Original Article

Medical Comorbidity of Nocturnal Enuresis in Children

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Abstract

Introduction: The purpose of this study was to evaluate the characteristics of patients with nocturnal enuresis (NE). **Methods:** We enrolled 403 children with NE referred to the Services of Pediatrics, Campus Bio-Medico University Hospital of Rome between June 2013 and July 2018. We excluded 2 children, respectively, with renal agenesis and chromosomopathy. **Results:** Of the 401 patients, 101 girls (25.2%) and 300 boys (74.8%), aged 5–16 years; mean age at first visit 8.8 ± 2.44 years. During the physical examination, we asked the patients and their parents specific questions to identify signs and symptoms of voiding disorders and comorbid conditions. In addition, we evaluated family history and behavioral characteristics of patients. In this study, NE was heredity in the 31.2% of cases. We found urogenital abnormalities in 15.7% of cases, constipation in 14.5% of cases, innocence heart murmur in 21.4% of cases and parasomnias in a good percentage of cases, especially snoring (13.7%), restless sleep (5.7%), somniloquy (23.7%) and bruxism (14.7%). **Conclusions:** Our experience demonstrates that there are a lot of comorbidities that are associated with NE and can influence the prognosis and the response to the therapy in these children.

Keywords: *Children, comorbidities, nocturnal enuresis*

Introduction

Nocturnal enuresis (NE), commonly known as bed wetting, is one of the most frequent pediatric disorder. According to the International Children's Continence Society, NE is defined as intermittent urinary incontinence while asleep, at least once a week and during a period of minimum three months, in children >5 years.[1] NE is considered mono-symptomatic (MNE) if it occurs without any other lower urinary tract symptoms (LUTS) and without a history of bladder dysfunction. NE in children with any other LUTS and with a history of bladder dysfunction is diagnosed as non-MNE NE (N-MNE). When MNE is diagnosed in children who have never achieved nocturnal urinary continence and have never been dry at night, it is defined as primary MNE (PMNE). Otherwise, secondary MNE (SMNE) describes children who experienced a previous dry period of at least 6 months and it is usually secondary to psychological stress or organic causes such as urinary tract infections, obstructive sleep hypoventilation, diabetes mellitus/insipidus, and neurogenic bladder. NE is a multifactorial disorder caused by three related mechanisms: nocturnal polyuria, bladder overactivity, and sleep disorder, which could be of urological, neurological, genetic, or psychological origin.[2,3]

Several studies have demonstrated the association between NE and specific comorbidities such as sleep disorders, encopresis, headache, and psychiatric and behavioral disorders.[4,5]

The purpose of this study was to evaluate the characteristics of enuretic patients and their natural history in order to enhance the knowledge of NE and its comorbidities.

Methods

We enrolled 403 children with NE referred to the Services of Pediatrics, Campus Bio-Medico University Hospital of Rome between June 2013 and July 2018. During the physical examination, we asked the patients and their parents, specific questions to identify signs and symptoms of voiding disorders and comorbid conditions. In addition, we evaluated family history and behavioral characteristics of patients. To diagnose constipation, we used the Rome III criteria. We excluded 2 children respectively with renal agenesis and chromosomopathy and we included

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401 patients, 101 girls (25.2%) and 300 boys (74.8%), aged 5–16 years; mean age at first visit being 8.8 ± 2.44 years. All the children included in our study had a good academic performance and they had not been exposed to any stress factor in the family and in the school environment.

Results

Of the 401 eligible patients, there were 327 (81.5%) patients with MNE [242 (74%) boys with mean age at first examination 9.1 years and 85 (26%) girls with mean age at first examination 7.8 years]; 74 (18.5%) children presented N-MNE [58/74 boys (78.4%) with mean age at first examination 9 years and 16 girls (21.6%) with mean age at first examination 8.4 years]; among the children with MNE, 322/327 (98.5%) had PMNE and 5/327 (1.5%) were diagnosed with SMNE.

Results are summarized in Tables 1-4. An association between parental and child NE was found in 125/401 (31.2%): 53.6% (67/125 children) had paternal heredity, 46.4% (58/125) in the maternal line, and 11.2% (14/125) had both paternal and maternal inheritance. Among children with NE, 180/401 (44.9%) had deep sleep, 55/401 (13.7%) snored, 23/401 (5.7%) had restless sleep, 12/401 (3%) had sleep apnea, 95/401 (23.7%) had somniloquy, and 59/401 (14.7%) had bruxism [Table 1].

Children suffered from headaches were 21/401 (5.2%): 4 suffered from tension-type headache (TTH) and 17 had benign migraine associated with familiarity. Considering family history, 112 (27.3%) had family history of headache: 37/401 (9.2%) had a paternal family history of headache, 55/401 (13.7%) had a maternal family history of headache, and 20/401 (5%) had someone in their family between sisters, brothers, uncles, and grandparents who suffered from headaches [Table 2].

Of the males, 47/300 (15.7%) had urogenital abnormalities, in particular 28/47 (59.6%) children had balanopreputial adhesions [Table 3].

Neurobehavioral conditions were associated in 23/401 (5.7%) and 12/401 children (3%) had a poor academic achievement. Cutaneous manifestations of spinal dysraphism such as pilonidal dimple, single and deflected intergluteal cleft, or double intergluteal cleft were found in 21/401 (5.2%) patients. Encopresis was found in 12/401 (3%) children and 58/401 (14.5%) suffered from constipation. About 31/401 (7.7%) children had polythelia and other 10/401 (2.5%) had hypertrophic tonsils or previous tonsillectomy. Lastly, a significant percentage of children presented innocent heart murmur (86/401 – 21.4%) [Table 4].

Discussion and Conclusions

In our study, children with MNE have paternal heredity in 15% of cases (49/327), maternal heredity in 9.8% of

Table 1: Comorbidities in nocturnal enuresis: sleep disorders and family history of nocturnal enuresis.

	MNE						N-MNE				MNE + N-MNE	
	Boys	Percentage of the total of boys with MNE (242 boys)	Girls	Percentage of the total of girls with MNE (85 girls)	Total	Percentage of the total of children with MNE (327)	Boys	Percentage of the total of boys with N-MNE (58 boys)	Girls	Percentage of the total of girls with N-MNE (16 girls)	Total	Percentage of the total of children with N-MNE (74)	Total	Percentage of the total of children with enuresis
Sleep disorders														
Restless sleep	8	3.3%	2	2.4%	10	3.1%	13	22.4%	0	0.0%	13	17.6%	23	5.7%
Deep sleep	92	38.0%	26	30.6%	118	36.1%	47	81.0%	15	93.8%	62	83.8%	180	44.9%
Snoring	26	10.7%	10	11.8%	36	11.0%	14	24.1%	5	31.3%	19	25.7%	55	13.7%
Sleep apnea	5	2.1%	0	0.0%	5	1.5%	5	8.6%	2	12.5%	7	9.5%	12	3.0%
Somniloquy	41	16.9%	17	20.0%	58	17.7%	25	43.1%	12	75.0%	37	50.0%	95	23.7%
Bruxism	31	12.8%	7	8.2%	38	11.6%	17	29.3%	4	25.0%	21	28.4%	59	14.7%
Family history of nocturnal enuresis														
Paternal	40	16.5%	9	10.6%	49	15.0%	13	22.4%	5	31.3%	18	24.3%	67	16.7%
Maternal	28	11.6%	4	4.7%	32	9.8%	19	32.8%	7	43.8%	26	35.1%	58	14.5%
Paternal and maternal	10	4.1%	1	1.2%	11	3.4%	2	3.4%	1	6.3%	3	4.1%	14	3.5%

MNE: Monosymptomatic nocturnal enuresis, N-MNE: Non-monosymptomatic nocturnal enuresis

Table 2: Comorbidities in nocturnal enuresis: headaches

	MNE						N-MNE						MNE + N-MNE	
	Boys	Percentage of the total of boys with MNE (242 boys)	Girls	Percentage of the total of girls with MNE (85 girls)	Total	Percentage of the total of children with MNE (327)	Boys	Percentage of the total of boys with N-MNE (58 boys)	Girls	Percentage of the total of girls with N-MNE (16 girls)	Total	Percentage of the total of children with N-MNE (74)	Total	Percentage of the total of children with enuresis
Number of patients	242		85		327 (81.5%)	100.0%	58		16		74 (18.4%)	100.0%	401	100.0%
Headache														
Episodes of headaches in the patient	2	0.8%	2	2.4%	4	1.2%	0	0.0%	0	0.0%	0	0.0%	4	1.0%
Paternal history of headaches	8	3.3%	0	0.0%	8	2.4%	1	1.7%	0	0.0%	1	1.4%	9	2.2%
Maternal history of headaches	7	2.9%	4	4.7%	11	3.4%	1	1.7%	0	0.0%	1	1.4%	12	3.0%
Paternal and maternal history of headaches	4	1.7%	0	0.0%	4	1.2%	1	1.7%	0	0.0%	1	1.4%	5	1.2%
Family history of headaches	0	0.0%	1	1.2%	1	0.3%	0	0.0%	0	0.0%	0	0.0%	1	0.2%
Migraine														
Episodes of migraine in the patient	12	5.0%	3	3.5%	15	4.6%	2	3.4%	0	0.0%	2	2.7%	17	4.2%
Paternal history of migraine	17	7.0%	9	10.6%	26	8.0%	2	3.4%	0	0.0%	2	2.7%	28	7.0%
Maternal history of migraine	27	11.2%	11	12.9%	38	11.6%	5	8.6%	0	0.0%	5	6.8%	43	10.7%
Paternal and maternal history of migraine	4	1.7%	1	1.2%	5	1.5%	0	0.0%	0	0.0%	0	0.0%	5	1.2%
Family history of migraine	14	5.8%	3	3.5%	17	5.2%	2	3.4%	0	0.0%	2	2.7%	19	4.7%
Headache and migraine														
Episodes of headache/ migraine in the patient	14	5.8%	5	5.9%	19	5.8%	2	3.4%	0	0.0%	2	2.7%	21	5.2%
Paternal history of headache/ migraine	25	10.3%	9	10.6%	34	10.4%	3	5.2%	0	0.0%	3	4.1%	37	9.2%
Maternal history of headache/migraine	34	14.0%	15	17.6%	49	15.0%	6	10.3%	0	0.0%	6	8.1%	55	13.7%
Both paternal and maternal history of headache/migraine	8	3.3%	1	1.2%	9	2.8%	1	1.7%	0	0.0%	1	1.4%	10	2.5%
Family history of headache/ migraine	14	5.8%	4	4.7%	18	5.5%	2	3.4%	0	0.0%	2	2.7%	20	5.0%

MNE: Monosymptomatic nocturnal enuresis, N-MNE: Non-monosymptomatic nocturnal enuresis

Table 3: Comorbidities in nocturnal enuresis: urogenital abnormalities

	MNE						N-MNE						MNE + N-MNE	
	Boys	Percentage of the total of boys with MNE (242 boys)	Girls	Percentage of the total of girls with MNE (85 girls)	Total	Percentage of the total of children with MNE (327)	Boys	Percentage of the total of boys with N-MNE (58 boys)	Girls	Percentage of the total of girls with N-MNE (16 girls)	Total	Percentage of the total of children with N-MNE (74)	Total	Percentage of the total of children with enuresis
Urogenital abnormalities	23	9.5%	2	2.4%	25	7.6%	24	41.4%	1	6.3%	25	33.8%	50	12.5%
Hyperemia or genital secretions	1	0.4%	2	2.4%	3	0.9%	2	3.4%	1	6.3%	3	4.1%	6	1.5%
Preputial phimosis	2	0.8%	0	0.0%	2	0.6%	3	5.2%	0	0.0%	3	4.1%	5	1.2%
Short preputial frenum	1	0.4%	0	0.0%	1	0.3%	0	0.0%	0	0.0%	0	0.0%	1	0.2%
Cleft of the prepuce	1	0.4%	0	0.0%	1	0.3%	0	0.0%	0	0.0%	0	0.0%	1	0.2%
Hypospadias	2	0.8%	0	0.0%	2	0.6%	2	3.4%	0	0.0%	2	2.7%	4	1.0%
Retractable testicles	1	0.4%	0	0.0%	1	0.3%	1	1.7%	0	0.0%	1	1.4%	2	0.5%
Hydrocele	0	0.0%	0	0.0%	0	0.0%	2	3.4%	0	0.0%	2	2.7%	2	0.5%
Balanopreputial adhesions	14	5.8%	0	0.0%	14	4.3%	14	24.1%	0	0.0%	14	18.9%	28	7.0%
Orchidopexy	1	0.4%	0	0.0%	1	0.3%	0	0.0%	0	0.0%	0	0.0%	1	0.2%
UTI	0	0.0%	0	0.0%	0	0.0%	2	3.4%	0	0.0%	2	2.7%	2	0.5%
Dysfunctional voiding	0	0.0%	0	0.0%	0	0.0%	2	3.4%	0	0.0%	2	2.7%	2	0.5%

MNE: Monosymptomatic nocturnal enuresis, N-MNE: Non-monosymptomatic nocturnal enuresis, UTI: Urinary tract infections

Table 4: Comorbidities in nocturnal enuresis: neurobehavioral alterations, spina bifida occulta, gastrointestinal system, cardiovascular system, and others

	MNE						N-MNE						MNE + N-MNE	
	Boys	Percentage of the total of boys with MNE (242 boys)	Girls	Percentage of the total of girls with MNE (85 girls)	Total	Percentage of the total of children with MNE (327)	Boys	Percentage of the total of boys with N-MNE (58 boys)	Girls	Percentage of the total of girls with N-MNE (16 girls)	Total	Percentage of the total of children with N-MNE (74)	Total	Percentage of the total of children with enuresis
Neurobehavioral alterations														
ADHD, language delay, dilslexia, dysorthography, stuttering, attention deficit, and anxiety	9	3.7%	4	4.7%	13	4.0%	9	15.5%	1	6.3%	10	13.5%	23	5.7%
Poor academic achievement	5	2.1%	1	1.2%	6	1.8%	6	10.3%	0	0.0%	6	8.1%	12	3.0%
Spina bifida occulta														
Pilonidal dimple	4	1.7%	1	1.2%	5	1.5%	3	5.2%	0	0.0%	3	4.1%	8	2.0%
Single and deflected intergluteal cleft	5	2.1%	1	1.2%	6	1.8%	4	6.9%	0	0.0%	4	5.4%	10	2.5%
Double intergluteal cleft	3	1.2%	0	0.0%	3	0.9%	0	0.0%	0	0.0%	0	0.0%	3	0.7%
Gastrointestinal system														
Fecal incontinence (encopresis)	3	1.2%	0	0.0%	3	0.9%	8	13.8%	1	6.3%	9	12.2%	12	3.0%
Constipation	15	6.2%	11	12.9%	26	8.0%	24	41.4%	8	50.0%	32	43.2%	58	14.5%
Others														

Contd...

Table 4: Contd...

	MNE						N-MNE				MNE + N-MNE	
	Boys	Percentage of the total of boys with MNE (242 boys)	Girls	Percentage of the total of girls with MNE (85 girls)	Total	Percentage of the total of children with MNE (327)	Boys	Percentage of the total of boys with N-MNE (58 boys)	Girls	Percentage of the total of girls with N-MNE (16 girls)	Total	Percentage of the total of children with N-MNE (74)	Total	Percentage of the total of children with enuresis
Polythelia	16	6.6%	3	3.5%	19	5.8%	12	20.7%	0	0.0%	12	16.2%	31	7.7%
Enlargement of the tonsils or tonsillectomy	6	2.5%	1	1.2%	7	2.1%	3	5.2%	0	0.0%	3	4.1%	10	2.5%
Cardiovascular system														
Innocence heart murmur	48	19.8%	18	21.2%	66	20.2%	15	25.9%	5	31.3%	20	27.0%	86	21.4%

MNE: Monosymptomatic nocturnal enuresis, N-MNE: Non-monosymptomatic nocturnal enuresis, ADHD: Attention deficit hyperactivity disorder

cases (32/327), and paternal and maternal heredity in 3.4% of cases (11/327). On the contrary, children with N-MNE have paternal heredity in 24.3% of cases (18/74), maternal heredity in 35.1% of cases (26/74), and paternal and maternal heredity in 4.1% of cases (3/327). In a sample of the Avon Longitudinal Study of Parents and Children, the prevalence of NE was 15.5%.[6] Of the 11,650 mothers and 7,897 fathers who provided information of their own NE, respectively, 8.8% and 9.6% had NE. The odds for severe child NE were 3.6 higher in maternal and 1.85 times higher in paternal NE. When both parents were enuretic, their children had a 77% risk of having NE.[7] The risk was 43% when one parent was enuretic and 15% when neither parent was enuretic. It was reported a positive family history in 65–85% of children with NE.

In MNE group, 38% (92/242) of boys and 30.6% (26/85) of girls have deep sleep. In N-MNE group, 81% (47/58) of boys and 93.8% (15/16) of girls have deep sleep. Other authors suggested that deep sleep is more frequent in MNE children (96.2%) than nonenuretic children (12.5%).[8] Snoring is more frequent in the N-MNE group (25.7% – 19/74) than the MNE group (11% – 36/327). Girls with N-MNE have snoring more frequent (31.3% – 5/16) than girls with MNE (11.8% – 10/85). About 3.3% (10/300) of boys and 2% (2/101) of girls have sleep apnea. It is more frequent in the N-MNE group, in which 12.5% (2/16) of females and 8.6% (5/58) of males are affected. In the MNE group, 2.1% (5/242) of males and none of the females have sleep apnea. About 2.1% (7/327) of children with NME and 4.1% (3/74) of children with N-MNE suffer or suffered from enlargement of the tonsils or have undergone tonsillectomy. Obstructive sleep-disordered breathing (SDB) is a syndrome characterized by snoring and increased respiratory effort caused by upper airway obstruction (UAO).[9] UAO occurs in 27% of the pediatric population and nasal or oropharyngeal pathologies. The most common cause is tonsil and adenoid enlargement. SDB may present as simple snoring or as obstructive sleep apnea syndrome (OSAS). In a study, OSAS occurs in 47.8% of children with NE and in 30.4% of children without NE. About 71.5% of patients with MNE who underwent an adenoidectomy had their NE resolve, which is much higher than the annual spontaneous resolution rate. In another study, 52% of the children with NE after tonsillectomy had complete resolution of NE.[10]

A study based on a large national population database has shown that OSAS and snoring are more common in the group with enuresis than in the control group (1.8% vs. 0.6%; 1.3% vs. 0.6%, respectively).[11] Respiratory problems in children may affect or worsen NE. The link between OSAS and NE is due to an increased respiratory effort against an obstructed airway in children with SDB that may cause increased release of both brain and atrial natriuretic peptides from cardiac myocytes after cardiac

wall distension owing to increased negative intrathoracic pressure. Relief of UAO is associated with significant improvement of NE.

Parasomnias are more frequent in the N-MNE group than the MNE group. About 50% of N-MNE children (37/74) and 17.7% of MNE children (58/327) are affected by somniloquy. It is more common in girls with N-MNE (75% – 12/16) than in girls with MNE (17/85 – 20%). Bruxism affects 28.4% of children with N-MNE (21/74) and 11.6% of children with MNE (38/327), especially boys (29.3% – 17/58) and girls (25% – 4/16) with N-MNE. In a group of primary school children, more than one awakening each night was found in 12.2% of children.[12] In the whole group, the prevalence of bed-wetting was 8.7%, sleep talking 20.9%, sleepwalking 3.2%, teeth grinding 15.4%, and nocturnal pavor 8.4%. Snoring was reported by 11.4% of children, and 6.3% reportedly struggled to breathe during sleep.

In a nationwide sample of Chinese primary school children, children with NE had slightly shorter sleep duration than those without NE.[13] The prevalence rates of bedtime resistance, sleep onset delay, sleep duration disorder, night awakening, sleep anxiety, SDB, parasomnias, and daytime sleepiness were much higher in children with NE than those without NE. Children with NE were more than 1.5 times more likely to have parasomnias, SDB, and night awakening such as sleep problems as compared to those without NE. Compared to girls, boys with NE had higher odds of suffering from most of the sleep problems and shortened sleep duration on weekends. However, compared to boys, girls with NE were more likely to have other types of parasomnias; 11–12-year-old children with NE had the highest odds of bedtime resistance, night awakening, sleep anxiety, SDB, and parasomnias among all age groups, which indicated that the relationship between NE and sleep problems might be more pronounced in older children. The link between NE and sleep disorders can be explained by the fact that bedwetting itself can cause 50% of all awakenings in children with NE, consequently leading to sleep deprivation and daytime sleepiness, by the fact that children with shortened sleep duration and some other sleep problems are inclined to suffer from sleep deprivation, which in turn causes an elevated arousal threshold or a reduced secretion of vasopressin during sleep, which would be the underlying pathophysiology to induce NE and by the fact that NE and certain sleep problems may share the same dysfunctional neural circuits, resulting in an increased rate of comorbidity.

In our study, MNE patients are more affected by headaches or migraine (5.8% – 19/327) than N-MNE patients (2.7% – 2/74). In the MNE group, headaches or migraine in the male and female groups are alike (5.8% vs. 5.9%). In the N-MNE female group, there is no inheritance for headaches or migraine, and in the N-MNE male group, paternal inheritance is 5.2% (3/58) and maternal inheritance is 10.3% (6/58). On the other hand, the MNE group maternal heredity for headache or migraine is more common (15% – 49/327) than paternal heredity (10.4% – 34/327); 14% (34/242) boys with MNE and 17.6% (15/85) girl with MNE have maternal inheritance for migraine or headaches, in contrast with paternal inheritance (10.3% and 10.6%, respectively). In MNE group, 11.6% (38/327) of children have maternal inheritance for migraine, higher than paternal inheritance for migraine (8% – 26/327), paternal inheritance for headache (2.4% – 8/327) and maternal inheritance for headache (3.4% – 11/327). The International Headache Society classification system is distinguished into primary and secondary headache disorders.[14] Migraine without aura and TTH, both primary disorders, are the two most common types of headaches in children and adolescents. Children suffered from headaches were 21/401 (5.2%): 4 suffered from TTH and 17 had benign migraine associated with familiarity. Our 17 children with benign migraine associated with familiarity had a recurrent tender or pulsating, moderate-to-severe, and often unilateral pain that lasts 4–72 h with complete freedom between the attacks (episodic). They preferred to lie still in a dark and quiet room and to avoid physical activity. On the other side, our four children with TTH had episodes of migraine without particular features and symptoms. There is contrasting theory about the onset of migraine or enuretic attacks during the night; in particular, micturition tends to occur during nonrapid eye-movement sleep, while migraine attacks seem to be linked to rapid eye-movement sleep stages. Moreover, recent neurometabolic studies have reported altered levels of melatonin both in migraine sufferers and enuretics. Children with NE may show signs of delayed maturation of the nervous system. The parasympathetic nervous system functions are hyperactive in children with NE. In migraine, sympathetic hyperfunction or parasympathetic dysfunction has also been reported. Altered levels of melatonin, an important metabolite for the regulation or arginine–vasopressin levels as well as for the regulation of the circadian rhythm, may affect nocturnal micturition continence. In contrast with our study, in this study, migraine is more common in females.

Innocent heart murmur is more common in the N-MNE group (27% – 20/74) than in the MNE group (20.2% – 66/327). Boys and girls are affected by the same percentage (21% vs. 22.8%). The most affected group is that of girls with N-MNE (31.3% – 5/16), followed by one of boys with N-MNE (25.9% – 15/58), one of girls with MNE (21.2% – 18/85), and one of boys with MNE (19.8% – 48/242). About 100% (16/16) of girls with N-MNE and 91.4% (53/58) boys with N-MNE have urgency. Boys and girls are wet in the afternoon sleep in the same percentage (3.7% vs. 2.9%). N-MNE children are wet in the afternoon sleep more frequent (13.5% – 10/74) than MNE children (1.2% – 4/327).

Male genital alterations are more common in males with N-MNE than in those with MNE. This was mainly observed for balanopreputial adhesions, which are present in 24.1% (14/58) of boys with N-MNE compared to the MNE group, where they are present in 5.8% (14/242) of boys with N-MNE. It was observed the same for preputial phimosis (5.2% vs. 0.8%), hypospadias (3.4% vs. 0.8%), and hydrocele (3.4% vs. 0%).

Boys are more affected by neurobehavioral abnormalities than girls. Attention deficit hyperactivity disorder (ADHD), language delay, dilslexia, dysorthography, stuttering, attention deficit, and anxiety are more common in the N-MNE group than the MNE group (13.5% vs. 4%). N-MNE boys (15.5% – 9/58) are more affected than N-MNE girls (6.3% – 1/16).

The prevalence of NE in patients with ADHD has been estimated to be 28–32%.[7] The presence of ADHD had a negative effect on the resolution of incontinence and treatment of urinary incontinence in children with ADHD compared to those without ADHD. Children with NE had lower birth weight than non-NE children, and also, children who were given birth by caesarian had a higher risk for developing NE. It has been shown that low birth weight was significantly associated with delay in achieving all developmental milestones including walking alone, meaning speech, and bedwetting cessation. We also investigated the correlation between parental education and NE and concluded that the lower parental educational level was associated with higher prevalence of NE in ADHD children. There is a meaningful association between family history of NE and developing NE in patients with ADHD. This may indicate the role of genetics in NE in children with ADHD. The attention deficit could be due to defects in the suppressive function of the brain stem of NE children.[15] Analysis of T1 data revealed that NE children showed lower gray matter density than normal control children in the right dorsolateral prefrontal cortex and left posterior lobe of cerebellum associated with the occurrence of working memory deficits. fMRI study performed indicated that NE children had deficits in working memory.

Pilonidal dimple is more frequent in the male group (2.3% – 7/300) than in the female group (1% – 1/101). It is observed in 5.2% (3/58) of boys with N-MNE, 1.7% (4/242) of boys with MNE, and 1.2% (1/85) of girls with MNE. Girls with N-MNE are not affected.

Among the group of patients, 3.2% (13/401) patients have alterations to the intergluteal cleft. Girls with N-MNE are not affected. Single and deflected intergluteal cleft is observed in 2.1% (5/242) boys with MNE, 1.2% (1/85) of girls with MNE, and 6.9% (4/58) boys with N-MNE. Double intergluteal cleft is observed in 1.2% (3/242) boys with MNE. No cases of double intergluteal cleft were seen in girls with MNE and in boys with N-MNE.

Spinal dysraphism refers to any fusion defect of vertebral arch and may be simply classified as open or closed spinal dysraphism.[16] Open spinal dysraphisms have distinct symptomatology, whereas closed spinal dysraphisms or spina bifida occulta (SBO) may cause insignificant symptoms and might be detected incidentally. Most of these children have normal neurological examination during neonate period but may be symptomatic as they grow up due to tethered cord syndrome, cauda equina syndrome, or split cord syndrome with the traction and deoxygenation of spinal cord. In the milder forms of SBO, there are even no neurological symptoms and urological findings may be the only symptomatic presentation. The prevalence of SBO in general population ranges between 1.2% and 50%, and this prevalence was reported to be higher in NE patients. This study shows that SBO is more frequent in N-MNE than in MNE (48% vs. 20.4%) and treatment success was significantly lower in this group because behavioral interventions alone would not be enough for patients with severe NE and patients with SBO.

The prevalence of SBO is between 12% and 23% and is more common in males.[17] In this study, this proportion was found to be 21.5%. It is most commonly seen at S1, L5, S2, and L4 vertebral levels. The frequency of SBO levels is similar in patients with and without NE. Patients with SBO and NE have higher rates of N-MNE than patients without SBO.

Encopresis is more common in N-MNE group (12.2% – 9/74) than the MNE group (0.9% – 3/327). Constipation affects N-MNE children more than MNE children (43.2% vs. 8%), especially girls with N-MNE (50% – 8/16) followed by boys with N-MNE (41.4% – 24/58), by girls with MNE (12.9% – 11/85), and by boys with MNE (6.2% – 15/242). Encopresis is more common in enuretic children than in the general population, both in males (5.1% vs. 0.2%) and females (3.8% vs. 0%).[18,19] Constipation is more frequent in MNE children (88.8%) than non-enuretic children (8.9%).

Children with encopresis and functional constipation have a significant incidence of such urinary disorders as NE, infection, vesicoureteral reflux, and hydronephrosis.[1,18,19] Constipation was defined as less than three bowel movements per week for a period of at least 6 months. In this study, 7% of children with enuresis and 1.5% of the control group had constipation, and the difference between the two groups was statistically significant. It is explained by the prolonged and frequent anal contractions seen in children with constipation, which cause involuntary bladder contractions, thus leading to incontinence.

In this study, all the children and adolescents with NE had rectal distension according to the rectal/pelvic outlet ratio, and 80% were constipated according to the Leech criteria.[19] Only 10% of the patient or families reported

clinical symptoms of constipation. Many children have daily bowel movements but do not fully empty their rectum and, therefore, retain stool, which can have a negative effect on bladder capacity. Rectal distension might lead to bladder overactivity, another known risk factor for NE, independent of its effects on bladder capacity. It is important to diagnose occult megarectum because when it is missed, children are often subjected to unnecessary therapies, for example, high doses of desmopressin or adenotonsillectomy in the hope that the treatment of obstructive sleep apnea might resolve the NE.

NE is a common disorder in childhood. Our study underlines the importance of motivational therapy in the management of NE and highlights the safety of treatment evaluating all the comorbidities.[20] Our experience demonstrates that there are a lot of comorbidities[21] that influence the prognosis and the response to the therapy in these children. Children with a family history of NE have shown a greater percentage of remission compared to children without a family history. Moreover, the relation between NE and ADHD has shown that the non-resolution or treatment of one disorder increases the risk for the other disorder.[5] In addition, children with SBO have lower treatment response.[17] On the other side, previous studies have shown that resolution of comorbidities, such as OSAS, leads to a better treatment success of NE.[9] Further studies on our sample might address the issue of evaluating the prognostic role of comorbidities associated with NE.

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Conflicts of interest

There are no conflicts of interest.

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