




A RETROSPECTIVE STUDY ABOUT INCONTINENCE AND ENURESIS IN THE SHADOW OF COVID19 PANDEMIC

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Abstract

Aim: Enuresis and/or incontinence are one of the most common problems that families seek professional help. In this study we wanted to evaluate the patients who applied to pediatric nephrology outpatient clinics with enuresis and/or urinary incontinence during Covid19 pandemic.

Methods: We retrospectively evaluated the patients with the ICD diagnoses of “Non-organic enuresis” and “Urinary incontinence”. The data regarding two hundred and four patients were analyzed and compared via dividing them into two groups as Group A (Primary enuresis nocturna) and Group B (other enuresis and incontinence types such as dysfunctional voiding, secondary enuresis, bladder and bowel dysfunction etc.).

Results: Mean age was significantly higher in Group A when compared with Group B (9.57 (± 2.78) vs. 8.67 (±3.27), p=0.036). In Group A male/female ratio was 61/43, in Group B male/female ratio was 36/64 (p<0.001). Family history was more prevalent in Group A (72% vs 31%) (p<0.001). In Group B, 25% of the patients had a history of at least one symptomatic urinary tract infection, and it is significantly higher than Group A (p=0.012). One-hundred and nine over 204 patients had applied for a control visit (53%). Overall treatment success rate in patients having at least one control visit was 82% and 72% in Group A and B respectively.

Conclusions: Urinary incontinence and enuresis are common problems in children. There are certain differences between nocturnal enuresis and day time incontinence in terms of their characteristics and the treatments as well. We usually demand a control visit since the treatment of enuresis and incontinence requires close follow-up, however only 53% of the patients applied for a control visit. This low rate of control visit might be attributed to the Covid19 pandemic since patients and families might have avoided to apply to hospitals with this “less serious” complaints when compared with an important contagious disease.

Keywords: Covid19, enuresis, incontinence, bed-wetting

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Introduction

Urinary incontinence is the uncontrolled leakage of urine, and enuresis is the urinary incontinence during sleep including naps. Diurnal enuresis (or enuresis diurna) is an obsolete term replaced with “functional daytime urinary incontinence” nowadays. Primary enuresis defines the habit of bedwetting since the time of toilet training. Secondary enuresis is bedwetting of a person who had been “dry” for at least six months¹⁻³. The prevalence of daytime urinary incontinence in children varies from 3.2% to 9%^{1,4-6}. Prevalence decreases with age, and is higher in girls^{1,4-7}. Prevalence of nocturnal enuresis is reported to be as 7.2-8% in children⁸.

Enuresis and/or urinary incontinence are caused by several etiologies. The largest group of patients applying to pediatric nephrology and urology clinics are the ones with monosymptomatic enuresis nocturna. Those patients do not have any other symptoms except bedwetting. Non-monosymptomatic nocturnal enuresis defines bedwetting with daytime lower urinary tract symptoms^{1,2}. On the other hand, secondary enuresis may be the result of urinary tract infections, pinworms or psychosocial problems. Diabetes mellitus, as well as diabetes insipidus, and renal insufficiencies may also present as urinary incontinence³.

In a child with enuresis and/or daytime incontinence, lower urinary system should be evaluated. Together with incontinence, the presence of urgency, frequency or recurrent urinary tract infections might indicate lower urinary tract dysfunction. Overactive bladder, dysfunctional voiding, underactive bladder, postponing of the voiding, stress incontinence, giggle incontinence, vesico-vaginal reflux are the most possible diagnoses in a child with lower urinary tract dysfunction¹. Nocturnal enuresis have been attributed to several reasons such as nocturnal polyuria, detrusor overactivity, increased arousal threshold during sleep, and genetic factors^{1,3}.

In this study we aimed to evaluate the profile of the patients with enuresis and/or incontinence in the shadow of Covid-19 pandemic.

Materials and Methods

Pediatric patients who applied to the outpatient clinics of pediatric nephrology department of Kayseri City Hospital between December 2019 and August 2021, during the most overwhelming times of Covid19 pandemic, with the ICD diagnoses of “Non-organic Enuresis” and/or “Urinary Incontinence” were retrospectively evaluated. Among all patients with those ICD codes, 204 patients who had detailed anamnesis on the online records of the hospital were chosen as study group. Since enuresis is defined by ICCS (International Children's Continence Society) in children who had passed their fifth birthday¹⁰, we evaluated the data of patients older than 5 years of age.

We recorded and analyzed the demographic data, laboratory data (kidney function tests, complete blood count, and urine density), radiological findings (urinary ultrasounds), the history of recurrent urinary tract infections, the main complaint at application, the presence of bowel dysfunction (in terms of constipation and fecal incontinence), the final diagnoses, the treatment modalities, and data regarding improvement of the symptoms.

The patients were divided into two groups as “primary enuresis nocturna group (defined as Group A)” and “other incontinence&enuresis types (defined as Group B)”, since primary enuresis nocturna can be speculated as a more benign condition. The data regarding the two groups were compared.

The data of 204 patients were evaluated with IBM SPSS for Windows (SPSS version 17.0). For the analysis of the categorical data in Group A and Group B Chi-square (χ^2) test was used. Student t test was performed for normally distributed data, and Mann-Whitney U test for nonnormally

distributed data. Frequencies and percentages were used as descriptive values in the categorical data.

Arithmetical mean±standard deviation was used for the normally distributed data, and median and interquartile range (IQR) were used for the non-normally distributed data. Statistical significance was accepted as 0.05.

Local Ethic Committee of Kayseri City Hospital approved the study, on 18 March 2021, with the decision number 331.

Results

Among 204 patients, 97 of them were male (47.5%), 107 were female (52.5%). Mean age of the patients were 9.1 years (±3.05). Mean age of the girls were 9.02 years whereas mean age of the boys were 9.2 years. Mean age for toilet training was 2.5 years (±0.8) (min-max: 1,5-5).

One-hundred and nineteen (58.3%) patients applied to the hospital with the complaint of bedwetting during sleep, 17 (8.3%) patients with daytime incontinence, 67 patients applied with the complaints of both nocturnal and day-time incontinence and one patient's complaint was incontinence during laughing. When the patients and their parents were questioned, 51% of the patients had the habit of postponing the voiding. Family history of an enuretic relative was found in 55% of the patients.

Table 1. Diagnoses of the patients

	n(%)
Primary enuresis nocturna	104 (51%)
Secondary enuresis nocturna	22 (10.8%)
Dysfunctional voiding	37 (18.1%)
Overactive bladder	12 (5.9%)
Enuresis diurna	14 (6.9%)
Giggle incontinence	3 (1.5%)
Bladder and Bowel Dysfunction	8 (3.9%)
Mental retardation and Learning disabilities	3 (1.5%)
Neurogenic bladder	1 (0.5%)

Constipation was an accompanying condition in 23 (11%) of the patients and fecal soiling in 14 (6.8%) patients. Among 197 patients who had at least one urinary ultrasonographic investigation in the medical records of the hospital's system, 165 (83.7%) had normal findings. Fourteen patients (6.8%) had thickening of the urinary bladder wall, whereas 7 patients (3.5%) were found to have hydronephrosis. Five patients had structural anomalies in kidneys and the urinary tract (excluding hydronephrosis). One patient with daytime urinary incontinence had an ultrasound imaging supporting ureterovaginal fistula, and that patient was referred to pediatric urology for further follow-up and treatment. Incidentally two patients were found to have microlithiasis and one patient was found to have unilateral simple kidney cyst. When we evaluate the medical history of the patients 36 (17.6%) of them had at least one symptomatic urinary tract infection in their life.

One-hundred and four patients (51%) were diagnosed as primary enuresis nocturna, 37 patients (18.1%) as dysfunctional voiding, 22 patients (10.8%) as secondary enuresis nocturna, 14 patients (6.9%) as enuresis diurna, 12 patients (5.9%) as overactive bladder. Eight patients were found to have bladder and bowel dysfunction (previously known as dysfunctional elimination syndrome), three patients were diagnosed as giggle incontinence, and another three patients had the diagnosis of specific learning disabilities. One patient was diagnosed as neurogenic bladder (Table 1).

When we divide the patients into two groups as primary enuresis nocturna (Group A) and other incontinence&enuresis types (Group B); mean blood urea nitrogen (BUN), serum creatinine, serum sodium, potassium, glucose, hemoglobin levels and mean urine density were similar between the two groups.

Table 2. Clinical and laboratory data of the groups.

N	Group A 104	Group B 100	p value
Age (years), Mean(\pm SD)	9.57 (\pm 2.78)	8.67 (\pm 3.27)	0.036
Male/Female ratio (n/n)	61/43	36/64	0.001
BUN (mg/dL)	10.3	10.8	>0.05
Serum creatinine (mg/dL)	0.47	0.45	>0.05
Serum sodium (mmol/L)	139	138	>0.05
Serum potassium (mmol/L)	4.5	4.4	>0.05
Serum glucose (mg/dL)	88	84	>0.05
Hemoglobin (g/dL)	13.5	13.2	>0.05
Hematocrit (%)	38.4	38.9	>0.05
MCV (fL)	78.6	78.5	>0.05
Urine density	1020	1019	>0.05
Toilet training age (years)(Mean)	2.5	2.5	>0.05
Family history (n)	45/62 (72%)	14/45 (31%)	<0.001
History of UTI (n of patients)	12/104 (11%)	24/95 (25%)	0.012
Voiding postponement (n)	29/104 (27.8%)	67/100 (67%)	<0.001
Constipation (n)	7/104 (6%)	16/93 (17%)	0.024
Fecal soiling (n)	-	14/94	<0.001
Urinary anomaly (including hydronephrosis)	5	7	
Bladder thickening	-	14	
Comorbid Conditions			
<i>Epilepsy</i>	-	4	
<i>ADHD</i>	1	2	
<i>Obesity</i>	1	3	
<i>Diabetes mellitus</i>	1 (MODY 5)	1 (Type 1 DM)	

Mean age in Group A was significantly higher than the mean of the Group B (9.57 years (\pm 2.78) vs. 8.67 years (\pm 3.27) $p=0.036$). Mean toilet training age was similar between the two groups (2.5 years). In Group A male/female ratio was 61/43, however in Group B female patients were dominant with a ratio of male/female ratio of 36/64. The difference is significant with a p value of 0.001.

Postponing of the voiding was seen in 29 patients (27.8%) in Group A, whereas 67 patients (67%) in Group B were found to have void postponement. This difference is also significant ($p<0.001$). In Group A, family history was found in 45 of 62 patients (72%), in Group B family history was found in 31% of the patients (14/45) ($p<0.001$).

The history of having at least one symptomatic urinary tract infections was found in 12/104 patients (11%). Among group B, 24 of 95 patients (25%) had a

history of urinary tract infection, the rate of urinary tract infections was significantly higher in that group when compared with the primary enuresis nocturna group (Group A) ($p=0.012$). Fecal incontinence was prominent in 14 patients among 94 patients in Group B whereas none of the patients had fecal incontinence in Group A ($p<0.001$). Constipation was seen in 7/104 (6%) in Group A whereas it was more prevalent in Group B 16/93 (17%) ($p=0.024$) (Table 2). Among all patients, oral desmopressin was administered to 86 patients (42%), behavioral modifications were the choice of treatment in 68 patients (33%), daily calendar in 18 (8%) patients, and 9 patients (4.4%) had been administered oxybutynin. Desmopressin was also the choice of medication in 10 patients with secondary enuresis nocturna, 7 of them benefited from the treatment, remaining three did not have a control visit. Desmopressin was administered after having the detailed anamnesis

and work-up to elucidate the exact etiology of secondary enuresis and when the behavioral modifications fail.

In Group A 76 patients were administered desmopressin treatment, 15 patients were treated with calendar method and 3 patients with alarm method. Ten patients only had suggestions about voiding with no other treatment methods applied. In Group B, 9 patients diagnosed as overactive bladder later, were administered oxybutynin and 58 patients were given advices on voiding habits and postures, with behavioral therapy (Table 3).

Totally, 109 over 204 patients had applied for a control visit (53%). Sixty-nine patients (66%) among 104 patients in Group A had at least one control visit. Among those 69 patients who had control visits, 57 of them were discovered to have responded well to therapy, making the success rate 82% in patients having control visits in Group A. Among 53 patients in Group A having desmopressin and applied for a control visit, 41 patients benefited from desmopressin treatment making the success rate 77%. Twelve among 15 patients benefited from calendar method (success rate is 80%) and 4 patients benefited from lifestyle modifications. In Group B, only 40 of 100 patients had control visits, and among those 40 patients 29 had benefited from the treatment the success rate 72% in this group. In Group A, one patient had been

discovered to have a rotational anomaly in his right kidney. An atrophic left kidney with a non-obstructive ureterovesical junction obstruction in right kidney was diagnosed in another patient. Two patients were discovered to have unilateral hydronephrosis, two patients had microlithiasis, one patient with unilateral kidney cyst had the diagnosis of MODY 5 with a HNF1Beta mutation. Two patients in Group A had renal microlithiasis. In Group B, 14 patients had thickening in bladder wall on their urinary ultrasound imaging, whereas none of the patients had thickened bladder wall in Group A. A 5-year-old girl with diurnal enuresis was found to have ectopic ureter opening to vagina wall and referred to pediatric urology. A patient with unilateral right renal agenesis and another one with unilateral two cysts in left kidney were the other urinary anomalies detected in ultrasound in Group B. Three patients had been found to have microlithiasis incidentally. Five patients had hydronephrosis in Group B.

Eight among 104 patients in Group A were referred to pediatric urology department due to unresponsiveness to desmopressin treatment. Twenty patients in Group B were referred to pediatric urology with the suspicion of bladder dysfunction and with the need of uroflowmetric and urodynamic tests.

Table 3. Treatment modalities and the prognosis of the patients

	Group A N (%)	Group B N (%)	p value
Behavioral modifications	10 (9.6%)	58 (58%)	<0.001
Desmopressin	76 (73%)	10 (10%)	<0.001
Oxybutynin	-	9 (9%)	0.001
Calendar Method	15 (7.3%)	3 (3%)	0.008
Alarm	3 (2.8%)	-	>0.05
Urology consultation	8 (unresponsive to desmopressin) (7.6%)	20 (20%)	0.019
Child psychiatry consultation	-	5 (5%)	0.031
Control visit	69/104 (66%)	40/100 (40%)	<0.001
Improvement with treatment modalities	57/69 (82%)	29/40 (72%)	>0.05
Total	104	100	

When we evaluate the comorbid conditions, in Group A there was one patient with obesity, whereas there were three obese patients in Group B. Four patients had epilepsy in Group B. Established diagnosis of attention deficit hyperactivity disorder (ADHD) was found in three patients (one in Group A vs two in Group B). Two patients (one in Group A and one in Group B) were on the follow-up of pediatric psychiatry with the diagnoses of generalized anxiety disorder and were on selective serotonin reuptake inhibitors treatment. One of them responded well to behavioral modifications and the other one benefited from desmopressin treatment. One patient in Group B had the established diagnosis of Type 1 diabetes and applied with the complaint of both daytime incontinence and nocturnal enuresis. The patient had a bad control on her blood sugar and benefited from behavioral modifications together with strict sugar control. Two patients with secondary enuresis with the suspicion of sibling rivalry disorder and three patients with possible learning disorder were referred to pediatric psychiatry department.

Discussion

Nocturnal enuresis is defined as urinary incontinence during sleep in children older than the age of five¹⁰⁻¹². Primary nocturnal enuresis can be defined when the child has never been dry more than 6 months. Enuresis can be further separated into monosymptomatic or non- monosymptomatic based on the presence of lower urinary tract symptoms or bladder dysfunction¹⁰⁻¹². Prevalence of nocturnal enuresis in children at 7 years of age changes between 15–22% among male children and 7–15% among female children^{9,13}. In align with that, in our cohort we also found a male dominance in primary nocturnal enuresis group (Group A) with a male/female ratio of 61/43. In a recent data, 10% of the children were found to have enuresis and at the age of seven 1% of the children presented with secondary enuresis^{14,15}. Among our cohort 22 patients

(10.8%) had secondary enuresis nocturna. Genetic predisposition, abnormally large production of urine, developmental issues, heavily sleeping, male gender, constipation, and low socioeconomic status are the known general risk factors associated with nocturnal enuresis⁹.

On the other hand, daytime urinary incontinence is an important issue in especially school-aged children affecting their quality of life¹. Day-time wetting accounts for 4.2%–32% of the total incontinence cases¹⁶. Daytime urinary incontinence in 7-year-old children has an overall prevalence rate of 3.2-9.0%, and almost 1% of the children experience daytime urinary incontinence in a considerable extent^{1,4-6}. Prevalence gets lower with increasing age. Prevalence of daytime urinary incontinence is higher in girls when compared with the boys, this discrepancy might be attributed to the dissimilarities in the anatomy of different genders^{1,5-7}. We also found a significant female predominance in Group B in which most of the patients have daytime urinary incontinence.

Family history might be positive for both enuresis nocturna and daytime urinary incontinence. In nocturnal enuresis heritance is more prevalent. Genes 8q, 12q, and 13q are demonstrated to be related with nocturnal enuresis¹⁷. In our cohort 72% of the patients in Group A (primary enuresis nocturna) had positive family history, whereas only 31% of the patients in Group B had a family member with incontinence. Our findings are consistent with previous data.

Urinary incontinence might also be associated with behavioral issues. Among incontinent children, increased prevalence of anxiety, attention, hyperactivity problems, and oppositional behavior were found when compared with continent children^{1,18}. Studies document that several developmental disorders such as ADHD has an association with enuresis^{14,18,19}. In addition, enuresis nocturna is associated with psychological disorders, and ADHD is present in as much as 20% of children with nocturnal enuresis^{2,9}. Despite the unclearness of the mech-

anism it is speculated that a delay in neuronal maturation might be related with it^{14,18,20,21}. In our study three patients had the established diagnosis of ADHD. Anxiety and psychological stress are known causes of overactivity in bladder²². In our study, two patients had the diagnosis of anxiety disorder and were using medications prescribed by a pediatric psychiatrist.

Dysfunctional voiding, overactive bladder, underactive (lazy) bladder, voiding postponement, stress incontinence, giggle incontinence, vesico-vaginal incontinence are the subtypes of daytime incontinence. In our study 37 patients had dysfunctional voiding, 12 patients had overactive bladder, 8 patients had bladder and bowel dysfunction, and three patients were found to have giggle incontinence. The signs and symptoms of dysfunctional voiding are post-void residue (poor bladder emptying), staccato or interrupted voiding, incontinence, enuresis, constipation, recurrent urinary tract infections. There is a functional incontinence arising from failure in coordinating the urinary tract between the detrusor and the sphincter ending in a dysfunction in the urinary phase. Overactivity in the pelvic muscles leads to infravesical obstruction^{16,23}.

Postponing the micturition via holding maneuvers defines voiding postponement and it is associated with low voiding frequency, urgency, and possible urge incontinence¹. Hydronephrosis may be seen in the children with holding maneuvers. Upper urinary system is strained by the dyssynergic lower urinary tract. In our cohort hydronephrosis was prevalent in 7 (3.3%) patients (two in Group A, five in Group B).

Stress incontinence is defined by the uncontrolled leakage of urine during a physical activity increasing intraabdominal pressure such as coughing or sneezing. Giggle incontinence (or enuresis risoria) is a rare, benign and self-limiting condition, seen usually in females, in which wetting occurs during laughing, although bladder function is otherwise normal. It is thought to be arised from centrally mediated and related to a receptor imbalance of cholinergic and mono-

aminergic systems that results in loss of the muscle tone^{16,24}. Among our study group there were three cases with giggle incontinence. For both stress and giggle incontinence, exact causes are unknown¹.

Another type of incontinence is vesico-vaginal (or urethro-vaginal) reflux or post-void dribbling especially in obese prepubertal girls. During urination, urine might flow towards vagina due to the compression of the thighs and wetting of the underwear occurs after urination^{2,16}.

Functional constipation develops in almost 50% of children with dysfunctional voiding^{2,10-12}. Constipation was found in 11% of our total cases (6% in primary enuresis group (Group A) vs 17% in Group B). Dysfunctional elimination syndrome term, used previously, is now replaced by the term "bladder and bowel dysfunction", and the new nomenclature is also recommended by The International Children's Continence Society^{2,10-12}. We had 8 patients diagnosed as bladder and bowel dysfunction which had daytime urinary and fecal incontinence. Anamnesis of the patient (including extensive history of urination and history of febrile urinary tract infections), physical examination (including the inspection of urogenital system to detect congenital malformations, and lumbosacral region examination), voiding diaries, questionnaires, uroflowmetry, and ultrasound are the diagnostic tools. According to ICCS guidelines, the diagnosis of overactive bladder does not require a test such as urodynamics. However if the physician is suspicious of autonomic dysfunction (detrusor overactivity), which is an important etiology of overactive bladder in childhood, cystometrics will be helpful¹⁰⁻¹². Urinary stream is recorded as a graphic in uroflowmetry, and it gives us data about urine volume, flow time, velocity at the beginning of micturition, maximum flow rate (mL/s), and flow pattern. A normal flow will have a bell-shaped pattern and will be completed within 20 seconds^{1,2}.

Treatment differs according to the types of enuresis and the etiology of daytime incontinence. Generally, clinicians tend to treat

primary enuresis nocturna cases with both behavioral therapy and medications. Behavioral therapy consists of recommendations on regular water intake and timed voiding during daytime and decreasing the amount of fluid intake in the evening. The calendar method in which the child marks the wet and dry nights is also helpful. We also found a success rate of 80% among patients with calendar method.

Desmopressin is known as the best medication for nocturnal enuresis. Due to the risk of water intoxication, patients must be warn about not drinking large volumes of fluid with the drug¹². Previous studies concludes the response rate of desmopressin in mono-symptomatic enuresis as 60–80%. In our study 77% of the patients among the ones with a control visit in Group A responded well to desmopressin treatment. Despite alarms are known as effective methods for the treatment of enuresis, in our patient group alarm method was not the mostly preferred one due to several known factors such as technical problems related with it such as child's sweat causing false alarms, or low battery time²⁵. We only had three patients treated with alarm method in our cohort. Most of the parents of enuretic children tend to prefer the combination of behavioral modifications and taking medications⁹. We did not prefer imipramine, which is originally a tricyclic antidepressant drug, due to its possible cardiac effects.

First choice of treatment of daytime enuresis is urotherapy which is a non-invasive treatment consisting of the education of the child, behavioral modifications and lifestyle changes regarding the arrangement of voiding frequencies, voiding habits and posture, and fluid intake in order to prevent incontinence episodes¹. Fecal impaction can cause pressure on bladder neck and urethra, resulting in lower urinary tract dysfunction, therefore medication for constipation may be added to urotherapy^{1,26-28}. In our patient group, 23 patients (11%) had constipation and were administered constipation therapy together with suggestions about life-style modifications as well as nutritional advices.

Since regular visits are recommended to evaluate progress and to prevent prolonged treatment (or change the treatment if necessary) we usually demand a control visit for our patients. A control visit will also identify the benefits of the treatment, motivate the patient and parents, and the physician will find the opportunity to strengthen the recommendations as well. However only 53% of the patients had the control visit in our cohort. We speculate that, this low control rate might be attributed to the ongoing Covid19 pandemic. Patients and families might have felt uncomfortable to go to hospitals with this “less serious” complaints regarding enuresis and urinary incontinence, when compared with a life threatening contagious disease.

The control rate was significantly higher in Group A, and the treatment success was also higher in this group. This may be related with the need of a prescription since medical treatment rate (mainly desmopressin) is higher in group A. In the shadow of a pandemic affecting the whole world, families might have been evaluated enuresis and/or incontinence as a benign condition and refused to apply to the hospital for a second visit. Due to the fact that anxiety is known as an enuretic issue, Covid19 pandemic might have an additional effect on incontinence and/or enuresis cases via causing anxiety in children, as well as treatment failure.

The limitation of our study is its retrospective nature. We have few missing data regarding the anamnesis of the patients. Besides we were not able to show the trends (whether there is increase or decrease) in the applications of incontinence and/or enuresis and we could not compare the patients with the number of total applications (per year) before the pandemic.

Conclusion

Treatment for enuresis and/or incontinence is multidisciplinary and requires expert knowledge. Urotherapy is a conservative treatment, which is the first choice for all

types of daytime incontinence. Primary enuresis nocturna can be treated with desmopressin and/or calendar method. We recommend to obtain routine biochemical tests and urinary ultrasound to identify urinary system anomalies and other conditions that may present as incontinence.

We believe that Covid-19 pandemic had affected the number of control visit applications as well as compatibility to treatment. Therefore, our study reconfirms the information of delayed health seeking behavior during pandemic. More studies are essential to show the effect of Covid19 on incontinence and/or enuresis.

Author contributions

OYA and FB were involved in the collection of the data and the clinical follow-up of the patients. OYA is the major contributor in writing the manuscript. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

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Ethical approval

The approval of the Local Ethical Committee was obtained (Kayseri City Hospital).

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