

# Relationship of Urinary Tract Infection to Lower Urinary Tract Dysfunction and Kidney Scar Formation in Children

## Abstract

**Background:** Urinary tract infection (UTI) is the most common infection during childhood. Lower urinary tract dysfunction (LUTD) is a broad term that indicates an abnormal voiding pattern in a child without anatomical and neurological impairment. The purpose of this study was to determine the relationship between UTI and LUTD. **Methods:** This study was conducted at the Children Medical Center Hospital in 2014–2016. The inclusion criteria of this study were at least one UTI confirmed by a positive urine culture and active urine analysis in children who were well toilet-trained previously. Complete physical examination of the genitourinary and skeletal systems was performed to identify patients with anomalies in these systems. The patients with genitourinary system anomalies and obvious and prediagnosed neurological defects of the urinary system such as neurogenic bladder were excluded from the study. To confirm the presence of LUTD, the scoring system of Akbal *et al.* was applied. **Results:** A total of 260 patients including 9.2% of males and 90.8% of females were included in this study. The prevalence of LUTD was 63.8% (166 cases) in these patients. In this study, the prevalence of LUTD in patients with a single episode of UTI was 50.5%, while in patients with recurrence of UTI it was 88.9%. In patients with unilateral kidney scar formation, 90.9% had a recurrence of UTI ( $P = 0.003$ ) which shows a strong correlation of unilateral scar formation with recurrence of UTI. **Conclusions:** These data suggest that there is a significant relationship between UTI and LUTD in children, so evaluation of voiding dysfunction is necessary in this group. With early diagnosis and appropriate treatment, we can reduce the possible serious and permanent sequels of LUTD in patients with UTIs.

**Keywords:** Children, lower urinary tract dysfunction, scar formation, urinary tract infection

## Introduction

The most common infection during childhood is urinary tract infection (UTI).<sup>[1]</sup> In recent studies, the number of emergency department visit and financial burden due to UTI have increased.<sup>[2,3]</sup> Lower urinary tract dysfunction (LUTD) is a broad term that indicates voiding pattern which is inappropriate to a child's age, but more precisely it means any abnormal holding and disturbed voiding pattern seen in a child without anatomical or neurological disease.<sup>[4-6]</sup> It also encompasses a wide range of symptoms, particularly wetting, urgency, frequency, nocturia, nocturnal enuresis, holding maneuvers, and straining.<sup>[5-7]</sup> Dysfunctional elimination syndrome is a condition in which LUTD is associated with constipation that shows a close relationship between two systems.<sup>[8]</sup> Uncomfortable symptoms of LUTD such as wetting and nocturnal enuresis induce

intense psychological burden on the child and his or her parents.<sup>[9-11]</sup> In children at school age, wetting is the third major stress after parent's death and blindness.<sup>[12]</sup> Due to the lack of precise definition and the lack of suitable criteria for the diagnosis and selection of patients, the exact epidemiology of LUTD was not available in the past.<sup>[13]</sup> However, in recent studies using more precise criteria, its prevalence is estimated to be 4.2%–32%.<sup>[14,15]</sup> Etiology of LUTD is not fully understood, but it seems that uncompromised contraction of pelvic floor muscle and muscles of the sphincter at the same time causes it.<sup>[6]</sup> Vesicoureteral reflux (VUR) means a retrograde flow of urine from the bladder to the ureters, and if it occurs recurrently and in the long term, it can lead to irreversible damage to the kidney tissues.<sup>[16]</sup> In previous studies, it has been shown that there is an association between UTI and LUTD.<sup>[6,7,17,18]</sup> But so far a few studies have been done to detect the association of UTI with LUTD, VUR,

Soroosh Alizadeh,  
Mehdi Farhangian,  
Mastaneh  
Moghtaderi<sup>1</sup>, Rasool  
Ghovvati, Zahra  
Noparast<sup>2</sup>, Fatemeh  
Ghafoorimehr<sup>3</sup>

Department of Pediatric Nephrology, Tehran University of Medical Science, Tehran, Iran, <sup>1</sup>Department of Pediatric Nephrology, Tehran University of Medical Science, Tehran, Iran, <sup>2</sup>Department of Pediatric Nephrology, Tehran University of Medical Science, Tehran, Iran, <sup>3</sup>Department of Pediatrics, Tehran University of Medical Science, Tehran, Iran

**Address for correspondence:**  
Dr. Mastaneh Moghtaderi,  
Children Medical Center  
Hospital, Qarib St. Tehran, Iran.  
E-mail: drmoghtaderi@gmail.  
com

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and renal scar formation. Also, we have done this study in middle-east Asian population for the first time.

## Methods

This study was carried out among children referred to the nephrology clinic of the Children Medical Center Hospital, Tehran, from 2014 to 2016. In all, 260 children age 3–14 years with at least one urinary tract infection episode confirmed by active urine analysis and positive urine culture were included in the study. Detailed clinical interviews were conducted and accurate histories were obtained. Then they underwent full examination of the genitourinary system and the skeletal system for the presence of any obvious concurrent anomalies.

The exclusion criteria of this study were the presence of neurogenic bladder, congenital anatomical abnormalities of the urinary system, acquired complications of the anatomy of the urogenital system (trauma, tumor), and patients with central nervous system diseases, chronic kidney disease, and diabetes mellitus. Patients with normal findings at first were included in the study.

The patient's parents were interviewed based on a questionnaire. A standardized questionnaire with 90% sensitivity and specificity with a score of 8.5 or greater that was designed by Akbal *et al.* was applied<sup>[19]</sup> [Table 1]. Patients with a score of 9 or higher were identified as LUTD. Radiological investigations include voiding cystourthrography and dimercaptosuccinic acid scanning (DMSA) performed when indicated like in pyelonephritis or hydronephrosis. The data were analyzed by Chi-square test.

## Results

The study population consisted of 260 patients including 9.2% males and 90.8% females (236). The mean age of patients was 6.4 years with a standard deviation of 3.2.

The prevalence of LUTD was 63.8% (166 cases). With a confidence interval of 95% per 1000, this prevalence was estimated to be 56.2%–72.3%. The prevalence of pyelonephritis (176 cases) was 67.7% and cystitis (84 cases) was 32.2%. Recurrent infection was observed in 34.6% of these patients. Of 118 patients who had VCUG to evaluate their pyelonephritis, 62 patients (52.5%) had VUR. Of 112 patients who had DMSA, 22 patients (19.6%) had unilateral renal scars. About 51.5% of the patients had constipation. In this study, the prevalence of dysfunctional elimination syndrome was 43.1%. Among patients with LUTD (166 cases), the prevalence of frequency was 97.6%, urinary urgency was 96.4%, straining maneuver was 76.2%, and history of daily wetting underwear was 49.4% [Table 2].

The prevalence of occult spina bifida, short sacrum, and dimple was 14.6%, 6.9%, and 53.8%, respectively.

In 156 patients in the age group of 3–7 years, 91% had pyelonephritis and only 9% had cystitis. The prevalence of LUTD in this age group was 56.4%. Of 86 patients in the age group of 7–11 years, 39.5% had pyelonephritis and 60.5% had cystitis. The prevalence of LUTD in this age group was 74%. Of 18 patients in the age group of 11–14 years, all of them had cystitis, and the prevalence of LUTD in this group was 77.8%. So the prevalence of cystitis and LUTD seems to increase with age [Figure 1].

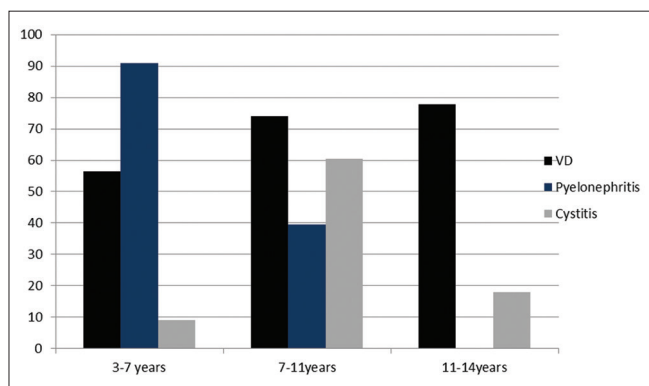
The prevalence of LUTD in patients with cystitis was 83.3% and in patients with pyelonephritis was 54.5%. There was a significant relationship between LUTD and cystitis ( $P = 0.001$ ). There was no significant relationship between dimple and type of UTI in this study. In this study, all patients with short sacrum (18 patients) had pyelonephritis ( $P = 0.026$ ). There was a significant relationship between constipation and LUTD, and hence

**Table 1: Standardized questionnaire designed by Akbal *et al.***

1. Does your child wet during the day?	No (0) Sometimes (1) 1–2 times/day (3) Always (5)
2. How wet is your child during the day?	Damp underwear (1) Damp pants only (3) Pants soaking wet (5)
3. Does your child wet during the night?	No (0) 1–2 Nights/week (1) 3–5 Nights/week (3) 6–7 Nights/week (5)
4. How wet is your child during the night?	Damp bed sheet only (1) Bed sheets soaking wet (4)
5. How many times does your child void?	Less than 7/day (0) 7 or more than 7/day (1)
6. My child strains during voiding.	No (0) Yes (4)
7. My child feels pain during voiding.	No (0) Yes (1)
8. My child voids intermittently.	No (0) Yes (2)
9. My child needs to go back voiding soon after finishes his/her pee.	No (0) Yes (2)
10. My child has a sudden feeling of having to urinate immediately.	No (0) Yes (1)
11. My child holds by crossing his/her legs.	No (0) Yes (2)
12. My child wets on the way to the toilet.	No (0) Yes (2)
13. My child misses his/her bowel movement every day.	No (0) Yes (1)
14. If your child experiences symptoms mentioned above, does it affect his/her family, social or school life?	No (0) Sometimes (1) Yes affects (2) Seriously affects (3)

**Table 2: Associated symptoms in children with voiding dysfunction**

Frequency	97.7%
Urinary urgency	96.4%
Straining maneuver	76.2%
Daily wetting underwear	49.4%

**Figure 1: Prevalence of cystitis and VD was increased with age**

83.6% of patients with constipation had LUTD. In other words, the prevalence of urinary tract disorder was higher in patients with constipation than in others ( $P < 0.001$ ). In this study, 88.9% of patients with recurrence of UTI had LUTD ( $P < 0.001$ ). In contrast to patients who did not recur, only 50.5% had LUTD, which indicate the correlation of recurrence of UTI with LUTD prevalence in this study. In this study, there was no significant correlation between VUR and LUTD and also between scar formation and LUTD. In patients with unilateral scar, 90.9% had recurrent UTI ( $P = 0.003$ ) which shows correlation of unilateral scar formation with recurrent UTI. In this study, all patients with scar formation had VUR. Also, 37.9% of patients who had VUR, had kidney scars, and in patients without VUR, scar was not observed which indicates that there is a significant relationship between scar formation and VUR ( $P = 0.001$ ).

## Discussion

It seems that there is a relationship between UTI and LUTD. In our study, the rate of symptoms associated with LUTD was evaluated. According to our study, frequency with 97.7% and urinary urgency with 96.4% were the two most commonly associated symptoms with LUTD. In Yüksel *et al.*'s study, the overall frequency of LUTD was 9.3%. While a 6-year-old children had the highest frequency (23.1%) of LUTD, this rate was 7.9% at the age of 10 years, and children age 14 years had the lowest frequency (4.9%).<sup>[20]</sup> In a study by Ramalingam *et al.*, prevalence of frequency and urgency were moderately lower (74% and 63%, respectively).<sup>[7]</sup> This difference could be due to the age difference of the studied population, because the prevalence of frequency and urgency is higher

in lower age groups and their prevalence decreases with age. Because from birth to about 12 years old, an average of about 1–2 ounces per year is added to the bladder volume;<sup>[4]</sup> while in our study, in contrast to Ramalingam *et al.*'s study, lower age groups are also investigated. In our study, 83.6% of patients with constipation suffered from LUTD and prevalence of constipation among patients with LUTD was 43.1% which is known as dysfunctional elimination syndrome. Prevalence of constipation in Ramalingam *et al.*'s study was 64% in patients with LUTD.<sup>[7]</sup> In our study, the prevalence of LUTD in patients with single episode of UTI was 50.5% and in patients with recurrence of UTI was 88.9%. The difference in the prevalence of LUTD between the group with single-episode UTI and the group with recurrence of UTI was significant, while in the same study by Ramalingam *et al.* The result was a reversal of our study.<sup>[7]</sup> It seems that the reason for this difference was a significant percentage of patients with recurrence of UTI (34.6%) in our study population. Also, in this study we performed DMSA scan to assess the effect of recurrence of UTI on scar formation, which showed that 90.9% of patients with unilateral scar formation had recurrent UTI. Also, in patients in whom there was no recurrence, only 6.3% had unilateral scars, which revealed a significant relationship between scar formation and recurrent UTI ( $P = 0.003$ ) which is similar to a study by Benador *et al.*<sup>[21]</sup> So, it is necessary to assess the children with recurrent UTI to find and prevent any scar formation at an earlier stage. In this study, all patients with scar formation had reflux. Also, 37.7% of patients with reflux had kidney scars, and in patients without reflux, the scar was not observed at all which indicates that there is a significant relationship between scar formation and VUR ( $P = 0.001$ ), similar to a study by Lee *et al.*<sup>[22]</sup> Contrary to what was mentioned in a study by van Gool JD *et al.*, in our study there was no significant correlation between LUTD and VUR.<sup>[23]</sup> Also, there was no association between LUTD alone and kidney scar formation in our study.

## Conclusions

These data suggest that there is a significant relationship between UTI and LUTD in children, so evaluation of LUTD is necessary for this group of patients. With early diagnosis and appropriate treatment, we can reduce the possible side effects of LUTD in patients with UTI.

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## Conflicts of interest

There are no conflicts of interest.

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