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Functional Bladder Capacity in Children with Primary Monosymptomatic Nocturnal Enuresis

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Abstract

Objective: To study the clinical profile and to assess the Functional Bladder Capacity by ultrasonography and uroflowmetry in children presenting with Primary Monosymptomatic Nocturnal Enuresis.

Methods: An observational study was carried out in children (aged 5 -15 years) presenting to Pediatrics OPD between November 2018 to February 2020 with PMNE. Detailed history using a Clinical Management Tool, clinical examination, UTI investigation, Ultrasonography of KUB done. Also, Urodynamic Studies done. A 48-hour bladder diary provided to measure intake of fluids and frequency/ volume of urine.

Results: 46 children with mean age of 9.61 years were included. Boys were more affected than girls. Significantly associated factors were younger age, families with low income, family history of bedwetting, 37 patients (80.4%) had low functional bladder capacity. In 21 out of 26 children in whom UDS done showed normal in 21 children and abnormal only in 5 children. A weak correlation noted between maximal voided volume by bladder diary and voided volumes by UDS and FBC by ultrasound respectively.

Conclusion: PMNE is a multi-etiological disorder results from the interaction of genetics, sleep and psychological disturbances. History taking and bladder diary are sufficient for diagnosis but ultrasound and uroflowmetry to be done where facilities are available since abnormal UDS can be seen in PMNE cases too and low FBC noted.

Keywords: PMNE • Clinical management tool • Functional bladder capacity • Urodynamic studies

Abbreviations and acronyms: PMNE: Primary Monosymptomatic Nocturnal Enuresis • PNE: Primary Nocturnal Enuresis • EBC: Expected Bladder Capacity • FBC: Functional Bladder Capacity • UDS: Urodynamic Studies • KUB: Kidney Ureter Bladder • UTI: Urinary Tract Infection • OPD: Out-Patient Department • F/V: Frequency volume chart

Introduction

Nocturnal enuresis (NE) is defined as urinary incontinence during sleep in a child five years or older [1]. Enuresis can be subdivided into primary *vs.* secondary and monosymptomatic *vs.* non-monosymptomatic types. Primary enuresis refers to children who have never achieved six months of continuously dry nights. Secondary enuresis refers to children who previously attained at least six months of night-time dryness before incontinence. In monosymptomatic enuresis, the only symptom is night time bed-wetting. Non-monosymptomatic enuresis involves daytime lower urinary tract symptoms or daytime incontinence, or holding maneuvers [2]. The prevalence of enuresis in India is 7.61%-16.3% as reported in various studies [3,4]. The exact cause for PMNE is unknown, but several factors may be contributory. Three pathophysiological mechanisms have been postulated which cause enuresis as abnormal circadian release of antidiuretic hormone (ADH) or arginine vasopressin (AVP) [5],"Small for age" bladder volume, and impaired arousal from sleep which prevents waking to void in the toilet [6,7]. Comorbid conditions include family history of enuresis [8], obesity, constipation, behavioral disorders like attention deficit hyperactive disorder, low socioeconomic status, obstructive sleep apnea syndrome often have a central role in the pathogenesis and potential therapy resistance of enuresis [9-11].

Low functional bladder capacity in enuretics is still an area of research with varied results. Thus, this study was conducted to assess functional bladder capacity by ultrasonography and uroflowmetry in children with primary nocturnal enuresis.

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Methods

Study design and patient groups

This was a prospective observational study conducted at tertiary care teaching hospital in New Delhi, India from November 2018 to February 2020 and was approved by Institutional Ethics Board. Written informed consent was obtained from the legal guardian of each child before enrollment. Children aged 5 to 15 years presenting to outpatient department with Nocturnal enuresis were screened for eligibility. Those children with primary nocturnal enuresis were included as study participants. Those with a) secondary enuresis b) growth retardation, kidney disease, thyroid disorder or epilepsy, congenital neurological and genitourinary anomalies were excluded from the study. Enuresis, its subtypes, and lower urinary tract terminology were defined as per International Children Continence Society Standardized (ICCS) terminology [1].

All children were screened by detailed history and clinical examination of abdomen, spine, genitalia using Clinical Management Tool (CMT) to look for

symptoms and signs of NMNE. Rome III criteria was used to define functional constipation. A 48-hour bladder diary with container was provided to children to measure intake of fluids and frequency/ volume of urine, maximal voided volume. Maximum voided volume (MVV) is defined as the largest volume of urine voided in a 24 h period, as documented in a bladder diary kept over 3-4 days, excluding first morning voids. The expected bladder volume was derived from formula (Age + 2) * 30. Frequent bedwetting was defined as >3 wet nights per week [12].

Ultrasonography

Those children who met the criteria of primary nocturnal enuresis underwent ultrasonography of Kidney, Ureter and Bladder (USG KUB) by single radiologist with patient lying supine with a ultrasound machine, model IU22 with transducers (frequency 3.5 MHz). Patient were asked to drink water volume at least more than the expected bladder capacity. Once there was desire to void, the parameters were recorded namely volume of urine in bladder to know the Functional Bladder Capacity (FBC), bladder wall thickness and post void residue. Post void residue was recorded immediately after voiding (<5 min). Expected bladder capacity (EBC) was calculated by the formula [(Age in years+2) x 30] in millilitres (ml)[1]. Low Functional Bladder Capacity was defined as less than 65% of expected bladder capacity. High Functional Bladder Capacity was defined as more than 150% of expected bladder capacity. Significant post void residual volume was defined as more than 10% of the EBC in 5 to 6-year-old and >20 ml in children aged 7-15 year. Bladder wall thickness ≥3 mm in distended bladder was considered abnormal.

Uroflowmetry

Noninvasive urodynamics (uroflowmetry) was performed on uroflowmeter machine (Aquarius XT Laborie) in few children. Curves with a voided volume of >50 ml urine were considered valid for analysis. Flow patterns, voided volumes, peak flow rate were recorded.

Statistical analysis

Statistical analysis was carried out done using Statistical Package for Social Sciences (SPSS) version 21.0. Continuous variables were presented as the Mean ± Standard Deviation (SD) or median (minimum–maximum) while categorical variables were presented as the frequency and percentage. For continuous variables, a P value was calculated by t test and Wilcoxon rank sum test while categorical variables were tested by Fischer's exact test. Correlation between FBC by ultrasonography and MVV by bladder diary was done by Pearson's coefficient correlation. Voided volume assessed by uroflowmetry and MVV by bladder diary were also correlated by same. A p value of <0.05 was considered to be statistically significant.

Results

Sixty-seven children presented with nocturnal enuresis to paediatric outpatient department at our hospital during the study period and were screened for eligibility. Forty-six treatment naive primary nocturnal enuresis children who met inclusion criteria were included for analysis. The mean age of the children in present study was 9.61 ± 2.02 years. There were 28 male and 18 females. There were 14 (30.4%) children in 5 to 8 years, 18 (60.9%) in 9 to 12 years and 4 (8.7%) in 13 to 15 years age group. The mean frequency of enuresis was 4.78 ± 2.11 per night per week. Frequent bedwetting was defined as >3 wet nights per week. 36 (78.2%) children were frequent bedwetters. 18(39.1%) children had the history of constipation. 12 (26.1%) children had family history of enuresis in first degree relative. The mean age of attaining dry nights of affected family member was 11.67±2.87 years. 22 (47.8%) children had history of snoring.4 children (8.7%) felt the sudden and urgent need to urinate. 12 children (26.1% of total) had associated behavioral problems in the form of inattention and scholastic backwardness as compared to their peers as observed by parents.16 (34.7%) patients had urinary frequency ≥ 8/day .4 children (8.7%) had history of holding maneuvers to postpone micturition (Table 1).

Voided volumes recorded from the bladder diary. The maximum voided volume was 490 ml and the minimum voided volume was 180 ml, obtained through 48-hour bladder diary. Voiding diary revealed 18 (39.1%) children with increased frequency (i.e., >8 times daytime voids) while CMT identified 16 (34.7%) children with increased frequency. None of the children had maximum voided volume >150% of expected bladder volume and approximately all 20 children (43.4%) had minimum voided volume less than 65% of expected bladder volume.

Ultrasonography was performed in all 46 study participants. Table 2 reveals the ultrasonographic findings of the study participants. 80.4% children had low FBC, 19.6% children had normal FBC and none of the children had high FBC. Bladder wall thickness was <3 mm in 84.8% and ≥ 3 mm in 15.2% children. Post Void Residue (PVR) was normal in all except 1 child. No other abnormalities were noted.

Table 1. Clinical Management Tool (CMT) of children participated in study.

Clinical Characteristics	Number of Children	(n=46)	Percentage (%)
How often (per night/per week)	>5 nights/week	34	73.9
	3 to 5 nights/week	2	4.34
	1 to 2 nights/week	10	21.7
Urinary frequency (# of voids) (>/= 8x/day)	>/= 8 times/day	16	34.7
	< 8 times/day	30	65.3
Voiding postponement	Yes	12	26.1
	No	34	73.9
Sudden and urgent need to urinate	Yes	4	8.7
	No	42	91.3
Family history- Did father/ mother/sibling have enuresis?	Yes	12	26.1
	No	34	73.9
History of constipation, Rome III criteria	Yes	18	39.1
	No	28	56.5
Any behavioral problems noticed by parents	Yes	12	26.1
	No	34	73.9
History of motor and/ or developmental delay	Yes	4	8.7
	No	42	91.3
Does child keep mouth open while sleeping/snoring	Yes	22	47.8
	No	24	52.1
Holding maneuvers (e.g., standing on tip toes, crossing legs, pressing hands on perineum etc.)	Yes	4	8.7
	No	42	91.3

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Table 3 shows concordance between frequency volume charts and ultrasonography. CMT classified as 54.3% as PMNE whereas ultrasonography classified 84.3% as PMNE. Diagnostic discordance between PMNE and non PMNE noted on CMT and ultrasound were 16 32.4% and 30.757.1% respectively (Table 3).

Uroflowmetry was performed in 26 children. Out of 26 children, the test was valid and reliable in 25 children. Since the voided volume was less than 50 ml in 1 child, it was not considered for analysis. Normal bell-shaped curve was found in 20 children and abnormal curve was recorded in 5 children. The maximum flow rate (Q max) was normal in 24 children and less in 2 children.

On correlation between maximal voided volume by 48-hour bladder diary with functional bladder capacity assessed by ultrasound a weak positive correlation with the Pearson test (r) = 0.255 (p <0.001) was found (Figure 1) and on correlation between maximal voided volume by bladder diary with voided volumes generated on uroflowmetry, a very weak positive correlation with the Pearson test (r) = 0.191 (p =0.026) were noted (Figure 2).

Discussion

The theory of the diminishing FBC can be the cause of primary enuresis is not new and the literature contributes with the controversial datum, some have measured it with voiding diaries (volume and frequency of urination) and a few reports exists with the measurement by ultrasound. The present study found 80.4% of children with PMNE to have low FBC similar to other literature published earlier [13-15].

This study shows a proportion of 1.5:1 with a higher number of males and an average age of 10. Male preponderance, family history, progressive decline with age is concordant with published literature [4,13,16,17]. Majority (60.9%) of PMNE children belonged to the lower middle class as our hospital is a tertiary care government hospital catering a large population belonging to middle class. Majority children belonged to poor socioeconomic class and least in upper middle class [18].

Table 2. Ultrasound KUB (Kidney, ureter and bladder)

Parameters		N (%)
Functional bladder capacity	<65% of EBC	37 (80.4)
	≥ 65% of EBC	9 (19.6)
	>150% of EBC	0
Bladder wall thickness	<3 mm	39 (84.8)
	≥ 3 mm	7 (15.2)
Post void residual urine in ml	≤ 10% of EBC	45 (97.8)
	>10% of EBC	1 (2.2)
	>20 ml	0
Other abnormalities	Normal	46 (100)
	Abnormal	0

Table 3. Label of PMNE and non PMNE by CMT and Ultrasonography.

Parameters	PMNE	Non-PMNE
CMT	25 (54.3%)	21 (45.6%)
Ultrasonography	37 (80.4%)	9 (19.5%)
Both CMT and Ultrasonography	22 (47.8%)	3 (6.5%)
CMT but not ultrasonography	4 (8.6%)	17 (36.9%)
Ultrasonography but not CMT	17 (36.9%)	4 (8.6%)

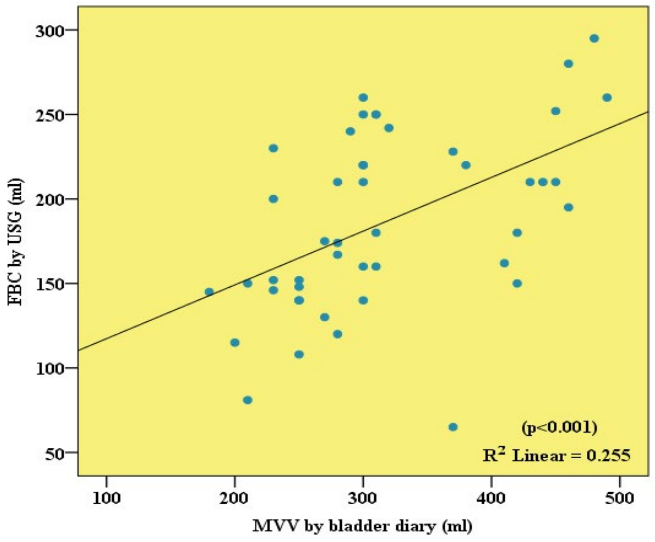

Figure 1. Correlation of MVV by bladder diary and FBC by USG in study population (n=46).

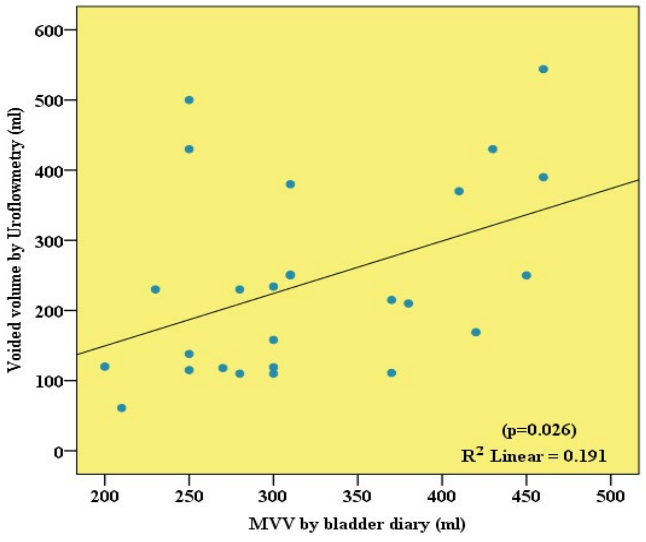

Figure 2. Correlation of MVV by bladder diary and Voided Volume (VV) by uroflowmetry (n=26).

The etiology of enuresis is multifactorial; however, it has been associated with heritage as an important factor. In the study it was found that one third of the children with enuresis had first-degree relatives (parents and brothers) with a history of enuresis, considering it as a factor of risk to develop the disease. Positive family history was noted in other studies as well but these had higher proportion of family members with NE than our study [3,4,19]. Approximately half of the children enrolled in our study had history of snoring similar to published literature [20]. One third of children had associated behavioral problems in the form of inattention and poor school performances were noted by parents.

From CMT, we noted that majority of the children (73.9%) were severe bed wetters. One third of children had increased urinary frequency. Only a few children (13%) had presence of holding maneuvers. A study done in 2017 by Haid B and Tekgül S [2] to differentiate between primary and secondary enuresis revealed the absence of holding maneuvers in primary enuresis while the holding maneuvers, daytime incontinence, dysfunctional voiding symptoms were present in secondary enuresis.

48-hour daytime recording of fluid intake, voided volumes, frequency done by parents showed increased urinary frequency in one third of children in our study but it was the only symptom besides bed wetting, urinalysis was normal and other lower urinary symptoms were absent. Approximately all children had maximal voided volume less than <65% of expected bladder volume suggestive of low functional bladder capacity.

Regarding the bladder wall thickness, which when it is increased (>3 mm), shows detrusor hypertrophy due to a probable obstruction of the urine stream or vesicle dysfunction, majority children with PMNE (84.7%) had normal bladder wall thickness, thus we can deduce that children with primary nocturnal enuresis are free of bladder dysfunction, at least with the ultrasonographic datum similar to few other studies done [6,13].

In this study, non-invasive uroflowmetry examination was done in 26 children due to time bound studies as well as poor compliance by parents to participate in further evaluation of PMNE. Out of 26 children, normal uroflowmetry studies were found in 21 children and abnormal in 5 children.

Only a weak correlation was found between maximal voided volume by 48-hour bladder diary with functional bladder capacity assessed by USG and between maximal voided volume by bladder diary (F/V chart) with voided volumes generated on uroflowmetry. For children with MNE, both bladder diary and uroflowmetry are reliable methods of maximum bladder capacity evaluation. For children with Overactive bladder or Dysfunctional Voiding, both methods may be necessary for accurate evaluation of decreased BC, as F/V chart and uroflowmetry results may not be comparable [21].

The bladder ultrasound is a non-invasive method that can estimate, with precision, the urinary volume and, at any given time, the bladder capacity. It can also guide to diagnosis a probable bladder dysfunction if the amount of residual urine (PVR) is increased and if the bladder wall thickness is also increased.

Our strength in this study was the correlation of maximal voided volumes assessed by bladder diary and to know the children with low Functional Bladder Capacity (FBC). Also, we tried to correlate maximal voided volumes recorded in Bladder diary with FBC by USG and voided volumes in uroflowmetry.

Our study has certain limitations. Being an outpatient clinic-based study, the true community prevalence of enuresis, PMNE or Voiding Disorder cannot be ascertained. Being a questionnaire, a recall bias does exist in CMT. The present study is limited by a small sample size hence limiting the adequate power to draw major statistical conclusions. Uroflowmetry could not be done in all children recruited for study. We used a simplified 2-day diary instead of an extensive one since a more rigorous and longer diary ran a risk of non-compliance and study drop outs. We sacrificed many additional parameters like nocturnal urine outputs for the sake of ease of administration and compliance to look for nocturnal polyuria which help in treatment outcome further.

Conclusion

The study concluded that history taking and bladder diary are sufficient for diagnosis of PMNE but ultrasound and uroflowmetry to be done where facilities are available since abnormal UDS can be seen in PMNE cases too and low functional bladder capacity noted.

Conflict of Interest

The authors declare no conflict of interest.

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None.

Ethical Approval

Institutional board ethics approval was taken for study (IEC/2018)

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