remaining 8 (27%) patients other causes included calcified granulomas and infarcts (3 patients each); head injury (n=1) and post surgery for craniopharyngioma (n=1).

There was equal distribution of nocturnal and diurnal periodicity of seizures (26.7% each). Seizures were well controlled in 20 (67%) patients; uncontrolled seizures occurred in 10 patients (33%). Most of the patients (n=24; 80%) required treatment with more than one AED. Six patients (20%) were receiving monotherapy with phenytoin, phenobarbitone and carbamazepine (2 patients each). Among patients receiving polytherapy, 18 were receiving 2 AEDs, while 6 patients were on triple drug regimen. Among patients receiving a 2-drug regimen, commonly used combination regimen was phenytoin plus carbamazepine (n=5) and phenobarbitone plus carbamazepine (n=4).

A family history of epilepsy was documented in 3 patients. A family history of obesity and snoring were observed in 9 patients and 4 patients respectively. Three patients had a family history of both obesity and snoring. Majority of the patients (n=26) had never smoked; three were past-smokers; and one male patient was a current smoker. Majority of the patients (n=26) had never consumed alcohol; two patients had consumed alcohol in the past and 2 other male patients were currently consuming alcohol.

Table 2: Demographic characteristics of 30 patients with epilepsy who underwent polysomnography

Variable	Value
Age (years)*	35.8±13.1
Male: Female	26:4
BMI (kg/m ²)*	22.9 ±4.6
Mid arm circumference (cm)*	26.8±4.6
Waist/hip ratio*	0.89 ±0.07

* expressed as mean ± SD; BMI=body mass index

Anthropometric measurements are shown in Table 3A. Only one patient had a neck circumference greater than 43 cm. As per the International Diabetes Federation (IDF) definition¹² *central obesity* observed in 12 (40%) patients (10 males). As per WHO criteria¹³ *abdominal obesity* was observed in 14 (47%) patients (11 males). As per the International Obesity Task Force Guidelines for Asians,¹⁴ BMI was in the normal range in 13 (43.3%) patients; 5 (16.7%) patients were overweight; 6 (20%) were categorized as obese I; 3 patients (10%) each were categorized as obese II; and underweight.

None of patients had craniofacial deformities and otorhinolaryngological examination was normal in all patients. The EEG was abnormal in 8 patients; 4 patients had epileptiform discharges and 4 patients had predominant slow waves. The EEG was normal in the remaining 22 patients. Eight (26.7%) patients had abnormal imaging findings. These included calcified granulomas (n=3); left MCA infarct (n=2); right MCA infarct; left temporal lobe contusion; sequelae of surgery for craniopharyngioma (n=1 patient each). Pulmonary function testing was normal in all the 30 patients.

The PSG data and prevalence of OSAS are presented in Tables 3B and 3C respectively. An

AHI of 5 or more was observed in 13 (43.3%) patients and all of them had evidence of EDS (ESS > 10). Thus, 43.3% of patients who underwent PSG had evidence of OSAS. Of these, 9 patients had mild OSAS; 3 had moderate OSAS and the remaining patient had severe OSAS (Table 3C; Figure 2). The patient with severe OSAS had no other risk factors except alcoholism.

Comparison of demographic, clinical, anthropometric and laboratory variables between patients with and without OSAS is shown in Tables 3D and 3E. All the patients diagnosed to have OSAS were men. On univariate analysis, there was no statistically significant difference between the two groups. There was no statistically significant difference in the prevalence of metabolic syndrome in epilepsy patients with and without OSAS in the present study (5/13 Vs 6/17; p=1.00). A higher proportion of patients with nocturnal seizures had OSAS compared with those with diurnal seizures and combined periodicity (7/8 Vs 6/22; p=0.009). Patients with uncontrolled seizures had a higher prevalence of OSAS (7/10 Vs 6/20; p=0.045). There was no statistically significant difference in the percentage of patients with OSAS between patients who required monotherapy and polytherapy with AEDs (3/7 Vs 10/13; p=0.66).

The correlation matrix showing correlation

Table 3A: Anthropometric measurements

Variable	Observations*
Body mass index (kg/m ²)	22.9 ± 4.6
Neck length (cm)	15.6 ± 2.4
Neck circumference (cm)	34.3 ± 4.2
Percent predicted neck circumference	132 ± 14.5
Total height/neck length ratio	10.6 ± 1.20
Mid-arm circumference (cm)	26.8 ± 4.6
Waist circumference (cm)	84.0±14.2
Waist/hip ratio	0.89±0.07

* data are shown as mean ± SD

Table 3B: Polysomnographic data in 30 patients with epilepsy with evidence of excessive

Variable	Median (IQR)
Total duration of study (min)	469 (445-484)
Total sleep time(min)	420 (360-450)
Desaturation index	14.3 (4.3-32.7)
Sleep efficiency (%)	90.7 (48.7-99.7)
Sleep onset latency (min)	1.5 (0.1-22.3)
Latency to stage 1 (min)	5.7 (0.1-202.8)
Latency to stage 2 (min)	8.0 (0.1-38)
Latency to stage ¾ (min)	47.8 (0.5-310.7)
Latency to REM (min)	96.5 (19.3-424.3)
Sleep stage % stage 1	16.3 (1-42)
Sleep stage % stage 2	61.8 (11.1-88.5)
Sleep stage % stage 3/4	0.60 (0-8.9)
REM sleep (%)	7 (2.9-14.6)
Arousal index-events/hour	37.4 (15.8-111.5)
Total number of arousals	234.5 (117-684)
Total number of awakenings	31.5 (2-75)
Isolated limb movements index-events/hour	4.6 (0.2 -13.9)
Periodic limb movements index-events/hour	3.1 (0-75.7)
Isolated limb movements with arousal-events/hour	1.2 (0-4)
Periodic limb movements with arousal-events/hour	0.9 (0-10.9)
Central apnoea/hypopnoea events/hour	0.5 (0-12)
Obstructive apnoea/hypopnoea events/hour	1.2 (0-8.2)
Mixed apnoea/hypopnoea events/hour	4.0 (0.2-36.2)

IQR = interquartile range; REM = rapid eye movement sleep; AHI = apnoea-hypopnoea index; OSAS = obstructive sleep apnoea syndrome

Table 3C: Prevalence of obstructive sleep apnoea syndrome in 30 patients with epilepsy and excessive of daytime sleeping

Variable	Observations
AHI [median (IQR)]	3.9 (1.4 - 11.5)
OSAS [No. (%)]	13/30 (43)
Mild OSAS (AHI > 5 <15)	09/30 (30)
Moderate OSAS (AHI > 15 <30)	03/30 (10)
Severe OSAS (AHI > 30)	01/30 (03)

IQR = interquartile range

between ESS AHI and other anthropometric variables is shown in Figure 3. A statistically significant positive correlation was observed between ESS and BMI ($p < 0.001$); MAC ($p = 0.001$); WC ($p = 0.001$); HC ($p = 0.004$); WHR ($p = 0.029$). There was no statistically significant association between ESS and NL

($p = 0.412$); H/NL ratio ($p = 0.059$); AHI ($p = 0.331$); and oxygen desaturation index (0.368).

DISCUSSION

The relationship between epilepsy and sleep is complex. Published data suggest that sleep

Table 3D: Comparison of demographic, clinical, anthropometric and laboratory variables between patients with and without OSAS

Variable	No OSAS (n=17)	OSAS (n=13)	p-value
Age at presentation (years)	32.5 ± 13.2	40.1 ± 12.1	0.18
Gender			0.113
Males	13	13	
Females	04	00	
Age at onset of seizures	26 ± 14.8	21.8 ± 15.2	0.462
Body mass index (kg/m ²)	23.2 ± 3.9	22.6 ± 5.5	0.09
Neck length (cm)	15.5 ± 1.8	15.7 ± 3.1	0.29
Neck circumference (cm)	33.8 ± 3.8	35.1 ± 4.8	0.61
PPNC	134.5 ± 16.9	130.1 ± 12.6	0.42
Height to neck length ratio	10.47 ± 0.98	10.67 ± 1.47	0.39
Mid arm circumference (cm)	26.8 ± 3.9	26.8 ± 5.5	0.44
Waist circumference (cm)	83.5 ± 12.5	84.6 ± 16.7	0.46
Waist-hip ratio	0.88 ± 0.08	0.90 ± 0.05	0.46
Serum total cholesterol	180.7 ± 39.8	177.4 ± 41.1	0.84
Serum triglycerides	185.1 ± 58.0	171.6 ± 38.6	0.49
Serum HDL-cholesterol	36.1 ± 1.8	37.3 ± 2.6	0.14

OSAS=obstructive sleep apnoea syndrome; PPNC=percent predicted neck circumference; HDL=high density lipoproteins

Table 3E: Comparison of proportion of patients with a high BMI, high WC and high WHR between patients with and without OSAS

Variable	No OSAS (n=17)	OSAS (n=13)	χ^2	p-value
BMI (kg/m ²)				
>25	05	05		
<25	12	08	0.271	0.446
High WC*				
Yes	07	05		
No	10	08	0.023	0.59
High WHR				
Yes	09	05		
No	08	08	0.621	0.339

* ≥ 90 cm for men, ≥ 80 cm for women

† > 0.90 cm for men, > 0.80 cm for women

BMI=body mass index; WC=waist circumference; WHR=waist-hip ratio; OSAS=obstructive sleep apnoea syndrome

deprivation may exacerbate seizures. Further, some seizures mainly occur during sleep. It is not uncommon for nocturnal seizures to be misdiagnosed as parasomnia and vice-versa. Recent observations indicate that primary sleep disorders such as OSA may aggravate epilepsy and treatment of these sleep disorders can

improve seizure control.¹⁸ The resulting disruption of normal sleep architecture may cause EDS, significantly affecting the quality of life. Given the paucity of data regarding the burden of SDB in patients with epilepsy from India, the present study was undertaken. Accurate identification and diagnosis of SDB

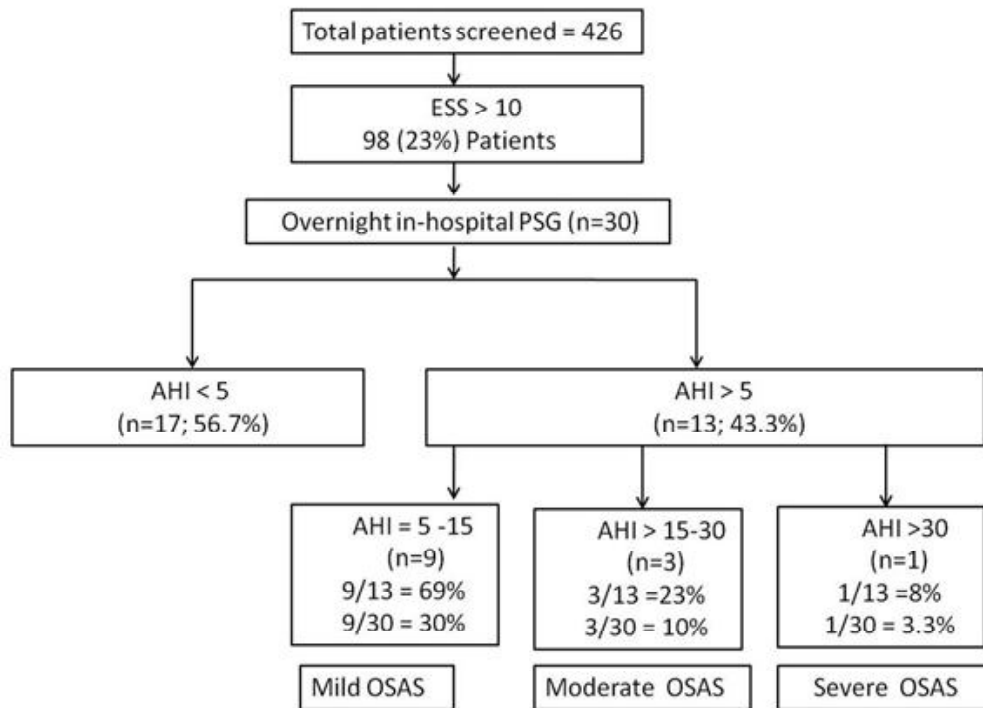


Figure 2: Burden of OSAS in patients with epilepsy
ESS=Epworth Sleepiness Scale; AHI=apnoea-hypopnoea index; OSAS=obstructive sleep apnoea syndrome

in patients with epilepsy is clinically important to ensure optimal treatment of both the conditions.

Some published questionnaire based studies¹⁹⁻²² had revealed a higher occurrence of EDS in patients with epilepsy. In the present study, among 426 patients with epilepsy who were screened, EDS was almost six-times more common compared to control subjects ($p < 0.0001$; Table 2).

Several causes, such as, manifestation of seizure disorder, adverse effect of AEDs, uncontrolled seizures, increased sleep latency and number of awakenings during night, reduction or fragmentation of REM sleep, among others have been postulated to be responsible for increased EDS in these patients.^{23,24} The observations from the present study indicate that the burden of EDS in Indian patients with epilepsy appears to be considerable and of similar magnitude to that observed in studies from the developed world even after allowing for the differences in the semiology of seizure disorders.

Since 1981, there have been anecdotal reports of epilepsy and OSA coexisting in the same subject.^{5,25,26} Subsequently, some published studies from the west^{19,27-30} had evaluated the problem of SDB in adult patients with epilepsy utilizing PSG. In-hospital overnight PSG is the method of choice for the diagnosis of SDB. However, PSG facilities are not widely available in public sector hospitals of Andhra Pradesh state, except at our institute. Given this limitation and the cost factor, in-hospital overnight PSG could be done in 30 of the 98 patients with EDS. In the present study 43.3% of patients who underwent PSG had evidence of OSAS. In comparison, in community based studies assessing the burden of OSAS published from India employing PSG, the prevalence of OSAS ranged from 3.6% to 17%.^{8,9,31} These observations suggest that SDB is an important underdiagnosed problem in patients with epilepsy.

OSA is more common in men and the prevalence is approximately 2 to 3 times that

	ESS	BMI	NC	NL	PPNC	H/NL	MAC	WC	HC	WHR	AHI	DI
ESS	1											
BMI	0.681 (0.000)	1										
NC	0.579 (0.001)	0.687 (0.000)	1									
NL	-0.156 (0.412)	-0.036 (0.850)	0.176 (0.353)	1								
PPNC	0.585 (0.001)	0.724 (0.000)	0.988 (0.000)	0.103 (0.588)	1							
H/NL	0.348 (0.059)	0.131 (0.489)	0.143 (0.451)	-0.867 (0.000)	0.157 (0.407)	1						
MAC	0.575 (0.001)	0.840 (0.000)	0.722 (0.000)	0.210 (0.265)	0.706 (0.000)	0.010 (0.958)	1					
WC	0.576 (0.001)	0.873 (0.000)	0.811 (0.000)	0.091 (0.633)	0.827 (0.000)	0.081 (0.671)	0.841 (0.000)	1				
HC	0.507 (0.004)	0.876 (0.000)	0.716 (0.000)	0.201 (0.288)	0.711 (0.000)	-0.015 (0.936)	0.902 (0.000)	0.883 (0.000)	1			
WHR	0.398† (0.029)	0.466 (0.009)	0.569 (0.001)	-0.106 (0.577)	0.606 (0.000)	0.175 (0.355)	0.368 (0.046)	0.718 (0.000)	0.310 (0.096)	1		
AHI	0.184 (0.331)	0.090 (0.635)	0.220 (0.242)	-0.025 (0.895)	0.206 (0.274)	0.183 (0.334)	0.093 (0.626)	0.184 (0.331)	0.171 (0.366)	0.097 (0.611)	1	
DI	0.171 (0.368)	0.150 (0.430)	0.345 (0.062)	0.280 (0.134)	0.347 (0.061)	-0.165 (0.383)	0.233 (0.216)	0.268 (0.152)	0.235 (0.212)	0.166 (0.380)	0.532 (0.002)	1

Figure 3: Correlation matrix showing correlation between ESS/AHI and other anthropometric variables

All data are expressed as r (p-value)

ESS=Epworth Sleepiness Scale; BMI=body mass index; NC= neck circumference (cm); NL=neck length; PPNC=% predicted neck circumference; H/NL=height to neck length ratio; MAC=mid-arm circumference; WC=waist circumference; HC=hip circumference; WHR=waist-to hip-ratio; AHI=apnoea-hypopnoea index; DI=desaturation index

observed among women.^{10,32} All the 13 patients who were diagnosed to have OSAS in the present study were men (Table 3D). Although it is not clear as to why OSA is more common in men than women, anatomical and functional properties of the upper airway, ventilatory response to the arousal from sleep, increased fat deposition around pharyngeal airway, hormonal differences, among others have been postulated to be the causes for male preponderance.³²

In the present study, majority of the patients (n=26) had never smoked and had never consumed alcohol. However, alcohol consumption was the only documented risk factor in a patient with severe OSAS. In susceptible subjects, alcohol has been shown to relax upper airway dilator muscles, increase upper airway resistance and induce OSA. Therefore, alcohol intake has the potential to prolong apnea duration, suppress arousals, increase frequency of occlusive episodes and worsen the severity of hypoxemia.^{32,33} It is likely that such factors could be operational in this patient.

Some studies^{28,34} have shown that patients with epilepsy and OSAS were older, had a higher BMI and had a later onset of seizures than people with epilepsy without OSAS.^{28,34} However, there was no statistically significant difference in the demographic, anthropometric and laboratory variables listed above between patients with and without OSAS (Tables 3D and 3E) in the present study. These associations were not significant in other studies^{35,36} as well. These issues need clarification in community based studies with a larger sample size.

In some studies carried out in subjects with OSAS, the ESS score significantly correlated with the oxygen desaturation index (ODI), AHI, and BMI.^{37,38} In the present study, a statistically significant positive correlation was observed between ESS and BMI (p=0.001); MAC

(p=0.001); WC (p=0.001); HC (p=0.004); WHR (p=0.029). There was no statistically significant association between ESS and NL (p=0.412); H/NL ratio (p=0.059); AHI (p=0.331); and desaturation index (0.368). As the sample size of patients with epilepsy who had undergone PSG in the present study is small (n=30), these correlations need to be further evaluated in studies with a large sample size.

There was no statistically significant difference in the mean serum lipid profile among epilepsy patients with and without OSAS in the present study (Table 3D). Furthermore, the prevalence of metabolic syndrome was similar in epilepsy patients with and without OSAS in the present study (5/13 Vs 6/17; p=0.99). These findings are similar to the observations from a study⁹ conducted at New Delhi in which the authors reported that OSA had no independent association with lipid abnormalities, insulin resistance, serum leptin and adiponectin levels.

In the present study, among the patients who have undergone PSG (n=30), a higher proportion of patients with nocturnal seizures had OSAS compared with those with diurnal seizures and combined periodicity (7/8 Vs 6/22; p=0.009). It has been reported that nocturnal seizures reduced the amount of stage II and IV sleep and increased the amount of stage I sleep with a consequent reduction in the sleep efficiency and increased drowsiness the day after.⁴⁰ However, such an association has not been documented in other studies.²⁸

A higher proportion of patients in uncontrolled seizures had OSAS as compared with those with controlled seizures in the present study (7/10 Vs 6/20; p=0.045). SDB is likely to have contributed to poor control of seizures in these patients. OSA has been observed to be more frequent among patients with refractory epilepsy, and has been reported in one third of patients investigated for epilepsy surgery.³⁴

AED use has been observed to have an adverse influence on OSAS. Barbiturates and

benzodiazepines by increasing upper airway collapsibility and depressing arousal mechanisms may worsen OSAS.⁴¹ AEDs, such as valproic acid and carbamazepine that can cause weight gain are also known to worsen OSAS.⁴² In the present study, there was no statistically significant difference in the prevalence of OSAS among patients receiving a single AED or those receiving more than one AED for seizure control (3/7 Vs 10/23; p=0.66). The effect of the AED on SDB should be kept in mind when patients with epilepsy, especially those with EDS are initiated on antiepileptic treatment.

In-hospital, overnight PSG could not be carried out in all the 98 patients with EDS (ESS >10) but could be done only in 30 patients due to logistic reasons. So, meaningful multivariable analysis for defining the predictors of OSAS among patients with epilepsy could not be done. The present study also did not attempt to study the effect of CPAP treatment on seizure control due to logistic reasons.

Our observations suggest that SDB appears to be an underdiagnosed disease in patients with epilepsy from India. Increased awareness regarding the condition, screening of patients with EDS and overnight in-hospital PSG can help in early recognition of this condition and may facilitate institution of CPAP treatment.

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