

**Correlation of nocturnal enuresis with obstructive sleep apnea syndrome in adults: a pilot study**

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**Abstract**

**Purpose:** Adult nocturnal enuresis (NE) is a poorly understood condition, and its association with obstructive sleep apnea syndrome (OSAS) has not been sufficiently investigated. This study aimed to explore the prevalence of OSAS and polysomnographic characteristics in adults with lifelong NE.

**Methods:** Adult patients (>18 years) presenting with lifelong NE were prospectively evaluated. Participants completed validated questionnaires including the Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Epworth Sleepiness Scale (ESS), and Incontinence Quality of Life questionnaire (I-QOL). All patients underwent overnight polysomnography. Patients were categorized into OSAS-positive and OSAS-negative groups based on AHI values.

**Results:** This study was completed with a total of 24 patients, 14 women (58.3%) and 10 men (41.7%). Among patients, 6 had OSAS (25.0%), while 18 did not have OSAS (75.0%). In the group who were OSAS (+), AHI rem ( $p=0.002$ ), AHI non-rem ( $p=0.003$ ), AHI total ( $p=0.005$ ), supine sleep duration ( $p<0.001$ ), desaturation index ( $p=0.007$ ) and obstructive apnea index ( $p=0.019$ ) were significantly higher than the OSAS (-) group.

For patients included in the study, according to BDI category, 14 had normal findings (58.3%), while 10 had depressive findings (41.7%). For patients, the median BDI score was 15 (6-21), BAI score was 12 (4-19), median ESS score was 4 (2-7) and median IQOL score was 49 (29-62).

**Conclusion:** One-quarter of adults with lifelong nocturnal enuresis were found to have coexisting mild OSAS. These findings suggest that sleep-disordered breathing may represent an overlooked comorbidity in adult NE and warrant further investigation in larger controlled studies.

**Keywords:** Nocturnal enuresis, obstructive sleep apnea syndrome, adult patient, polysomnography

## Introduction

Nocturnal enuresis (NE) is defined as the complaint of intermittent urinary incontinence occurring during the main sleep period [1]. Adults with NE complaints are frequently seen to have low self-respect, experienced bullying and disrupted family life. Studies related to NE have generally been performed with children. The studies about NE observed in adults are very limited and most studies in adults researched nocturia. Studies show that NE may affect 2-6% of adults [2, 3]. Though there are sufficient guidelines about diagnosis and disease management for NE in children, there is insufficient information about the pathophysiology, diagnosis and treatment of NE observed in adults [4].

Generally NE is a complicated clinical situation with several potential causes [4]. Insufficient arousal mechanisms during sleep are an important part of NE. Additionally, NE may be due to multifactorial etiologies like lower urinary tract dysfunction, neurogenic diseases, psychiatric drugs and sleep disorders [5]. To provide the best care to these patients, a comprehensive and multidisciplinary approach is required.

Obstructive sleep apnea syndrome (OSAS) is a ventilation disorder progressing with apnea and hypopnea of ventilation while the patient sleeps. In OSAS patients, intermittent hypoxia causes hypercapnia, hypoxemia, increased respiratory effort, repeated night wakings and sympathetic nerve activity [6, 7]. Population-based studies in different geographical regions show OSAS comprises a serious public health problem. OSAS can be seen in all age groups. OSAS affects 26% of the middle and older age populations in the United States of America and 48.9% of the

population living in Russia [8, 9]. The incidence of OSAS varies with age, sex, ethnic group and obesity. This variable data from geographical regions are due to risk factors affecting the incidence of OSAS and also to differences in methodology between studies [10].

NE is associated with various sleep disorders, particularly OSAS [11, 12]. OSAS disrupts the normal structure of sleep and contributes to a higher arousal threshold and a predominance of deeper sleep stages. Furthermore, the associated increase in intrathoracic pressure causes elevated levels of atrial natriuretic peptide, which exceeds functional bladder capacity and predisposes individuals to nocturnal urination [11]. Furthermore, OSAS can lead to bladder instability as a consequence of recurrent hypoxic episodes, ultimately manifesting nocturia and NE [13].

In this study, we researched whether patients over 18 years of age attending our hospital with NE complaints had OSAS or not and their depression and anxiety levels.

### **Material and Methods**

This study was permitted with decision 2016/303 by Selcuk University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee. Our study was explained to patients attending Health Science University Konya Training and Research Hospital Clinic of Urology with NE complaints (these patients had NE since childhood). Patients accepting participation signed an informed consent form appropriate to the World Medical Association Helsinki Declaration. Patients had height, weight, waist circumference and neck circumference measured.

The BMI values for patients were calculated with the formula: weight (kilogram) / height (meter)<sup>2</sup>. Patients filled the Beck Depression Inventory (BDI)<sup>[14]</sup>, Beck Anxiety Inventory (BAI) [15], Epworth Sleepiness Scale (ESS) [16] and Incontinence Quality of Life Questionnaire (IQOL) [17]. Our patients were examined by a urology expert and it was confirmed they did not have any urological disease. Then patients underwent polysomnography (PSG) tests in the sleep laboratory. The test results were interpreted by a clinician who was an expert in chest diseases.

### **Exclusion criteria**

Patients with diabetes mellitus and diabetes insipidus, with prostate hypertrophy, stenosis of any site in the lower urinary tract, with urinary system stones, with any muscular disease, using

diuretics, drinking alcohol, with disease affecting cognitive functions (Alzheimer, dementia, mental retardation), younger than 18 years, and older than 65 years were excluded.

### **Polysomnography**

Polysomnography is the standard diagnostic test for OSAS in adult patients [18]. In our study, PSG was applied for the whole night. Patients went to sleep from 22:00-23:00 and were woken at 07:00.

Polysomnography procedures were completed with a Compumedics brand 58-channel E-series device. Six channel (C4-M1, C3-M2, OI-M2, O2-M1, F4-M1, F3-M2) electroencephalography, submental and tibialis anterior electromyography, electrocardiography, bitemporal electrooculography, oximetry, air flow, abdominal and chest respiration effort tape recordings and snoring microphone records were obtained. Patients were recorded with video images for at least 6 hours during sleep. Sleep levels and Apnea-Hypopnea Index (AHI) values were manually assessed by a certified sleep expert according to the 2007 American Academy of Sleep Medicine criteria.

Apnea is a lack of air flow through the mouth and nose for 10 seconds or longer. Hypopnea is a 3% fall in oxygen saturation and development of at least a 30% fall in air flow lasting 10 seconds or longer and waking. The Apnea-Hypopnea Index is calculated by dividing the total number of apnea and hypopnea incidences by the hours of sleep. If the AHI is less than 5, OSAS is not considered, while scores from 5-15 indicate mild OSAS, 16-30 indicate moderate OSAS and 30 and above indicate severe OSAS.

### **Statistical analysis**

All statistical analyses were completed using SPSS 22.0 (IBM Inc., Armonk, NY, USA) software. The assumption of normality for the study groups was evaluated with the Shapiro-Wilk test and the Kolmogorov-Smirnov test. Comparison of data without normal distribution in the study groups used the Mann Whitney U test. Comparisons of categorical data in the study used Fisher's exact test. Descriptive statistics are given as frequency and percentage for categorical data and as median (IQR<sub>25-75</sub>) for numerical data. All statistical analyses used in the study were double-tailed with 5% significance limit and in the 95% confidence interval.

## Results

The study included 31 patients. Seven patients did not attend their PSG appointments and were excluded. This study was completed with a total of 24 patients, 14 women (58.3%) and 10 men (41.7%).

Of patients included in the study, 21 were single (87.5%), 12 were high school graduates (50.0%), 20 had no disease in their history (83.3%), 6 were using desmopressin (25.0%), 1 was using sodium valproate (4.2%), and 17 were not using any medications (70.8%). Of patients, 6 had NE history among first degree relatives (25.0%), while 3 had history in second degree relatives (12.5%). The sociodemographic data for patients participating in the study and comparison of group data are shown in Table 1.

The median age of patients included in the study was 20.0 (18.0-23.0) years. Among patients, median weight was 65.0 (54.0-70.0) kg, median height 167.0 (160.0-172.0) cm, median BMI 22.8 (20.8-24.5), median neck circumference 31.0 (30.0-34.0) cm and median waist circumference 79.0 (74.0-84.0). The age and anthropometric measurements for patients participating in the study and comparison of group data are shown in Table 2.

For patients included in the study, according to BDI category, 14 had normal findings (58.3%), while 10 had depressive findings (41.7%). For patients, the median BDI score was 15 (6-21), BAI score was 12 (4-19), median ESS score was 4 (2-7) and median IQOL score was 49 (29-62). The BDI, BAI, ESS, and IQOL scores for patients participating in the study and comparison of data between groups are shown in Table 3.

Among patients, 6 had OSAS (25.0%), while 18 did not have OSAS (75.0%). For patients with OSAS diagnosis, all had mild OSAS (AHI 5-15). In the group who were OSAS (+), AHI rem ( $p=0.002$ ), AHI non-rem ( $p=0.003$ ), AHI total ( $p=0.005$ ), supine sleep duration ( $p<0.001$ ), desaturation index ( $p=0.007$ ) and obstructive apnea index ( $p=0.019$ ) were significantly higher than the OSAS (-) group. The comparison of PSG results for the study groups is shown in Table 4.

## Discussion

In this study, the presence of OSAS, anxiety and depression was researched in adults with NE disease. When the literature is investigated, previous studies researched the correlation of OSAS and NE in children. To the best of our knowledge, the correlation between OSAS and nocturia was investigated in adults, while there is no study researching OSAS in NE patients. There are

case reports about OSAS accompanying NE. McInnis et al [19] and Kramer et al [20] published two series comprising 5 patients each with NE and diagnosis of OSAS using polysomnography with NE complaints resolving with continuous positive airway pressure (CPAP) treatment [19] We believe this study is the first to research OSAS in adults with NE.

The results of a systematic investigation by Di Bellow et al. reported nearly one third of OSAS patients experienced nocturia, while less than 1% of nocturia patients had OSAS [21] Kasynak et al. reported the nocturia incidence was between 50-70% in OSAS patients [22] In this study, 25.0% of patients with NE were found to have OSAS.

Koo et al. researched the correlation between NE with OSAS risk factors in postmenopausal women. They reported that OSAS risk factors (obesity, snoring, poor sleep quality, sleep disruption, daytime sleepiness) were associated with NE in postmenopausal women [11] In this study, patients did not have polysomnography performed and only the correlation with OSAS risk factors was researched.

For OSAS, age and BMI are identified as risk factors [23, 24] In this study, in spite of the high mean age in the group with OSAS, there was no statistically significant difference between the groups. In the case series published by McInnis et al. [19] and Kramer et al. [20], all cases were obese (BMI >30.0). In this study, while the mean BMI values of the study groups fell within the normal weight category, patients with OSAS demonstrated significantly higher BMI compared to those without OSAS.

Oztura et al. researched the correlation with nocturia in OSAS patients. They reported there were significant correlations between the urination frequency at night with mean age, BMI, respiratory distress index (RDI), AHI, respiratory effort index (REI) and low oxygen saturation [25].

The series published by Kramer et al. reported the mean AHI was  $107.7 \pm 7.7$ . with mean minimum  $\text{SPO}_2$   $73.2 \pm 2.7$  for OSAS patients [20]. McInnis et al. gave PSG results separately for each case in their report. The mean AHI in this series was found to be 57.1 [19]. In this study, the median AHI value was 6.2, with median minimum  $\text{SPO}_2$  value of 91 for OSAS patients. The reason for this may be that patients in the other two case series were morbidly obese, while OSAS patients in this study had median BMI value of 24.5.

When the sleep architecture of patients included by McInnis et al. in their series is investigated, they reported no notable pattern was observed before or after beginning CPAP [19]. In this

study, the patient groups had less stage 1 sleep duration, and generally sleep architecture was not degraded in the patient groups. In the group with OSAS, respiratory events in sleep were not observed significantly more in the rem and non-rem periods. In the group with OSAS, it was observed that oxygen desaturation indexes significantly fell simultaneously.

Yazilitaş et al. reported that the depression and anxiety scale scores for children with primary NE and their mothers were significantly higher than the healthy control group [26]. A study of children by Eray et al. did not find significant differences for depression and anxiety scores between children with primary NE diagnosis and the control group; however, social anxiety scores were higher in the primary NE group [27]. Quiroz-Guerrero et al. reported mothers of child with NE experienced moderate and severe levels of state anxiety [28]. In this study, 10 out of all participants (41.7%) appeared to have depressive findings, with no significant difference observed between the study groups for depressive findings.

The present study should primarily be interpreted as a hypothesis-generating investigation. Due to the small sample size and the absence of a control group, causal inferences cannot be established. Nevertheless, the detection of OSAS in 25% of adults with lifelong nocturnal enuresis using objective polysomnography suggests a potentially clinically relevant association that deserves further evaluation in larger, controlled, and prospective studies.

This study has several important limitations. First, the sample size is small, which limits statistical power and increases the risk of type II error. Second, the absence of a healthy control group prevents direct comparison of OSAS prevalence with the general population. Third, the cross-sectional design does not allow causal interpretation of the relationship between OSAS and nocturnal enuresis. Finally, treatment outcomes such as the effect of CPAP on enuresis frequency were not evaluated.

In conclusion, a considerable proportion of adults with lifelong nocturnal enuresis were found to have coexisting mild OSAS. While these findings do not establish causality, they highlight the potential relevance of sleep-disordered breathing in this population and support the need for further large-scale and interventional studies.

### **The author contribution**

Solak I: Data curation, Formal analysis, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing

Ergun O: Data curation, Writing – review & editing

Sumer A: Data curation, Writing – review & editing

Bekci TT: Data curation, Writing – review & editing

Eryilmaz MA: Formal analysis, Writing – review & editing

Solak A: Writing – original draft, Writing – review & editing

### **Financial disclosure**

No funding was received for this research.

### **Conflict of Interest**

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

### **Ethical approval**

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Selcuk University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

### **Informed consent**

Informed consent was obtained from all individual participants included in the study.

### **Data availability**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## Tables

**Table 1: Comparison of sociodemographic data in the study groups**

		All patients n=24	OSAS (-) n=18(75.0%)	OSAS (+) n=6(25.0%)	
Sex	Woman	14(58.3%)	12(85.7%)	2(14.3%)	0.192
	Man	10(41.7%)	6(60.0%)	4(40.0%)	
Marital status	Married	3(12.5%)	2(66.7%)	1(33.3%)	0.597
	Single	21(87.5%)	16(76.2%)	5(23.8%)	
Education	Primary education	9(37.5%)	7(77.8%)	2(22.2%)	0.931

	High School	12(50.0%)	9(75.0%)	3(25.0%)	
	University	3(12.5%)	2(66.7%)	1(33.3%)	
	Student	11(45.8%)	9(81.8%)	2(18.2%)	
Occupation	Unemployed	4(16.7%)	4(100.0%)	0(0.0%)	0.123
	Employed	9(37.5%)	5(55.6%)	4(44.4%)	
History	No	20(83.3%)	15(75.0%)	5(25.0%)	1.000
	Yes	4(16.7%)	3(75.0%)	1(25.0%)	
	Epilepsy	1(4.2%)	0(0.0%)	1(100.0%)	
	Asthma	1(4.2%)	1(100.0%)	0(0.0%)	
	Allergic rhinitis	1(4.2%)	1(100.0%)	0(0.0%)	
	Migraine	1(4.2%)	1(100.0%)	0(0.0%)	
Drugs used	No	17(70.8%)	13(76.5%)	4(23.5%)	0.343
	Yes	7(29.2%)	6(85.7%)	1(14.3%)	
	Desmopressin	6(25.0%)	6(100.0%)	0(0.0%)	
	Valproic acid	1(4.2%)	0(0.0%)	1(100.0%)	
NE history in family	No	15(62.5%)	11(73.3%)	4(26.7%)	0.832
	Yes	9(37.5%)	7(77.8%)	2(22.2%)	
	1st degree relative	6(25.0%)	5(83.3%)	1(16.7%)	
	2nd degree relative	3(12.5%)	2(66.7%)	1(33.3%)	

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Fisher's Exact Test

**Table 2: Comparison of anthropometric measurements in the study groups**

	All patients n=24 Median(IQR <sub>25-75</sub> )	OSAS (-) n=18(75.0%) Median(IQR <sub>25-75</sub> )	OSAS (+) n=6(25.0%) Median(IQR <sub>25-75</sub> )	p
Age, years	20.0(18.0-23.0)	19.5(18.5-22.5)	23.0(18.0-26.0)	0.207
Weight, kg	65.0(54.0-70.0)	60.8(50.0-69.9)	70.0(64.5-75.0)	0.046
Height, cm	167.0(160.0-172.0)	163.5(157.0-172.5)	169.0(167.0-172.0)	0.309
BMI, kg/m <sup>2</sup>	22.8(20.8-24.5)	21.5(2.24-23.3)	24.5(23.6-25.0)	<b>0.030</b>
Neck circumference, cm	31.0(30.0-34.0)	31.0(30.0-34.0)	35.0(31.0-36.0)	0.183
Waist circumference, cm	79.0(74.0-84.0)	77(72.5-81.5)	84.0(80.0-91.0)	0.116

Mann Whitney U Test

**Table 3: Comparison of scale scores in the study groups**

		OSAS (-) n=18(75.0%)	OSAS (+) n=6(25.0%)	All patients n=24	p
Beck Depression category <sup>1</sup>	Normal	11(78.6%)	3(21.4%)	14(58.3%)	0.665
	Depressive findings	7(30.0%)	3(30.0%)	10(41.7%)	
		Median(IQR <sub>25-75</sub> )	Median(IQR <sub>25-75</sub> )	Median(IQR <sub>25-75</sub> )	
BDI <sup>2</sup>		15(6-22)	16(12-20)	15(6-21)	0.548
BAI <sup>2</sup>		12(3-18)	11(4-20)	12(4-19)	0.920
Epworth Sleepiness Scale <sup>2</sup>		4(1-7)	6(3-7)	4(2-7)	0.537

Incontinence Quality of Life<sup>2</sup> 55(30-65) 39(24-50) 49(29-62) 0.217

<sup>1</sup> Fisher's Exact Test, <sup>2</sup>Mann Whitney U Test. BDI: beck depression inventory; BAI: beck anxiety inventory

**Table 4: Comparison of polysomnography results for patients with and without OSAS**

	OSAS (-) n=18(75.0%) Median(IQR <sub>25-75</sub> )	OSAS (+) n=6(25.0%) Median(IQR <sub>25-75</sub> )	p
Total sleep duration, min	297.6(264.1-329.0)	292.6(228.8-325.8)	0.790
Sleep efficiency, %	87.8(78.3-94.9)	89.5(79.1-94.2)	0.894
Total rem duration	8.9(0.0-15.5)	23.8(12.4-34.7)	0.088
Stage N1%	1.6(0.6-2.6)	1.3(0.3-1.9)	0.422
Stage N2%	61.6(54.6-68.8)	61.6(48.5-72.1)	0.894
Stage N3%	31.0(22.9-36.5)	27.4(20.1-43.6)	0.973
AHI rem	0.0(0.0-0.0)	3.9(1.9-23.3)	<b>0.002</b>
AHI non-rem	1.4(0.2-2.2)	5.9(4.1-9.7)	<b>0.003</b>
AHI total, events/h	1.7(0.3-2.3)	6.2(5.6-10.5)	<b>0.005</b>
Supine sleep duration	0.8(0.2-1.8)	7.7(5.3-33.0)	<b>&lt;0.001</b>
Supine AHI	0.1(0.0-2.7)	3.1(0.0-9.0)	0.285
PLM	2.9(2.0-5.2)	3.1(2.5-90.5)	0.709
Basal oxygen SPO <sub>2</sub> , %	95.0(94.0-96.0)	95.0(93.2-97.0)	0.610
Desaturation index	1.0(0.0-2.0)	3.6(2.0-7.5)	<b>0.007</b>
Obstructive apnea index	0.1(0.0-0.2)	0.5(0.2-0.8)	<b>0.019</b>
Mean SPO <sub>2</sub> , %	96.0(94.0-96.0)	95.5(94.0-96.0)	0.691

Minimum SPO <sub>2</sub> , %	92.0(91.0-93.0)	91(90.5-92.0)	0.589
Aurosolin index, events/h	3.6(0.7-5.1)	3.8(0.0-9.0)	0.974

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Mann Whitney U Test. N1: non rapid-eye movement sleep stage 1; N2: non rapid-eye movement sleep stage 2; N3: deepest non rapid-eye movement sleep stage3; REM: rapid eye movement; AHI: apnoea–hypopnoea index; PLM: periodic leg movements; SPO<sub>2</sub>: oxygen saturation measured by pulse oximetry