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ORIGINAL PAPER

Clinical characteristics, diagnostic patterns, and treatment strategies in siblings with nocturnal enuresis: an 11-year single-centre experience

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ABSTRACT

Introduction: Nocturnal enuresis (NE) is a common paediatric problem associated with hereditary factors significantly affecting the physical and psychosocial well-being of children and their families. The aim of this retrospective study was an analysis of the medical records of siblings diagnosed with NE at the Department of Paediatric Nephrology, Medical University of Lublin, from January 2013 to December 2023, focusing on clinical characteristics, type concordance, uroflowmetry patterns, and treatment outcomes.

Material and methods: Siblings aged ≥ 5 years with a diagnosis of NE according to the Polish Society of Paediatric Nephrology guidelines were included in the study. The cohort comprised 41 children (18 girls, 23 boys) from 20 families. Clinical data included age at first admission, NE type, lower urinary tract symptoms, uroflowmetry curves, and pharmacotherapy. Treatment response was assessed at follow-up. Descriptive and comparative statistics were applied.

Results: Participants at first admission were aged 5.25–12.67 years (mean 7.88). Monosymptomatic NE and non-monosymptomatic NE (NMNE) were identified in 19 and 22 children, respectively, with type concordance in 12 sibling pairs. Primary NE was diagnosed in 31 children and secondary NE in 7; data were unavailable for 3. Urgency was the predominant symptom among NMNE patients (77%). Uroflowmetry curves were physiological in 75.6% of children, and 77.8% of sibling pairs presented concordant patterns. Oxybutynin was the most commonly used therapeutic agent, both as monotherapy and in combination, with beneficial effects in the majority of patients. Concordant treatment and therapeutic response were observed in 60% of sibling pairs, including differing NE types.

Conclusions: The familial occurrence of NE highlights the role of genetic and shared environmental factors. Its manifestation among siblings warrants consideration of family patterns in understanding the pathophysiology and guiding management. Simultaneously, clinical similarities and differences highlight individual variability in NE phenotypic expression.

KEY WORDS:

nocturnal enuresis, children, siblings.

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INTRODUCTION

Nocturnal enuresis (NE) is one of the most common paediatric problems, affecting approximately 10–16% of 7-year-old children worldwide, with significant psychosocial consequences for affected individuals and their families [1, 2].

It is defined as involuntary urination during sleep in a child who is at least 5 years old or has already completed toilet training [3]. Nocturnal enuresis can be classified as either monosymptomatic (MNE) or non-monosymptomatic (NMNE), and it can be further categorised as primary (PNE) or secondary (SNE) [3, 4].

Monosymptomatic NE is characterised by bedwetting that occurs exclusively during sleep, without the presence of any additional lower urinary tract symptoms (LUTS). It is typically associated with nocturnal detrusor overactivity, which may result in multiple episodes of enuresis throughout the night, or with a nocturnal vasopressin deficiency, leading to bedwetting episodes several hours after sleep onset [3, 5],

In contrast, NMNE is associated with additional LUTS, including daytime urinary incontinence, recurrent urinary tract infections (RUTIs), constipation, urgency, increased voiding frequency, and other manifestations of dysfunctional voiding, such as holding manoeuvres or squatting behaviours [3, 5].

Secondary NE refers to a recurrence of bedwetting after a consecutive period of at least 6 months of nocturnal dryness. In contrast, PNE describes NE in a child who has never maintained a prolonged period of nighttime dryness [3].

Although NE is often approached as an individual issue, it is highly heritable. However, to date, only a few studies have specifically explored NE within sibling sets, limiting understanding of familial phenotypic variability and treatment response [1, 6, 7].

This retrospective study of a single-centre 11-year experience aims to analyse clinical characteristics, NE type concordance, uroflowmetry curve patterns, and treatment outcomes in siblings diagnosed with NE, contributing novel insights into the familial nature of NE.

MATERIAL AND METHODS

The objective of the study was a retrospective analysis of medical records of siblings diagnosed with NE and treated at the Department of Paediatric Nephrology, Medical University of Lublin, between 1 January 2013 and 31 December 2023.

Inclusion criteria encompassed siblings aged 5 or more years diagnosed with NE in accordance with the guidelines of the Polish Society of Paediatric Nephrology [3]. The study cohort comprised 20 sibling groups, totalling 41 children (18 girls and 23 boys). This included 2 sets of twins (one pair of female twins and one pair of male twins), 4 sister pairs, 6 brother pairs, 7 mixed-sex (sister–brother) pairs, and one sibling group consisting of 1 sister and 2 brothers (Table 1).

The clinical data comprised: age at first admission, NE type classification (MNE vs. NMNE; PNE vs. SNE), accompanying LUTS, uroflowmetry curve patterns, and pharmacological therapy.

Uroflowmetry was performed using standard protocols, with curves classified as bell-shaped (BS), high-peak (HP), plateau (PL), or staccato (ST). Pharmacotherapy included oxybutynin, desmopressin, doxazosin, solifenacin, and amitriptyline tailored to individual clinical presentation. Treatment response was assessed during follow-up visits.

Statistical analysis included descriptive statistics (mean, median, standard deviation, percentages) and group comparisons using the Mann-Whitney *U* test, Fisher's exact test, χ^2 test, and one-sided Wilcoxon signed-rank test. Analyses were performed using standard statistical software.

RESULTS

PARTICIPANTS AGE CHARACTERISTICS

The study group consisted of children aged 5.25–16.27 years at the time of initial admission (boys: 5.5–12.5 years; girls: 5.25–12.67 years). The mean age was 7.88 years (boys: 7.62, SD 2.13; girls: 8.21, SD 2.4), and the median age was 7.08 years (boys: 7.00; girls: 8.29) (Figure 1).

Because the assumptions of normality within gender groups and homogeneity of variance were not fulfilled, the Mann-Whitney *U* test for independent samples was applied. The analysis showed that the difference in age at first admission between boys and girls was not statistically significant (U = 234, $p = 0.24$, $r = 0.18$).

ENURESIS TYPE DISTRIBUTION AND CONCORDANCE AMONG SIBLINGS

In the study cohort, NE was classified clinically as MNE or NMNE, and according to onset as PNE or SNE.

Primary NE was diagnosed in 31 children (13 girls, 18 boys) and SNE in 7 children (3 girls, 4 boys), while diagnostic data were unavailable for 3 children (2 girls, 1 boy) residing in institutional care (Figure 2).

Monosymptomatic NE was diagnosed in 19 children (8 girls and 11 boys), and NMNE in 22 (10 girls and 12 boys) (Figure 2). Notably, concordance in enuresis type was observed in 12 sibling sets: MNE in 5 and NMNE in 7. In contrast, the remaining 9 sets exhibited differing types among siblings (Table 1).

Notably, among 12 same-sex sibling pairs, 9 pairs (75%) exhibited the same type of NE: 5 pairs MNE, and 4 pairs NMNE. The remaining 3 pairs (25%) showed discordance in enuresis type, where one sibling had MNE

TABLE 1. Clinical characteristics of the study cohort

Sibling ID	Patient ID	Gender	Age of first admission [years]	NE type	Symptoms	Type – PNE/SNE	Uroflow type	Treatment
S1	S1-A	F	5.25	MNE	–	PNE	BS	OXYB
	S1-B	M	5.5	MNE	–	PNE	BS	OXYB, AMIT
	S1-C	M	12.08	NMNE	DTINC	PNE	PL	OXYB, DESM
S2	S2-TA	F	9.5	NMNE	CONST	PNE	BS	OXYB, DESM
	S2-TB	F	9.5	MNE	–	PNE	BS	OXYB, DESM
S3	S3-TA	M	6.17	MNE	–	PNE	BS	OXYB
	S3-TB	M	6.17	MNE	–	PNE	BS	OXYB
S4	S4-A	F	9.08	MNE	–	PNE	HP	OXYB, DESM
	S4-B	F	6.08	MNE	–	PNE	HP	OXYB
S5	S5-A	F	8.83	MNE	–	UNK	HP, ST	OXYB, DESM
	S5-B	F	6.25	MNE	–	UNK	BS	DESM
S6	S6-A	F	6.5	NMNE	FRQ	PNE	BS	OXYB, DESM
	S6-B	F	5.5	NMNE	URG, RUTIs, CONST	SNE	BS	OXYB, DXN, ABP, SOLI, SENN
S7	S7-A	F	12.67	NMNE	URG	PNE	UNK	OXYB
	S7-B	F	10.5	NMNE	URG	PNE	BS	OXYB
S8	S8-A	M	5.75	MNE	–	PNE	BS	OXYB
	S8-B	M	8	NMNE	URG, RUTIs	PNE	BS	OXYB, ABP
S9	S9-A	M	7.75	NMNE	URG	PNE	BS	OXYB, DESM
	S9-B	M	5.83	NMNE	URG	PNE	BS	OXYB, DESM
S10	S10-A	M	9.92	MNE	–	UNK	BS	OXYB, DESM, SOLI
	S10-B	M	6.08	MNE	–	SNE	BS	OXYB
S11	S11-A	M	7.75	MNE	–	PNE	PL	OXYB
	S11-B	M	11.17	MNE	–	PNE	BS	OXYB
S12	S12-A	M	10.33	NMNE	URG	PNE	BS	OXYB, DESM
	S12-B	M	7.08	MNE	–	PNE	BS	OXYB, DESM
S13	S13-A	M	6.5	NMNE	URG	PNE	BS	OXYB, DESM
	S13-B	M	6.42	NMNE	FRQ	PNE	BS	OXYB
S14	S14-A	M	8.08	NMNE	CONST, URG	SNE	BS	OXYB, DESM, MGOL
	S14-B	F	6.5	NMNE	URG	SNE	BS	OXYB, DESM
S15	S15-A	F	5.92	NMNE	URG	PNE	BS	OXYB, DESM
	S15-B	M	5.83	NMNE	URG	PNE	BS	OXYB, DESM
S16	S16-A	F	7.75	NMNE	URG	PNE	BS	OXYB, DESM, AMIT
	S16-B	M	5.5	NMNE	URG	PNE	UNK	OXYB
S17	S17-A	M	7.58	MNE	–	PNE	PL	OXYB, AMIT
	S17-B	F	10.75	NMNE	FRQ, DTINC	PNE	PL	OXYB
S18	S18-A	F	12.58	MNE	–	PNE	BS	OXYB
	S18-B	M	7	NMNE	URG	PNE	BS	OXYB, MGOL
S19	S19-A	M	12.5	MNE	–	SNE	BS	OXYB, DESM
	S19-B	F	5.67	NMNE	URG	PNE	HP	OXYB, DESM
S20	S20-A	F	8.92	MNE	–	SNE	BS	OXYB
	S20-B	M	6.25	NMNE	URG	SNE	BS	OXYB

A, B, C – patient numbering, ABP – antibacterial prophylaxis, AMIT – amitriptyline, BS – bell-shaped/normal (uroflowmetry curve), CONST – constipation, DESM – desmopressin, DTINC – daytime incontinence, DXN – doxazosin, F – female, FRQ – frequency, HP – high-peak (uroflowmetry curve), INT – interrupted (uroflowmetry curve), MGOL – macrogol, M – male, MNE – monosymptomatic nocturnal enuresis, NMNE – non-monosymptomatic nocturnal enuresis, OXYB – oxybutynin, PNE – primary nocturnal enuresis, PL – plateau (uroflowmetry curve), RUTIs – recurrent urinary tract infections, S – sibling numbering, SENN –Sennae folium, SNE – secondary nocturnal enuresis, SOLI – solifenacin, ST – staccato (uroflowmetry curve), TA, TB – twin siblings numbering, UNK – unknown, URG – urgency

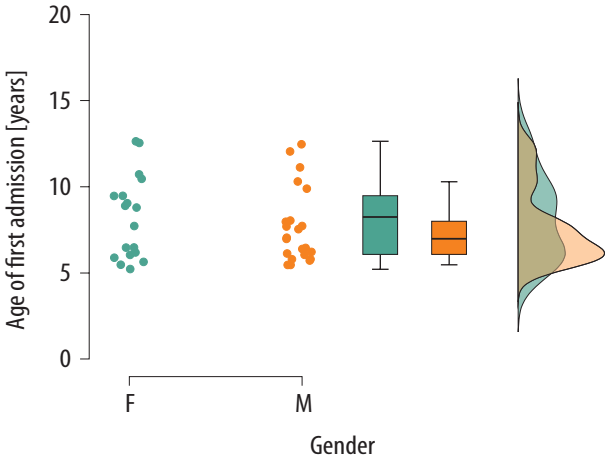

FIGURE 1. Raincloud plot showing the distribution of age at first admission in the study cohort by sex

F – female, M – male

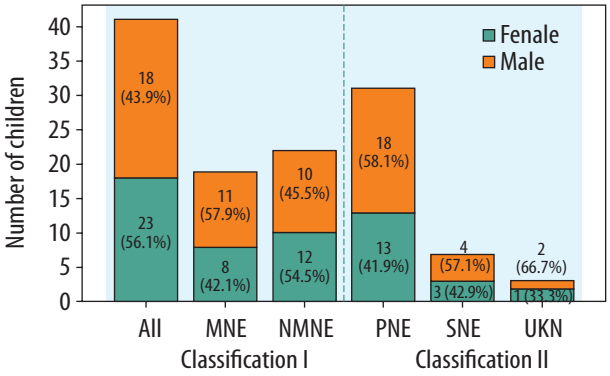

FIGURE 2. Distribution of the study cohort by two classifications and sex

All – the total population, UKN – unknown
Classification I includes monosymptomatic nocturnal enuresis (NE) and non-monosymptomatic NE. Classification II includes primary NE (PNE) and secondary NE (SNE) (unknown: cases where PNE and SNE could not be distinguished).
Bars represent absolute counts by sex; percentages indicate the proportion of each sex within the representative bar.

TABLE 2. Distribution of accompanying symptoms in siblings with non-monosymptomatic nocturnal enuresis

Symptoms	Overall	Male	Female
URG	14	8	6
URG, RUTIs	1	1	0
URG, CONST	1	1	0
URG, RUTIs, CONST	1	1	0
DTINC	1	1	0
CONST	1	0	1
FRQ	2	1	1
FRQ, DTINC	1	0	1

CONST – constipation, DTINC – daytime incontinence, FRQ – frequency, RUTIs – recurrent urinary tract infections, URG – urgency

TABLE 3. Distribution of uroflowmetry curve patterns in the study group

Uroflow curve patterns	Overall	Male	Female
BS	31	19	12
HP	3	0	3
PL	4	3	1
HP, ST	1	0	0
UNK	2	1	1

BS – bell-shaped/ normal, HP – high-peak, PL – plateau, ST –staccato, UNK – unknown

and the other NMNE. In contrast, among 7 opposite-sex sibling pairs, 3 pairs (42.9%) had the same enuresis type (all NMNE), and 4 pairs (57.1%) were discordant. Additionally, one family with 3 siblings demonstrated variability in enuresis type: 2 children had MNE, and one child had NMNE.

Given the limited subgroup sizes, Fisher's exact test was applied. The resulting p-value ($p = 0.18$) provides no evidence of a statistically significant increase in concordance of enuresis types among same-sex sibling pairs. Nevertheless, the possibility of such an association cannot be excluded and may emerge in studies with larger cohorts.

SYMPTOM PROFILE OF CHILDREN DIAGNOSED WITH NON-MONOSYMPTOMATIC NOCTURNAL ENURESIS

Among patients with NMNE, urgency was the most prevalent symptom, reported in 17 children (77%). In 3 male patients, urgency co-occurred with additional LUTS.

Although urgency was more prevalent in boys (84.6%) than in girls (66.6%) (Tables 1, 2), the χ^2 test indicated that this difference was not statistically significant ($\chi^2(1, 41) = 0.09$, $p = 0.77$).

Notably, 14 of the 22 children (63.6%) diagnosed with NMNE belonged to 7 sibling pairs, comprising 2 pairs of brothers, 2 pairs of sisters, and 3 mixed-sex pairs.

Simultaneously, the siblings of the remaining 8 children presented with MNE, comprising 2 pairs of brothers, 1 pair of sisters, 4 mixed-sex pairs, and 1 mixed-sex trio (Table 1).

DISTRIBUTION OF UROFLOWMETRY CURVE PATTERNS AND CONCORDANCE AMONG SIBLINGS

Physiological, BS uroflowmetry curves were observed in the majority of patients (75.6%), including 82.6% of boys and 66.7% of girls. Abnormal patterns: HP, PL, and a combined HP and ST were identified in 3, 4, and 1 patient(s), respectively. In 2 cases, uroflowmetry could not be reliably assessed due to the patients' non-compliance (Tables 1, 3).

As many as 14 sibling pairs exhibited the same uroflowmetry curve pattern, whereas in 4 sibling sets the children showed discordant curve shapes (including 1 sibling trio, 1 pair of brothers, 1 pair of sisters, and

1 mixed-gender pair). In 2 additional sibling pairs, uroflowmetry could not be performed in 1 of the children due to a lack of cooperation (Table 1). Among 18 sibling sets with available uroflowmetry data, 14 (77.8%) demonstrated concordant flow curve patterns, whereas 4 (22.2%) were discordant.

Based on Fisher's exact test with Monte Carlo simulation, no statistically significant association was observed; however, a trend toward higher concordance of urethral flow curve patterns among siblings was noted ($p = 0.51$).

TREATMENT PATTERNS AND THERAPEUTIC RESPONSE IN SIBLINGS

Oxybutynin was the most frequently used pharmacological treatment, administered to 40 children (23 boys and 17 girls). In 36 children, oxybutynin was introduced during the first admission, with improvement in 33 patients. Interestingly, desmopressin was administered to fewer patients than oxybutynin, i.e. only to 20 children (10 boys and 10 girls), and in just 3 cases it was prescribed during the first visit.

Monotherapy with oxybutynin was effective in 43.9% of children (47.8% in boys and 38.9% in girls). In comparison, desmopressin alone was sufficient in only 1 female patient. Therapy with both oxybutynin and desmopressin was necessary in 41.5% of cases (39.1% in boys and 44.4% in girls) due to an insufficient response to monotherapy. Other pharmacotherapy, including amitriptyline, doxazosin, and solifenacin, was used in more complex and treatment-resistant cases (Tables 1, 4).

The one-sided Wilcoxon signed-rank test for dependent samples demonstrated a statistically significant predominance of oxybutynin use compared with desmopressin and other medications in the study cohort ($V = 69$, $p < 0.05$).

Notably, in 12 (60%) sibling pairs, comprising 5 brother pairs, 2 sister pairs, and 5 mixed-sex pairs, the same treatment regimen was administered, yielding a favourable and consistent therapeutic response in both children. Interestingly, in half of these sibling pairs, despite differing enuresis types (MNE vs. NMNE), comparable therapeutic responses to the prescribed treatment were observed (Table 1).

Additionally, children with concomitant constipation were treated with macrogols and Sennae folium, while those with RUTIs received prophylactic doses of furazidine or sulfamethoxazole with trimethoprim (Table 1).

Although non-pharmacological management, including motivational therapy for NE, was recommended for all siblings, it proved insufficient as a standalone treatment.

TABLE 4. Pharmacotherapy in the presented group of siblings

Pharmacotherapy	Overall	Male	Female
OXYB	18	11	7
DESM	1	0	1
OXYB, DESM	17	9	8
OXYB, AMI	2	2	0
OXYB, DESM, AMI	1	0	1
OXYB, DXN, SOLI	1	0	1
OXYB, DESM, SOLI	1	1	0

AMI – amitriptyline, DESM – desmopressin, DXN – doxazosin, OXYB – oxybutynin, SOLI – solifenacin

DISCUSSION

Nocturnal enuresis is a distressing and often underrecognised public health issue, causing significant emotional burden for affected children and their families [8]. Recently, Adisu *et al.* [9] conducted a systematic review and meta-analysis of 128 studies, including 445,242 individuals from 39 countries, and reported an overall NE prevalence of 7.2% among children and adolescents. Nocturnal enuresis decreases with age and affects approximately 0.5–1% of adults [1]. Notably, the prevalence of NE varies across regions and is influenced by socioeconomic factors [10].

Epidemiological data indicate a higher prevalence of NE in boys compared with girls, whereas affected boys more often exhibit a poorer response to treatment [11]. Interestingly, all candidate "enuresis genes" are located on autosomes. Given the lack of clear sex differences in nocturnal polyuria and nocturnal detrusor overactivity, it has been hypothesised that girls may be protected by more efficient arousal mechanisms. Consequently, girls might exhibit a better response to alarm-based therapy [1]. Consistent with these findings, boys predominated in our study group of siblings with NE, comprising 56.1% of participants. Due to the retrospective design of the study, data regarding the presence of other, non-enuretic siblings and their sex were not available.

Mild LUTS are common in children with NE, affecting up to two-thirds of cases, and their identification and management are crucial for successful treatment [5]. Recently, in a pilot retrospective study of 629 patients with NE, Ata *et al.* [12] identified NMNE in 57.7% of cases, with a slight predominance of females (54.8%). In line with these observations, our study found that siblings with NMNE predominated, comprising 53.7% of the cohort, highlighting the clinical relevance of addressing LUTS in this population. However, although girls accounted for approximately 45.5%, the small size of the study group does not allow this difference to be meaningfully interpreted.

Notably, in the general paediatric population, PNE is twice as common as SNE. Children with SNE may have a precipitating factor such as an unusually stressful event (e.g. birth of a sibling, death of a family member, parental divorce, school trauma, or sexual abuse) [11]. In the study cohort of siblings, SNE was diagnosed in only 17%. Due to the retrospective nature of the study, no information was available regarding potential factors contributing to

the development of SNE. Although children with enuretic siblings share the same household, such a significant predominance of PNE in the study cohort suggests that genetic and developmental factors may play a stronger role than environmental influences.

Currently, NE is considered a polygenic disorder in which genetic susceptibility is combined with environmental and developmental influences. The inheritance of NE appears to follow an autosomal dominant pattern in many families, with varying penetrance. This suggests that one copy of a faulty gene may be sufficient to predispose an individual to the condition, although not all children with genetic risk will develop NE. The variable expression and incomplete penetrance are characteristics of complex genetic disorders, and further research is required to understand how different genetic variants and environmental factors interact to influence the risk of NE [1]. To date, several genetic loci have been identified as potentially associated with NE. These loci are often involved in the regulation of bladder function, urine production, and the circadian rhythm of urine output. Consequently, patients with NE often have a functional bladder disorder and/or a maturational delay in nocturnal arginine vasopressin secretion [13]. Jørgensen *et al.* [1] performed a genome-wide association study of NE in iPSYCH2012, a large Danish population-based case cohort established to investigate mental disorders. The genome-wide association study included 3882 NE cases and 31,073 controls. They found two loci at chromosome 6 and chromosome 13 significantly associated with NE.

Recent literature emphasises that a positive family history of NE significantly increases the risk of enuresis in relatives [10]. The incidence of enuresis is 15% among children from families with no history of NE, compared to 44% and 77% in patients with one or both parents affected, respectively [14, 15]. Von Gontard *et al.* [4] identified familial patterns in a large, representative sample of more than 8000 children enrolled in the prospective Avon Longitudinal Study of Parents and Children. They observed a stronger link between maternal and childhood enuresis than between paternal cases and affected children. In our retrospective study, the documentation regarding bedwetting in the participants' parents was fragmentary and incomplete, making it impossible to assess any potential association with parental enuresis.

While much is known about the familial occurrence of enuresis in relation to parents, relatively few studies have investigated its prevalence and concordance among siblings. Bakwin [16], in his historical twin studies from 1971, compared the incidence of enuresis in monozygotic and same-sex dizygotic twins, in which NE was present in 146 of 676 twin children after their fourth birthday. Monozygotic twins were concordant for enuresis about twice as frequently as dizygotic twins.

In another study, Schaumburg *et al.* [17] assessed phenotypic characteristics in 3 large families with hereditary NE, including 98 living members, of whom 34 were affected. Notably, the clinical phenotype, encompassing bladder capacity, nighttime urine production, and response to desmopressin, was heterogeneous both between and within families. Moreover, there were no differences between affected and unaffected family members for night-time urine production. Our dataset included only 2 twin pairs, monozygotic and dizygotic. Remarkably, 12 of 20 sibling sets in our cohort showed concordance in NE type (MNE or NMNE), while 9 were discordant, i.e. with one sibling presenting with MNE and the other with NMNE. This partial discordance is consistent with findings reported by Schaumburg *et al.* [17]. Notably, a higher concordance in the type of NE was observed among same-sex sibling pairs (75%) compared with opposite-sex pairs (42.9%). However, this difference did not reach statistical significance.

Genes responsible for NE are not directly related to the presence of PNE vs. SNE, nor MNE vs. NMNE. Nevertheless, there might be genetically determined differences in nighttime diuresis and/or bladder capacity [17]. These results support the theory that while genetics plays a strong role, NE is multifactorial. Epigenetic modifications, which are changes in gene expression due to environmental factors, may influence the expression of genes related to NE. This highlights the complex interaction between genetics and environment in the pathophysiology of NE [9]. Siblings with NE share a similar environment, which, alongside genetic predisposition, may modulate the clinical course of the disorder. Nevertheless, precisely delineating the relative contributions of genetic, epigenetic, and environmental factors to the patients' phenotype remains challenging, and addressing this issue requires well-designed population-based studies.

The majority of children with NE exhibit normal uroflow patterns, particularly in cases of MNE. This finding was confirmed in our study, in which over 75% of children exhibited normal BS uroflow curves. Most sibling pairs displayed the same curve type, with only 20% of patients showing differing curve patterns within the sibling sets. Prgomet *et al.* [18] described clinical characteristics and bladder assessment in children with NMNE in the coastal region of Croatia. The uroflow pattern in children with NMNE was abnormal in 42% of all children, more often in children with SNE than in children with PNE. Conversely, in our study, 77.3% of children with NMNE demonstrated normal uroflow curves. Only 3 patients exhibited abnormal patterns, while their siblings consistently displayed normal curves. Uroflowmetry was not performed in 2 children. Notably, in the MNE group, 73.7% of children showed normal uroflow curves. Abnormal patterns were observed only in 1 sibling pair and 3 children whose siblings exhibited normal curves, underscoring variability in bladder function even within families. Only 17% of participants exhibited SNE, including 2 sibling pairs. The remaining 3 children had

siblings with PNE. Interestingly, all patients with SNE demonstrated normal uroflowmetry curves; however, we consider that the study group was too small to allow for generalisation of these results or to regard them as representative.

Recently, Cammisa *et al.* [19] conducted a systematic review of studies published from 2000 to 2024, assessing the treatment of NE. Non-pharmacological interventions offer effective, safe options for managing this common paediatric problem, particularly when used in combination. Enuresis alarm therapy, considered the first-line therapy, has demonstrated success rates of 50–70% in patients [20]. The treatment aims to replace NE with controlled nighttime voiding (nocturia). When the first drops of urine appear, the enuresis alarm awakens the child, who should then go to the bathroom and consciously void [3]. However, many families find the use of the alarm too disruptive to established sleep routines and too demanding in terms of energy and time. Consequently, the dropout rate in clinical trials is approximately 30% [5].

Surprisingly, in our study, the medical records contained no information regarding the use of an enuresis alarm, suggesting either that it was not employed or that relevant data were unavailable. This management approach may reflect the centre's experience and preferences, or parental choice. Another explanation may also involve the challenges associated with the simultaneous use of enuresis alarms in both siblings, particularly when they share the same bedroom. Activation of the alarm could awaken not only the concerned patients but also their siblings, potentially compromising the effectiveness of the therapy.

Pharmacological management of NE primarily involves the use of desmopressin and anticholinergics [11, 19]. Desmopressin remains the first-line pharmacological treatment for NE, particularly recommended in cases of nocturnal polyuria [3]. Success rates of desmopressin treatment for enuresis reported by Cammisa *et al.* have ranged from 10–65%, with relapse occurring in up to 80% of patients after discontinuation of therapy [19]. Surprisingly, in our study, only one patient achieved successful treatment with desmopressin monotherapy. In contrast, monotherapy with oxybutynin was effective in nearly 44% of patients. Such a high response rate may be attributed to nocturnal detrusor overactivity in the described siblings.

Notably, a subset of children with nocturnal polyuria co-exhibit detrusor overactivity, and optimal therapeutic outcomes may be achieved only through combination therapy with desmopressin and anticholinergics. Dual therapy has consistently demonstrated superior efficacy and more rapid clinical responses compared to monotherapy [19, 21]. Recently, these findings have been reinforced by the first prospective, randomised controlled trial conducted by Shim *et al.* [22], which reported higher response rates and lower relapse rates with desmopressin plus anticholinergic combination therapy relative to desmopressin monotherapy when used as first-line treatment in children with primary MNE. Consistent with these reports, dual therapy with desmopressin and oxybutynin achieved efficacy in 41.5% of patients in our study.

Imipramine, a tricyclic antidepressant, is a second-line option for NE, benefiting up to 50% of therapy-resistant cases [23]. Because imipramine is unavailable in Poland, 3 children with treatment-resistant NE in our study received amitriptyline, another tricyclic antidepressant with a comparable pharmacological profile, resulting in clinical improvement.

Interestingly, in the majority of sibling pairs, the same treatment regimen was implemented and proved effective, yielding consistent responses, independent of enuresis type (MNE vs. NMNE) and its concordance within the sibling pairs. Sibling pairs exhibiting different enuresis types demonstrated similar treatment responses, particularly to oxybutynin and desmopressin. These findings, analogous to the study by Schaumburg *et al.* [17], suggest that phenotypic heterogeneity in enuretic families does not necessarily preclude comparable therapeutic pathways.

Importantly, our research provides novel insights by specifically examining the response to pharmacological interventions in sibling pairs, highlighting the potential role of familial or genetic factors in treatment outcomes and representing one of the first studies to address NE management in this unique patient population.

Children with NE often experience low self-esteem, shame, and social withdrawal, while their parents report feelings of helplessness and frustration [9, 24]. Managing NE in multiple siblings can disrupt family routines, elevate parental stress, and affect sibling relationships; however, these aspects remain underexplored. In our cohort, only 5 children were documented as receiving psychological support, highlighting the need to increase awareness among families and healthcare providers and improve access to such care.

Despite the clinical significance of NE, research on families with multiple affected children is limited, leaving gaps in understanding the specific challenges they face. Future prospective multicentre studies with standardised clinical protocols are needed to confirm these findings, assess long-term treatment outcomes, examine the impact of psychological interventions, and clarify the genetic and environmental factors contributing to NE among siblings.

LIMITATIONS

This study has several limitations that should be considered when interpreting the findings. First, its retrospective design and relatively small study group limit both the generalisability of the results and the statistical power to detect subtle differences between subgroups. Moreover, due to incomplete clinical documentation, other important data, such as parental history of enuresis, presence

of nocturnal polyuria, bladder capacity, treatment adherence, and long-term outcomes, were not consistently available. Finally, the study's single-centre setting may have contributed to the limited sample size and introduced institutional practice patterns that could influence the observed outcomes. Consequently, this study may be considered a pilot investigation, providing a foundation for the design and implementation of a subsequent prospective study with a rigorously defined clinical protocol.

CONCLUSIONS

Nocturnal enuresis remains a prevalent and clinically significant paediatric condition, imposing substantial emotional and psychosocial burdens on affected children and their families. Research specifically addressing sibling populations is limited, but such studies are essential for understanding familial patterns, genetic predisposition, and treatment responses. Our retrospective 11-year analysis of sibling sets demonstrated partial concordance in the clinical characteristics of NE, supporting a strong familial or genetic influence while highlighting the multifactorial nature of the disorder. Pharmacological interventions, including desmopressin, oxybutynin, and combination therapy, were generally effective, with comparable outcomes across different NE types and sibling concordance patterns. These findings underscore the importance of addressing both the clinical and psychosocial dimensions of NE in families with multiple affected children.

DISCLOSURES

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4. Conflicts of interest: None.

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