Original Article

Monosymptomatic and Non–monosymptomatic Nocturnal Enuresis: A Clinical Evaluation

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Abstract

Background: Nocturnal enuresis is divided into monosymptomatic nocturnal enuresis (MNE) and non-monosymptomatic nocturnal enuresis (NMNE). This study reviews clinical and ultrasonography (US) findings in enuretic children, and compares the organic and functional pathologies of the lower urinary tract (LUT) in children with MNE to those who have NMNE.

Methods: We enrolled 111 neurologically normal children with chief complaints of enuresis in this study. Participants included 60 boys and 51 girls, aged 5 – 17 years. There were 43 (38.8%) patients diagnosed with MNE and 68 (61.2%) with NMNE. Urine analysis, urine culture and kidney–bladder US were performed for patients. Some patients underwent a voiding cystoureterography (VCUG), urodynamic study (UDS), or both.

Results: Patients were divided into three groups: i) MNE, ii) NMNE without daytime incontinence (NMNE – daytime incontinence), and iii) NMNE plus daytime incontinence (NMNE + daytime incontinence). Constipation ($P = 0.011$), encopresis ($P = 0.003$) and urge incontinence ($P = 0.001$) were significantly more frequent in patients with NMNE +daytime incontinence. Bladder wall thickness (BWT) was the most common US finding. One patient with MNE and 9 with NMNE+ daytime incontinence had vesicoureteral reflux (VUR; $P = 0.016$). Posterior urethral valve (PUV) was reported in one patient with NMNE. Evidence of bladder dysfunction was noted in about half of the patients who underwent UDS, with a higher prevalence in cases that had NMNE +daytime incontinence ($P = 0.297$). Bowel symptoms and VUR were significantly more prevalent in cases with NMNE + daytime incontinence.

Conclusion: We recommend VCUG in enuretic children who have daytime incontinence. In addition our study has revealed that symptoms suggestive of an overactive bladder (OAB) are not good indicators for bladder dysfunction.

Keywords: Enuresis, MNE, NMNE, urological abnormalities

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Introduction

Acquisition of urinary control is complex and has not been completely understood. This process consists of different developmental stages, in which the final stages are usually achieved at the age of 3 to 4 years when the majority of children develop an adult pattern of urinary control.[1] Nocturnal enuresis affects 5% – 10% of younger school-age children.[2] Daytime urinary incontinence of varying severity occurs in 2% – 20% of school-age children and 0.7% wet daily.[3] Bedwetting is more common in boys whereas daytime incontinence is more common in girls.[4] Nocturnal enuresis is divided into monosymptomatic nocturnal enuresis (MNE) with no daytime urinary symptoms and non-monosymptomatic nocturnal enuresis (NMNE) that is accompanied by daytime urinary symptoms.[5]

This study was designed to review clinical and ultrasound (US) findings in childhood enuresis and compare organic and functional pathologies of the lower urinary tract (LUT) in the subtypes of enuresis.

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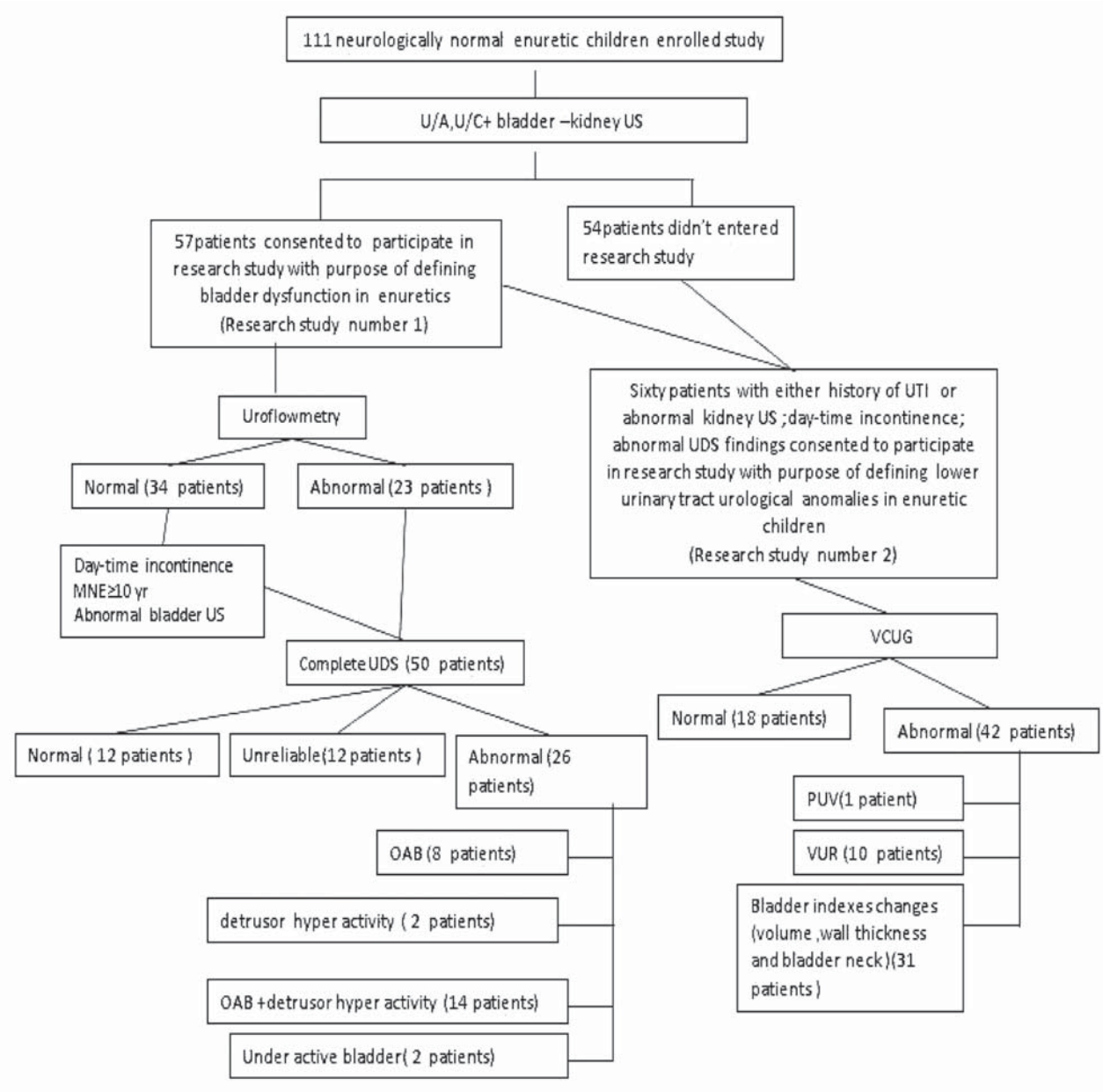
Materials and Methods

During a three-year period (2007 – 2009), neurologically normal children who consulted the Nephrology Clinic at a tertiary care center with chief complaints of enuresis were evaluated. International Children's Continence Society (ICCS) criteria were used to define enuresis and its subtypes; constipation and encopresis were defined according to ICD-10 and DSM-IV criteria.[5] Children with neurologic deficits (myelodysplasia, spinal cord disorders and mentally retarded children) were excluded from the study. The majority of patients referred to the clinic as a secondary referral center. A total of 67 (60.4%) received no prior medical treatment, whereas 24 (21.6%) previously received one conventional therapy and 8 (7.2%) had undergone two conventional therapies. In 12 (10.8%) children, parents were uncertain about their medical treatments. Urinalysis, urine culture and kidney–bladder US were performed for all children. US was performed in patients diagnosed with MNE since the majority of them had not undergone perinatal US Bladder volumes (BV) were matched for age and reported as normal, increased and decreased.[6] Bladder wall thickness (BWT) $\geq$3 mm in a filled bladder was considered as increased and post-voiding residual urinary volume (PVRUV) $\geq$ 15 cc was defined as abnormal. Voiding cystoureterography (VCUG) was used to evaluate the anatomy of the LUT and urodynamic studies (UDS) were performed to assess bladder function.

Flow Chart A illustrates the methods used for patient assessments.



Flow Chart A. Study design and method for patients' evaluations.

Criteria for the performance of a VCUG were a history of urinary tract infection (UTI), NMNE plus daytime incontinence (NMNE + daytime incontinence), abnormal UDS, and abnormal renal US (small-sized kidney, hydronephrosis, hydroureter, and hydroureteronephrosis). Uroflowmetry was performed in 57 patients who had participated in a research study funded by a grant from Mashhad University of Medical Sciences. Cystometrography (CMG) and pelvic floor electromyography (EMG) were done in cases of abnormal uroflowmetry results, abnormal bladder US findings, BWT, decreased or increased BV or PVURV ≥ 15 cc, NMNE + daytime incontinence, and MNE in children ≥ 10 years of age. A frequency-volume chart was not obtained since patients and their parents did not express interest in cooperating. Oral consent was taken from parents and older children.

For the uroflowmetry test, children were asked to wait until they felt a strong desire to void. The uroflowmetry test was performed for three consecutive times. CMG was done as a conventional method that involved a dual lumen urodynamic catheter and a rectal catheter. The bladder was filled slowly with saline warmed to 37°C while patients were in the supine position.[7] simultaneously, intravesical and abdominal pressures were recorded and the detrusor pressure derived. Abdominal pressure was estimated from the rectal catheter. Urodynamic tests were performed when patients were in an aroused state. Pelvic floor EMG was done by spacing skin electrodes .We used Koff's formula to measure bladder capacity:[7]

Volume (ml) = (Age + 2× 30)

The volume in the filling phase at which the patient felt the first desire to void (FDV) was defined as bladder capacity.[8] Measured capacities less than 65% and > 150% of the age-calculated value

Table 1. Clinical details of patients.

Variable	MNE (N/%)	NMNE – daytime incontinence (N/%)	NMNE + daytime incontinence (N/%)
Age ≤10 years	36 (83.8)	11 (64.7)	42 (82.4)
Age > 10 years	7 (16.2)	6 (35.3)	9 (17.6)
Male	31 (72.1)	12 (70.6)	17 (33.3)
Female	12 (27.9)	5 (29.4)	34 (66.7)
Positive family history of enuresis*	29 (67.5)	11 (64.7)	32 (66.7)
Negative family history of enuresis	13 (30.2)	1 (5.9)	8 (15.7)
Primary enuresis	38 (88.4)	15 (88.2)	41 (80.4)
Secondary enuresis	5 (11.6)	2 (11.8)	10 (19.6)
Total number	**43 (100)**	**17 (100)**	**51 (100)**

*In 17 cases (1, 5, and 11 patients from groups 1–3, respectively) parents were unsure about family history.

Table 2. Urinary and bowel symptoms in our series.

Symptoms	MNE (N/%)	NMNE - daytime incontinence (N/%)	NMNE + daytime incontinence (N/%)
Increased voiding frequency	0	8 (47)	13 (24.5)
Straining	0	1 (9.5)	1 (2)
Constipation	3 (7)	0	11 (21.6)
Encopresis	1	2 (11.8)	13 (24.5)
Wetting during nap	5 (11.6)	3 (17.6)	15 (29.4)
Urge incontinence	0	3 (17.6)	18 (35.3)
Holding maneuvers	0	3 (17.6)	7 (13.7)
Dribbling	0	1 (5.9)	3 (5.9)
Giggle incontinence	0	2 (11.8)	1 (2)
Decreased voiding frequency	0	1 (5.9)	3 (5.9)
Encopresis +constipation	0	0	6 (11.8)
Urge incontinence + increased voiding frequency	0	1 (5.9)	3 (5.9)
Intermittency	0	0	3 (5.9)
Total	**43 (100)**	**17 (100)**	**51 (100)**

were defined as small and large capacities.[5] Detrusor over activity was defined as involuntary detrusor contractions during the filling phase that involved a detrusor pressure increase of > 15 cm of water above baseline. Detrusor under activity was defined as a contraction of decreased strength that resulted in prolonged bladder emptying and/or failure to achieve complete bladder emptying. Overactive bladder (OAB) was defined as involuntary detrusor contractions, small bladder capacity, and urethral instability.[5]

Children were divided into the following three groups. Group 1 consisted of patients diagnosed with MNE; group 2 patients had NMNE but did not wet during the day (NMNE - daytime incontinence); and group 3 consisted of patients with NMNE who also had daytime incontinence (NMNE + daytime incontinence). To analyze data, we used the Fisher's exact, Chi -square and t-tests. A *P*-value < 0.05 was considered significant.

Results

There were 111 children who met the inclusion criteria and enrolled in the study. Participants included 60 boys and 51girls, of which 43 (38.8%) were diagnosed with MNE and 68 (61.2%) with NMNE. Children's ages ranged from 5 – 17 years (mean: 8.66 ± 2.24 years in those with MNE and 8.2 ± 2.5 years in those with NMNE). Children wet the bed 1 – 7 nights per week (mean: 5.58 ± 1.98 in children with MNE and 5.36 ± 2.17 in those with NMNE). Primary enuresis was noted in 94 (84.7 %) and secondary in 17 (15.3 %). A total of 72 (64.9%) patients had histories of nocturnal enuresis in their close relatives. In 22 (19.9%), the family histories were negative and in 17 (15.3%) parents were uncertain about family history.

Tables 1 and 2 illustrate clinical details, urinary and bowel symptoms in patients. In a comparison of patients with no daytime incontinence (groups 1 and 2) with those who wet during the day (group 3), it was observed that constipation ($P = 0.011$), encopresis ($P = 0.003$), and urge incontinence ($P = 0.001$) were significantly more frequent in group 3. Although symptoms indicative of OAB, such as increased urinary frequency and holding maneuver[5] were more frequent in children with daytime incontinence ($P = 0.332$) compared to those with daytime continence ($P = 0.144$), the differences were not significant.

Secondary enuresis was noted to be slightly more common in patients with NMNE than those with MNE ($P > 0.05$). BWT was the most common finding in all groups and a PVRU ≥ 15 cc was more common in children with MNE ($P = 0.388$ for total US findings). VCUG was performed in 60 patients, whereas 50 underwent EMG + CMG.

Table 3 shows the VCUG results. Vesicoureteral reflux (VUR) was reported in 10 patients and one case had a posterior urethral valve (PUV). One (2%) patient with MNE and 9 (17.6%) patients from the third group had VUR ($P = 0.016$). Within the group diagnosed with VUR, 5(50%) had positive histories of UTI, whereas 4 (40%) had no history of any UTI; amongst children without VUR, 17 (34%) had positive histories of UTI and 32 (64%) children had no UTI history ($P = 0.494$). For 2 patients, we were unable to determine a history of UTI. In the VUR group, enuresis was primary in 40 (80%) and secondary in 9 (18%) patients ($P = 0.333$). Parents were uncertain whether enuresis was primary or secondary in one child. VUR was reported in 10 patients and 12 kidney ureter unit (KUU). VUR was graded as follows: I (1), III (7), IV (2), and V (2).

Uroflowmetry was performed in 27 patients from group 1, 6 from group 2, and 24 patients from group 3. The results were normal in 17 (63%) group 1 patients, all group 2 patients, and 10 (41.6%) patients from group 3. The following conditions were noted in group 1 patients: outflow tract obstruction (4; 14.8%), staccato voiding (2; 7.2%) and detrusor sphincter dyssynergia (DSD) (2; 7.2%). The third group had the following patterns: outflow tract obstruction (8; 33.3%), high pressure (2; 8.3%), and staccato voiding (1; 4.1%).

Table 3. Results of VCUG and US in patients.

	MNE (N/%)	NMNE - daytime incontinence (N/%)	NMNE + daytime incontinence (N/%)
Findings of VCUG			
Normal	11 (52.4)	6 (35.3)	1 (40.6)
Irregularity of bladder wall	2(9.5)	6 (35.3)	6 (18.7)
Vertical bladder	2 (9.5)	2 (11.8)	1 (3)
Widening of bladder neck	3 (14.3)	0	5 (15.6)
Unilateral VUR	1 (4.8)	0	6 (18.7)
Bilateral VUR	0	0	3 (9.4)
Spinning top deformity	1 (4.8)	0	1 (3)
Enlarged bladder	1 (4.8)	1 (5.9)	0
PUV	0	1 (5.9)	0
Bladder diverticulum	(4.8)	0	2 (6.2)
Total	**21 (100)**	**17 (100)**	**32 (100)**
Bladder US findings			
Normal	10 (23.2)	3 (17.6)	6 (11.8)
Increased bladder wall thickness (BWT)	27 (62.8)	9 (53)	37 (72.5)
Post voiding urinary residue	10 (23.2)	4 (23.5)	8 (15.7)
Decreased bladder volume (BV)	4 (9.3)	1 (5.9)	3 (9.5)
Increased BV	1 (2.3)	0	0
Widening of bladder neck	3 (7)	1 (5.9)	1 (2)
Total	**43 (100)**	**17 (100)**	**51 (100)**

Table 4. Urodynamic findings in study patients.

Findings of urodynamic Studies	MNE (N/%)	NMNE - daytime incontinence (N/%)	NMNE + daytime incontinence (N/%)
Group 1 (normal UDS)	7 (33.3)	2 (28.6)	3 (13.6)
Group 2 (OAB)	2 (9.5)	3 (42.9)	3 (13.6)
Group 3 (OAB +detrusor hyperactivity)	5 (23.8)	0	9 (40.9)
Group 4 (detrusor hyperactivity)	0	0	2 (9)
Group 5 (Underactive bladder)	2 (9.5)	0	0
Un-reportable	5 (23.8)	2 (28.6)	5 (22.7)
Total	**21 (100)**	**7 (100)**	**22 (100)**

Discussion

In our series, bedwetting was more common in boys (60 out of 111 total cases) than girls (M/F = 1.1/1) at a 95% CI of 0.447 – 0.633. However in the group with daytime incontinence the majority were girls (F/M = 2/1; 34 out of 51 total cases), with a 95% CI of 0.578 – 0.754. Frequency and severity of wetting episodes progressively increases with age, and children >10 years of age have significantly more daytime urinary symptoms and incontinence.[9,10] In our cases 15 out of 22 (68%) patients aged ≥ 10 years old exhibited daytime symptoms. Of these, there were 16 %of children in group 1(MNE) compared to 22% in the NMNE group who were aged ≥ 10 years. This might be the result of the lower annual rate of spontaneous resolution of NMNE.

Constipation is frequent in enuretic patients and closely related to LUT symptoms.[11] in our series, abnormal bowel symptoms were noted in approximately one-third of cases that had constipation or encopresis. Mostly children in group 3 had abnormal bowel symptoms ($P < 0.05$). The higher prevalence of bowel symptoms in this group suggested that constipation was a factor that exaggerated daytime symptoms in enuretic children.

VUR has been reported in 2% – 10% of patients with enuresis.[12] Urological evaluation of enuresis has been recommended in cases with a history of UTI,[13] in NMNE,[14] in children with irritable bladder symptoms,[15] secondary enuresis,[16] and those who failed conventional medical therapy.[17] Kajiwara observed the presence of mechanical urethral obstruction and VUR more frequently in children with NMNE than those with MNE.[11] In contrast to our findings that VUR was only present in cases with primary enuresis, Abrams et al. have proposed that secondary enuresis was more likely to be associated with an organic cause.[4] In support of a study by Husman, we found significant urological abnormalities in a minority of children with primary MNE.[18] In contrast to previous studies,[13-16] we did not observe any correlation between a history of UTI ($P = 0.052$), form of enuresis (secondary compared to primary; $P = 0.494$), or bowel symptoms (constipation and encopresis; $P = 0.333$) and VUR. However daytime urinary incontinence was significantly more common in enuretic children who had VUR ($P = 0.016$).

In the current study, all VUR cases were enuretic girls ($P = 0.003$), which might be related to the observation that the majority of enuretics who wet during the daytime were girls. Tafuro t al. have found a meaningful correlation between BV wall thickness index on US with over activity, bladder capacity, and high voiding detrusor pressure on UDS.[19]

Tanaka, has recommended US for diagnosis and follow up of NMNE, which is preferable to UDS.[20] In our study, bladder US measurements showed similarities between children with MNE and NMNE. US findings were not helpful in the differentiation of those with bladder dysfunction from patients with normal bladder function (Table 3).

It has been suggested that enuretics with OAB symptoms should be classified as NMNE.[2] However in the study by Watanabe, it was determined that children diagnosed with MNE who have no diurnal symptoms may have OAB.[21] CMG recordings during sleep have indicated uninhibited bladder contractions in 30% – 32% of children with enuresis.[22] It has been reported that one-third of enuretic children have nocturnal detrusor overactivity.[23]

In our study, UDS evaluation in the arousal state has revealed abnormalities in 43% of MNE and 53% of NMNE patients, which shows that abnormal UDS is as common in MNE as in NMNE. Medel et al. have assessed urodynamics in patients with MNE and

NMNE with the intent to define a prognostic indicator of detrusor instability.[24] They found detrusor instability or decreased bladder compliance in 49% of patients with MNE and in 79% of those with NMNE. These researchers have concluded that maximum bladder capacity as determined by cystometry is a good indicator of bladder dysfunction In the study by Hann-Chorng, 63% of children with urinary incontinence and 73.3% of those with VUR had evidence of voiding dysfunction seen on video urodynamics.[25] In our study, the majority (53.9%) of patients with abnormal UDS had small capacity and low compliance bladders which was indicative of an OAB Although abnormal UDS was more frequent in cases with diurnal incontinence, the difference was not significant ($P = 0.297$). Therefore, patients who have either MNE or NMNE with daytime continence have a similar risk of association with LUT urological abnormalities. Cases with day- and nighttime incontinence seem to represent a completely different entity, thus a revision in enuresis subtypes should be considered as follows: MNE, NMNE with daytime continence and NMNE with daytime incontinence. Using this classification will enable health care providers to discern patients who need to be evaluated urologically.

Based on our study results, VCUG is recommended in patients with NMNE who have daytime incontinence.

Future studies should be conducted to determine if enuretic girls are at greater risk for urological abnormalities and which groups of enuretic children should be considered for urodynamic testing.

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