Central European Journal of Urology

ORIGINAL PAPER

FUNCTIONAL UROLOGY

The role of primary nocturnal enuresis in the aetiology of overactive bladder syndrome

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Citation: Çakıoğlu B, Arıkan MG, Taş T, Bilir B. The role of primary nocturnal enuresis in the aetiology of overactive bladder syndrome. Cent European J Urol. 2023; 76: 207-211.

Article history
Submitted: Mar. 28, 2023
Accepted: Aug. 28, 2023
Published online: Sept. 9, 2023

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Introduction The aim of this study was to investigate the effect of nocturnal enuresis (NE) in childhood on the development and course of overactive bladder (OAB) in adulthood.

Material and methods Between January and September 2021, data from patients who visited the Urology Outpatient Clinic with OAB symptoms were collected. Patients with a history of diabetes mellitus, neurological diseases, bladder outlet obstruction, active urinary system infection, or previous medical treatment for OAB and those who did not agree to join the study were excluded. Patients with a diagnosis of NE in childhood were classified as group 1, and patients without a diagnosis of NE were classified as group 2. Demographic data were recorded. Frequency of incontinence, and the number of daytime voids and nocturia were evaluated according to a three-day voiding diary. In addition, the maximum urinary flow ratio (Qmax), bladder wall thickness, and postvoid residual volume were determined using uroflowmetry and pelvic ultrasound.

Results After applying the inclusion/exclusion criteria, the mean age of the study group of 103 patients, consisting of 34 women and 69 men, was 32.85 ±11.20 years (18–65), and the mean BMI of both groups was 26.62 ±3.34 (19.49–39.18). Sixty-five of 103 patients (63.1%) had a history of childhood NE diagnosis. Patients in the group with a history of NE were younger than those without a history of NE.

Conclusions The earlier onset and more intense course of OAB symptoms in patients diagnosed with NE in childhood suggests that NE may be a triggering factor in the aetiology of OAB.

Key Words: overactive bladder ‹› primary nocturnal enuresis ‹› treatment ‹› aetiology

INTRODUCTION

Overactive bladder (OAB) is a disorder consisting of frequent urination and nighttime urination, accompanied by a sense of urgency [1]. The aetiology of OAB is unclear, but it has been suggested that it may be associated with some conditions [2]. The prevalence of OAB in the United States has been reported to be 16% in men and 16.9% in women [3]. OAB is a condition that increases with age and significantly affects quality of life [4]. For the diagnosis of OAB, first, urinary tract infection or similar complaints should be excluded, and it can be made with a detailed history, urological examination, and urinalysis [5].

The aetiopathogenesis of OAB is not fully understood, but the triggering mechanisms of OAB have been suggested [2]. More than one contributing factor to OAB phenotypes has been identified, and these factors have been proposed as the 5 main hypotheses: myogenic hypothesis, urotheliogenic hypothesis, urethrogenic hypothesis, supra-spinal hypothesis, and detrusor insufficiency [6–11].

Nocturnal enuresis (NE) is called urinary incontinence during sleep. The aetiology of NE is multifactorial, but its aetiology has not been fully

elucidated, and it is more common in girls [12, 13]. The prevalence of NE decreases gradually with age; it is 15–20% until 5–6 years of age, and it regresses to 1% at 17 years of age. NE resolves spontaneously at a rate of 14% per year. Three important criteria have been described in the pathophysiology of NE: excessive nocturnal urine production, decreased or increased bladder capacity, insufficient detrusor activity, and arousal disorder [13].

There are many studies investigating the relationship between NE and OAB, but these studies are mostly in the theory stage, so more studies are needed on this subject. Therefore, the development of OAB at an advanced age in patients with NE symptoms in childhood indicates that NE may be a triggering factor. There are few studies available in the literature about the possibility of having bladder dysfunction in children with NE [14–17]. We aimed to investigate the effect of NE in childhood on the development and course of OAB in adulthood.

MATERIAL AND METHODS

Ethical approval of the study was obtained from Trakya University Faculty of Medicine (IRB: 28.10.2019.5/30) and recorded on the ClinicalTrials.gov website (NCT05151081). Between January and September 2021, the data of patients who presented to the Urology Outpatient Clinic with OAB symptoms were collected prospectively. Patients with a history of diabetes mellitus, neurological diseases, bladder outlet obstruction, active urinary system infection, or previous medical treatment for OAB and those who did not agree to join the study were excluded. The patients were divided into 2 groups according to the diagnosis of childhood NE. The patients who received NE in childhood comprised group 1 (n = 65), and the patients without a diagnosis of NE formed group 2 (n = 38). Demographic data were recorded. Frequency of incontinence, and the number of daytime voids and nocturia were evaluated according to a three-day voiding diary. In addition, the Qmax, bladder wall thickness, and postvoid residual volume were determined using uroflowmetry and pelvic ultrasound.

According to International Continence Society, we defined NE as involuntary urinary incontinence occurring more than once a month during the main sleep period (bed-wetting) in children older than 5 years of age. OAB is defined as an increase in daytime frequency and/or urge urinary incontinence that occurs at least once a month, as in other important publications in the literature [18, 19]. Urgency and true stress urinary incontinence were not included in the definition of OAB. Additionally, the diagnosis of patients with OAB was made by history, symptom questionnaires (OAB Questionnaire: OAB-q), physical examination, and urinalysis. The Overactive Bladder Symptom Score (OABSS) questionnaire was used to evaluate OAB [20].

In addition, it was evaluated with the Turkish OABSS questionnaire validated by Çulha et al. [21], and scores between 0 and 15 were given according to this questionnaire.

Statistical analysis

All analyses were performed using SPSS 25.0 (Statistical Package for Social Sciences, Chicago, USA). The differences between the measurable data of the patient groups were analysed by Student's t test (independent samples test). The difference in group data percentages was analysed with the chi-square test. Descriptive statistics were presented as the mean ±SD for continuous variables, and numbers and percentages for categorical data. The results were considered significantly different when the p value was below 0.05.

RESULTS

A total of 103 patients, comprising 34 (33%) women and 69 (67%) men, were included in the study; 65 (63.1%) of these patients had a history of NE

Table 1. *Data on patients with overactive bladder with and without enuresis*

	Group I (N = 65) patients with enuresis	Group II (N = 38) patients without enuresis	p Value
Gender (M/F)	47 (72.3%)/ 18 (27.7%)	22 (57.9%)/ 16 (42.1%)	0.133
Age (years)	31.0 ±10.3	37.1 ±11.1	0.006*
BMI	26.07 ±3.18	26.90 ±3.66	0.233NS
Nocturia	1.24 ±1.11	1.52 ±1.26	0.246NS
Frequency	9.32 ±2.24	10.44 ±2.63	0.024**
Lifequality	2.54 ±0.66	2.30 ±0.78	0.106NS
Thickness	4.59 ±0.89	5.16 ±1.15	0.006*
Residüel Urine (mL)	22.4 ±11.6	27.3 ±34.9	0.346NS
Urine Volume (mL)	263.3 ±57.7	264.3 ±66.9	0.938NS
Qmax	33.03 ±5.89	32.18 ±6.48	0.500NS
Qave	19.00 ±4.10	18.39 ±4.90	0.504NS

BMI – body mass index; Qmax – maximum urine flow rate; Qave – average urine flow rate; NS – not significant
Independent Samples T Test (mean ±SD) *p <0.001, **p <0.05,
Chi-Square Test [Gender (Male/Female)]

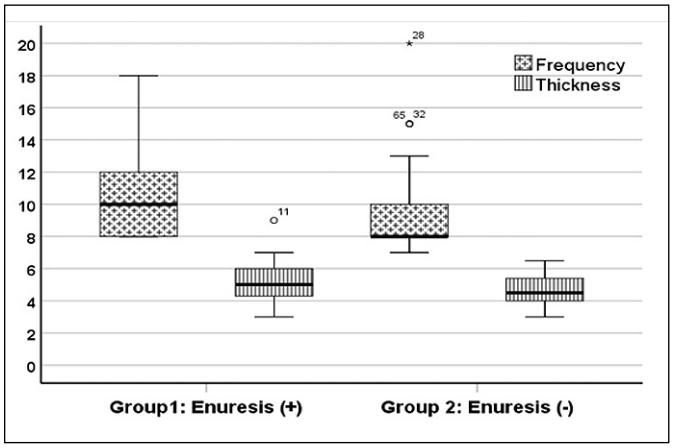

Figure 1. *Box plot graph of frequency and thickness data in patients with overactive bladder with and without enuresis.*

Table 2. *Statistical comparison of data differences between male and female patients with overactive bladder*

	Male Group (N = 69) overactive bladder	Female Group (N = 34) overactive bladder	p Value
Age (years)	30.7 ±9.8	38.2 ±11.4	0.001*
BMI	26.20 ±3.22	26.74 ±3.67	0.442NS
Nocturia	1.15 ±1.10	1.73 ±1.23	0.019**
Frequency	9.24 ±2.06	10.73 ±2.85	0.003*
Lifequality	2.59 ±0.62	2.18 ±0.80	0.006*
Thickness	4.60 ±0.99	5.20 ±0.99	0.005*
Residüel urine (mL)	28.5 ±22.4	15.5 ±28.8	0.013**
Urine volume (mL)	266.1 ±52.5	258.8 ±75.9	0.572NS
Qmax	32.02 ±5.89	34.11 ±6.35	0.103NS
Qave	18.71 ±4.51	18.91 ±4.24	0.828NS

BMI – body mass index; Qmax – maximum urine flow rate; Qave – average urine flow rate; NS – not significant
Independent Samples T Test (mean ±SD) *p <0.001, **p <0.05

and 38 (36.9%) had no history of NE. The mean age of the patients was 32.85 ±11.20 years (18–65), and the mean BMI of both groups was 26.62 ±3.34 (19.49–39.18). The mean nocturia was 1.26 ±1.22 (0–6), the mean frequency was 9.86 ±2.53, and the mean incontinence was 0.31 ±0.47. The mean OABSS-total score of the patients was 4.66 ±4.03 (1–15). When the data of both groups were compared, it was seen that the mean age in the NE group was lower: 31.0 ±10.3 and 37.1 ±11.1 years, respectively (p = 0.006). Urinary frequency was 9.32 ±2.24 in the NE group and 10.44 ±2.63 (p = 0.024) in the non-NE group, and bladder wall thickness was 4.59 ±0.89 mm in the NE group and 5.16 ±1.15 mm (p = 0.006) in the non-NE group (Figure 1). Both parameters were found to be statistically significant. Nevertheless, there was no significant difference between the 2 groups in terms of BMI, nocturia, quality of life, residual urine volume, Qmax, average flow rate (Qave), and maximum bladder capacity (Table 1). When comparing data between male and female patients with OAB, there was a statistically significant difference in age, nocturia, quality of life, bladder wall thickness, and residual urine between males and females in both groups. However, there was no statistically significant difference between BMI, maximum bladder capacity, Qmax, and Qave (Table 2, Figure 2).
The percentages of incontinence with and without enuresis in patients with OAB were 23.07% and

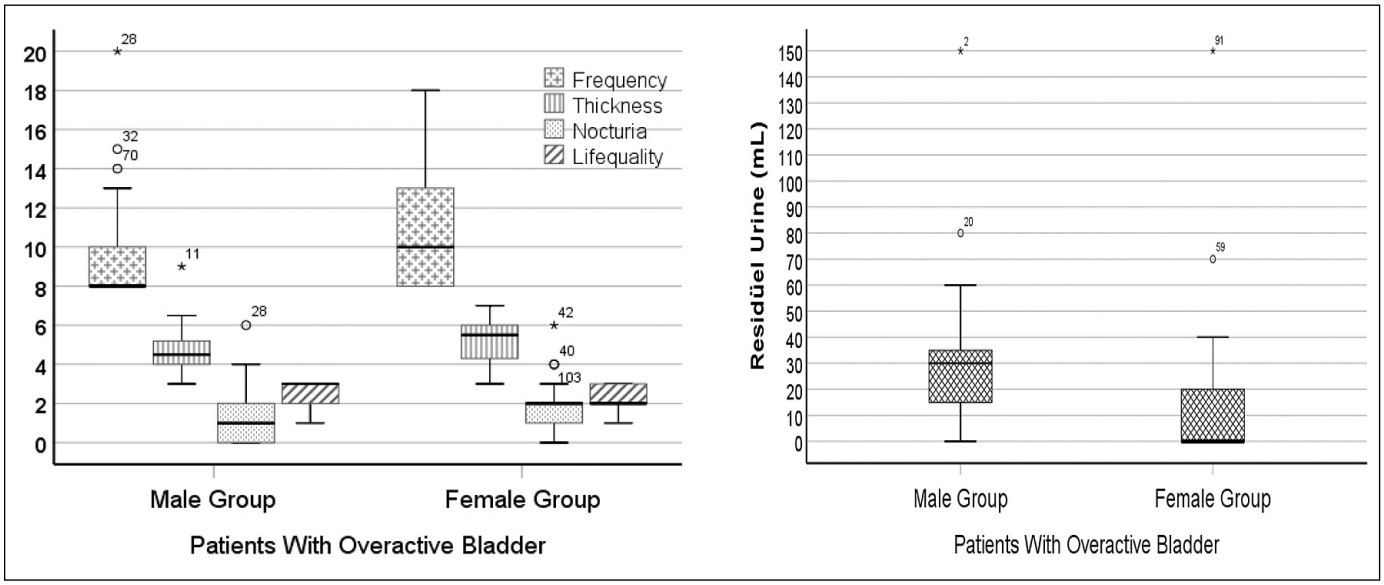

Figure 2. *Box plot of data for male and female patients with overactive bladder.*

36.84%, respectively. However, there was no significant difference in statistics (p: 0.134).
In addition, the percentages of patients with OAB who were unsatisfied with and without enuresis were 84.61% and 71.05%, respectively, but it was not statistically significant (p = 0.099).

DISCUSSION

The current results suggest that OAB patients diagnosed with NE in childhood face more severe symptomatology and earlier admission to a urology outpatient clinic.
Overactive bladder is defined as a symptom complex that includes urgency, frequency, urge incontinence, and nocturia [22]. The aetiopathogenesis of OAB is not fully understood, and studies on its aetiology are continuing. Among these studies, in a cohort study investigating the prevalence of long-term nocturia in children with nocturnal enuresis in the past, with a mean follow-up of 7 years, urgency, pollakiuria, urinary incontinence, and nocturia were found in 8–35% of adults treated for NE during childhood and whose symptoms resolved [23]. In a study conducted by Suditu et al., it was found that 34.38% of patients with childhood NE were diagnosed with OAB. Expressing this situation as follows, after the age of 25 years, the circadian rhythm of melatonin and vasopressin changes, but childhood NE patients will have symptoms such as nocturia and increased urination frequency in adulthood [16]. In our study, although there was no significant difference in the frequency of nocturia between the groups with and without NE, the frequency of nocturia was higher in the group with NE.
One of the major patterns of OAB is nocturia. The results of a study, which reported that the diagnosis of nocturnal enuresis in childhood and nocturia seen in adolescence and young adulthood is 35%, are in line with our results [24]. This seems to be a very high rate compared to other studies. Although our study was similar in terms of the mean age of the population, the small patient population may have caused the difference in the results [23]. In addition, patients diagnosed with NE in childhood had OAB symptoms at a younger age, had more urgency and incontinence, and had greater bladder wall thickness measurements. This indicates that NE remission is the beginning of the effect on lower urinary tract symptoms, and that the risk of developing OAB symptoms in the following years is high. There is a partial connection between the 5 main hypotheses proposed for the aetiology of OAB and that of NE, such as increased nighttime urination, underactive detrusor, and impaired sleep stimulation [13, 23].
The mean age of patients with OAB symptoms was 32 years, and the adults who had NE in childhood were younger compared to adults without NE in childhood. It was reported in a 2019 study that children with NE symptoms had OAB symptoms in early adulthood. In another study, the frequency of OAB in patients aged 35–44 years and patients aged 45–54 years was reported to be 22.8% and 17.2%, respectively [3]. Therefore, because NE can be considered a triggering factor for OAB, patients with NE during childhood who had OAB symptoms at an early age gained importance.
Determining the factors that play a role in the pathophysiology of OAB is an important goal in the treatment of the disease. However, the results of the studies on OAB have differed. Age, sex, low education level, obesity, multiple births, and difficult vaginal delivery are generally assumed to be risk factors for OAB [25].
Overactive bladder has a significant impact on patients' quality of life and therefore has a significant burden on the budget of this patient group. A study in 6 economically developed countries observed that the diagnosis and treatment of OAB have a major effect on the financial burden of the countries [26]. The relationship between OAB and NE revealed in our study is very important for clinicians, to inform parents and for follow-up.
The small number of patients in our study is the most important limitation, and another important limitation is the lack of urodynamic examinations of the patients. In our patient group, urodynamics was not used in the diagnosis of overactive bladder. Although we report this as a limitation, OAB is defined as an increase in daytime frequency and/or urge urinary incontinence that occurs at least once a month, as in other important publications in the literature [18, 19]. Urgency and true stress urinary incontinence were not included in the definition of OAB.

CONCLUSIONS

In conclusion, the earlier onset and more intense course of OAB symptoms in patients diagnosed with NE in childhood suggests that NE may be a triggering factor in the aetiology of OAB. It is very important for clinical practices to transfer this relationship to the clinics, to inform and follow the parents. More research is needed to clarify the relationship between NE and OAB.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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