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Measurement of the Knowledge of Pediatric Residents about the Urinary Tract Infection in Children

ABSTRACT

Objectives: Urinary tract infection (UTI) is one of the most common infectious diseases in children. However, although several specific guidelines have been published, the management of UTI has not been standardized. In this study, we evaluated the knowledge of residents about UTI using an online questionnaire. It was aimed to increase the interest and attention of residents on UTI.

Methods: The questionnaire consisted of 42 multiple-choice and true/false questions prepared through "Google Forms." The questions were sent to resident physicians working in Ankara province through various "WhatsApp" groups. Participation in the survey was voluntary.

Results: Ninety-three research assistants participated in the survey. The proportion of physicians in the first 2 years of residency training was 29.1%, and in the last year was 54.9%. 25.8% of residents felt competent about UTI. Bladder-bowel dysfunction, vesicoureteral reflux, and obesity were confirmed as risk factors by 98.9% of residents. However, 35.5% of the residents stated that fever is not seen in lower urinary tract infection and 5.4% stated that pyuria is sufficient for the diagnosis of UTI. The use of prophylaxis was thought to prevent renal scarring by 78.5%. Probiotic/prebiotic use was reported to be protective by 40.9%.

Conclusion: UTI can be managed differently depending on the level of knowledge and experience of physicians. In addition to correct answers, incorrect/incomplete answers were also noteworthy in our survey. Collaboration among physicians caring for pediatric patients and agreement on common guidelines are thought to provide more appropriate management of pediatric UTIs.

Keywords: Pediatrics, prophylaxis, residency training, urinary tract infection

Urinary tract infection (UTI) is one of the most common infectious diseases in childhood. It is divided into two main groups according to the site of occurrence. Upper urinary tract infection is an infection of the renal pelvis and/or renal parenchyma, while lower urinary tract infection is limited to the bladder and urethra (1). The clinical picture is quite heterogeneous, and symptoms such as dysuria, frequent urination, and incontinence are observed in lower urinary tract infections, whereas fever and flank pain are usually present in upper urinary tract infections (2). UTI affects 2.8% of children each year, with a recurrence risk of up to 30% (3). The prevalence of UTIs shows a bimodal distribution, reaching peak levels in the first year of life and during toilet training between 2-4 years of age. In the first 6 months of life, UTI is more common in uncircumcised male infants, whereas it is more common in girls after the age of one year (4).

Urine sampling is very important for the diagnosis of UTI. The technique used to obtain a urine sample for urinalysis or culture affects the contamination rate and may lead to misinterpretation of the results. Suprapubic aspiration and bladder catheterization have low contamination rates, but being invasive procedures, they cause various difficulties in daily use. Obtaining a urine sample with a plastic bag attached to the genital area is the most commonly used method, but it is simple and noninvasive with a high contamination rate. Therefore, the bag method should not be used for urine culture (5). A positive urinalysis for nitrite or nitrite with leukocyte esterase has a high specificity for the diagnosis of UTI and initiation of empirical antibiotic treatment (6).

In terms of UTI treatment, most guidelines recommend different molecules for empirical treatment selection (7). The antibiotic to be used should be selected according to

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local resistance patterns. The most common bacterial cause of UTI in infants and children is Escherichia coli (E. coli). Approximately 50 percent of E. coli are resistant to amoxicillin or ampicillin. In addition, the frequency of E. coli producing extended-spectrum beta-lactamase is increasing, leading to higher rates of resistance to amoxicillin-clavulanate. Resistance rates to trimethoprim-sulfamethoxazole have also increased in some populations in recent years. Therefore, cephalosporin group antibiotics are recommended as first-line oral agents in the treatment of UTI in children (8). Antibiotic prophylaxis can be used in the presence of a history of recurrent UTI (≥3 episodes per year), in the presence of high-grade vesicoureteral reflux (VUR) (stage 4-5), or until voiding cystourethrography (VCUG) is performed when indicated. Although there has been a recent trend to decrease the use of prophylactic antibiotics, prophylaxis in selected cases may protect against long-term adverse outcomes (9).

Although several specific guidelines have been published in recent years, UTI management has not been standardized (10-14). In this study, we evaluated the knowledge level of residents working as research assistants in the Departments of Pediatrics in university and training and research hospitals in Ankara province in terms of diagnosis and treatment of UTI using an online questionnaire. It was aimed to increase the interest and attention of resident physicians on UTI by drawing attention to various guidelines on the subject.

METHODS

The questionnaire study, aimed at measuring the level of knowledge of residents working as research assistants in the Department of Pediatrics in terms of diagnosis, treatment, and follow-up of UTI, was a multicenter cohort study in Ankara province. The questionnaire consisted of 42 questions with multiple choice and true/false options prepared through "Google Forms." The questions could be answered in 10-15 minutes. The survey was sent to resident physicians via various "WhatsApp" groups. Participation in the survey was voluntary. Before starting to answer the survey questions, the participants were asked for their place of work information, and the data were stored electronically.

In the first part of the questionnaire, the participants were asked about the year of their residency training, whether they were working in the Pediatric Nephrology service or outpatient clinic, and whether they felt competent in terms of UTI management. In the following questions, their level of knowledge about the definition and risk factors of UTI, the gold standard method for urine sampling, the conditions required for definitive diagnosis of infection, treatment, imaging methods, indications for starting prophylaxis, and other preventive measures for UTI were questioned (10-14).

Ethical approval for the study was obtained by the Gazi University Ethics Commission on 05.10.2023 with the research code 2023-1135.

Statistical Analysis

In the presentation of descriptive statistics, categorical data were presented as number (percentage). Cross-tabular analyses and Fisher's exact Chi-square tests were used to compare the qualitative characteristics of the groups. The Shapiro Wilks test was used to determine the normal distribution of numerical measurements in the groups. Two groups were compared using independent samples t-test and Mann-Whitney U test for those not normally distributed. IBM SPSS Statistics version 22 package program was used for all statistical analyses. The significance level was taken as $p<0.05$.

Table 1. General characteristics of the pediatric residents who participated in the survey

Sex	**%**
Female	75.3
Time spent in specialized training	
0-1 year	14
1-2 years	15.1
2-3 years	16.1
3-4 years	54.8
Units in the Department of Pediatric Nephrology	
Pediatric Nephrology inpatient clinic	86
Pediatric Nephrology outpatient clinic	73.1
Both	67.7
Feeling competent in the diagnosis/treatment/ prophylaxis of urinary tract infection	25.8

RESULTS

A total of 93 residents working as research assistants in the Department of Pediatrics in Ankara participated in the survey (Female/male: 3.2). The proportion of physicians in the first 2 years of residency training was 29.1% and 54.9% in the last year. The majority of the physicians worked in the Pediatric Nephrology service or Pediatric Nephrology outpatient clinic during their residency training (86% and 73.1%, respectively). The proportion of residents who had worked in both units was 67.7%. However, only 25.8% of the participants felt competent in the diagnosis, treatment, and follow-up of UTI (Table 1).

Bladder-bowel dysfunction, VUR, and obesity were confirmed as risk factors for UTI by 98.9% of the residents. However, 45.2% of the residents stated that the frequency of UTI was higher in girls in the first year of life, 35.5% stated that fever was not seen in lower urinary tract infection, and 5.4% stated that pyuria alone was sufficient for the diagnosis of UTI. When evaluated according to the duration of residency training, physicians in the first year of residency gave more incorrect answers to these questions than physicians in the last year of residency, although not statistically significant [46.4% versus 37.3% (p=0.329), 43.1% versus 30.8% (p=0.369), and 15.4% versus 5.9% (p=0.237), respectively].

Suprapubic aspiration as the gold standard for diagnosis was correctly answered by 72%. While 15.1% of the participants stated that urine sampling by urethral catheterization and 12.9% stated that midstream urine sampling was the gold standard, no physician chose the bag urine method. In the evaluation according to the duration of specialty training, although not statistically significant, physicians in the first year of specialty training correctly accepted suprapubic aspiration as the gold standard at a lower rate than physicians in the last year of specialty training (61.5% vs. 74.5%, p=0.905). These percentages were similar between physicians who had not yet worked in the Department of Pediatric Nephrology and

physicians who had worked in this department (66.7% vs. 74.6%, p=0.691).

More than one-third of the participants (n=34, 36.6%) thought that the growth of 100,000 colonies of bacteria per mL in a bagged urine sample was accurate for the definitive diagnosis of UTI. In cases of pyuria in midstream urinalysis, 52.7% and 60.2% of the residents answered correctly that the growth of 50,000 colonies of bacteria per mL in culture and 1,000-10,000 colonies of bacteria in urethral catheterization would be sufficient for the diagnosis of UTI. More than one-fifth of the participants (n=21, 22.6%) reported that asymptomatic bacteriuria should be treated. Residents in their first year of residency training were more likely to have incorrect knowledge on this topic than those in their final year of training (46.2% vs. 19.6%, p=0.159). Residents who had worked in the Department of Pediatric Nephrology were more likely to know that asymptomatic bacteriuria did not need to be treated than those who had not yet worked in the department (77.6% vs. 62.5%, p=0.335). Almost all residents correctly answered that indications for intravenous treatment include severe patient presentation, vomiting and/or non-compliance with oral therapy, and that neonates and infants younger than 2 months should be treated parenterally due to the risk of urosepsis and severe pyelonephritis (97.8% and 96.8%, respectively).

It was known by 57% of the participants that all pyelonephritis cases should be evaluated with urinary tract ultrasonography (USG) after the first UTI. This was significantly higher among last year residents than first year residents (70.6% vs. 38.5%, p=0.016). Similarly, physicians who had worked in both the Pediatric Nephrology outpatient clinic and the Pediatric Nephrology service were more likely to confirm the need for urinary tract USG after pyelonephritis than physicians who had not worked in these departments (65.1% vs. 40%, p=0.022). Almost all participants correctly answered that VCUG can detect changes consistent with VUR, urethral obstruction due to posterior urethral valves, ureterocele, and/or neurogenic bladder (93.5%).

The rate of residents who thought that prophylactic antibiotics should be initiated in patients with 3 or more UTIs per year was 80.6%. No significant difference was found in the evaluations comparing the necessity of initiating prophylactic antibiotics in patients with recurrent UTI in terms of the time spent in the specialty training process, and the rates of physicians who stated that prophylaxis was necessary were numerically similar (84.6% among residents in the first year of specialty training, 78.6% among residents in 1-2 years, 73.3% among residents in 2-3 years, and 82.4% among residents in the last year of training, p=0.855). Almost all of the participants were aware that prophylactic antibiotics should be initiated in patients with stage 4-5 VUR on VCUG (95.7%). However, the necessity of short-term prophylaxis due to VCUG was correctly answered by 23.7%. This rate was 23.1% and 25.5% in first and last year residents, and although not statistically significant, it was similar in all groups (p=0.969). The rate of residents who reported that every patient undergoing clean intermittent catheterization should receive long-term prophylaxis was 80.6%. The proportion of residents in the first year of residency training who thought that long-term prophylaxis should be used in every patient was higher compared to residents in the last year of residency training (92.3% vs. 76.5%, p=0.586).

Almost all residents correctly recognized that amoxicillin, trimethoprim/sulfamethoxazole, or nitrofurantoin are the antibiotic options for long-term prophylaxis (96.7%). However, the rate of physicians who thought that trimethoprim/sulfamethoxazole should be used for prophylaxis in the first two months of life was 31.2%. Prophylaxis is thought to prevent renal scarring by 78.5%. This misconception was slightly higher among first-year residents compared to last-year residents (84.6% vs. 72.5%, p=0.483). While 23.5% of the residents who had worked in a pediatric nephrology service or outpatient clinic knew that antibiotic prophylaxis does not prevent renal scarring, none of the residents who had not yet worked in this department answered this question correctly (p=0.043). Vitamin A supplementation can be used to reduce scar formation was known by 22.6% of the participants. In the comparisons made among residents in terms of this knowledge, it was observed that the duration of specialty training or whether or not they worked in the Pediatric Nephrology department did not make a significant difference (14.3% among residents in the first year of specialty training, 28.6% between 1-2 years, 19.4% between 2-3 years, 23.5% among residents in the last year, p=0.153; 22.5% among physicians who had worked in the Pediatric Nephrology service and 23.1% among physicians who had not, p=0.604; 19.1% among physicians who had worked in the Pediatric Nephrology outpatient clinic and 32% among physicians who had not, p=0.188).

When other factors other than antibiotic prophylaxis that may be protective in terms of UTI were questioned, prevention of constipation and circumcision in male patients with recurrent UTI or high-grade VUR were known to prevent the development of infection by the majority of the physicians surveyed (94.6% and 88.2%, respectively). Consumption of cranberry fruit/juice, probiotic/prebiotic use, and short-term application of local steroid cream to the tip of the penis in boys with physiologic phimosis were correctly recognized by 26.9%, 40.9%, and 22.6%, respectively.

The correct and incorrect statements among the items asked to the Pediatric Health and Diseases resident physicians in order to measure their level of knowledge about the diagnosis, treatment, and prophylaxis of urinary tract infections are presented in Table 2 and Table 3, respectively.

DISCUSSION

UTI, which is a very common bacterial infection in the pediatric population, constitutes an important cause of antibiotic use and hospitalization in children. It is known that the risk of UTI in infants up to the age of one year is higher in boys, especially in uncircumcised male infants, and after the age of one year, the male-female ratio reverses (7). However, approximately half of the resident physicians who participated in our survey stated that the frequency of UTI was higher in girls in the first year of life, suggesting that their level of knowledge about gender distribution in UTI was insufficient.

The diagnosis of pediatric UTI is challenging due to its non-specific clinical presentation. Fever may be the sole clinical symptom, particularly in young children. UTI should be considered in the differential diagnosis of children presenting with fever without an apparent source (15). Neonates and infants under three months typically present with non-specific symptoms such as feeding difficulties, restlessness, jaundice, or vomiting, and sometimes hypothermia. Older

Table 2. Correct statements and the proportion of participants selecting the relevant option when asked to measure their level of knowledge about the diagnosis, treatment and prophylaxis of urinary tract infections by pediatrics residents

General Informations Related to Urinary Tract Infection:	**%**
Bladder-bowel dysfunction, vesicoureteral reflux, and obesity are some of the risk factors for urinary tract infections.	98.9
Newly developed enuresis nocturna with a diagnosis of urinary tract infection suggests lower urinary tract infection.	75.3
A fever of 38.5°C and above is indicative of pyelonephritis.	97.8
Informations Directed for the Diagnosis of Urinary Tract Infection:	
The presence of 100,000 colony-forming units of bacteria per milliliter (mL) in midstream urine confirms the diagnosis of urinary tract infection.	77.4
In the presence of pyuria, the presence of 50,000 colony-forming units of bacteria per milliliter (mL) in midstream urine confirms the diagnosis of urinary tract infection.	52.7
The presence of 1,000 to 10,000 colony-forming units of bacteria per milliliter (mL) in urethral catheterization confirms the diagnosis of urinary tract infection.	60.2
In infants under 4 months of age, the presence of 1,000 colony-forming units of bacteria per milliliter (mL) in urine obtained by urethral catheterization confirms the diagnosis of urinary tract infection.	31.2
Informations Directed for the Treatment of Urinary Tract Infection:	
Indications for intravenous therapy include the appearance of a severely ill patient, vomiting, and/or non-compliance with oral therapy.	97.8
Newborns and infants under 2 months of age should be treated parenterally due to the risks of urosepsis and severe pyelonephritis.	96.8
If sensitive according to the antibiogram, no antibiotic has superiority over another.	53.8
There is no difference in efficacy between starting with parenteral treatment and switching to oral treatment after the third day.	61.3
Informations Directed for Imaging Methods after Urinary Tract Infection:	
In patients diagnosed with urinary tract infection, imaging should be performed in the presence of pseudohypoaldosteronism to assess obstructive uropathy.	36.6
All cases of pyelonephritis should be evaluated with urinary system ultrasonography (USG) after the first infection.	57
Voiding cystourethrography (VCUG) can detect changes consistent with vesicoureteral reflux (VUR), posterior urethral valves (PUV) in male children, ureteroceles, and/or neurogenic bladder.	93.5
Informations Directed for Prophylaxis of Urinary Tract Infection:	
Planning for VCUG is one of the indications for starting antibiotic prophylaxis.	23.7
Detection of grade 4-5 VUR in VCUG is one of the indications for starting antibiotic prophylaxis.	95.7
Having a history of 3 or more urinary tract infections per year is one of the indications for starting antibiotic prophylaxis.	80.6
Vitamin A prophylaxis reduces scar formation after urinary tract infection.	22.6
Options for antibiotic prophylaxis include amoxicillin, trimethoprim/sulfamethoxazole, and nitrofurantoin.	96.7
Nitrofurantoin and cotrimoxazole doses can be applied as 2 mg/kg/day.	58.1
In cases where urinary tract infection occurs 2 or more times under prophylaxis, the active substance used in prophylaxis should be changed.	80.6
Informations Items Directed for Factors That Can Be Protective against Urinary Tract Infection:	
Circumcision in male patients with recurrent urinary tract infections or high-grade VUR is protective against urinary tract infections.	88.2
The use of topical steroid cream on the tip of the penis in male children with phimosis is protective against urinary tract infections.	22.6
Consumption of cranberry juice/fruit is protective against urinary tract infections.	26.9
The use of probiotics/prebiotics is protective against urinary tract infections.	40.9
Prevention of constipation is protective against urinary tract infections.	94.6

children may exhibit lower urinary tract symptoms like increased frequency of urination, dysuria, and continence disorders, along with complaints of abdominal pain and lower back pain. The risk of upper urinary tract infection is higher if the patient has a fever of 38°C or higher, but fever can also occur in lower urinary tract infections. Therefore, in many pediatric cases, it is not possible to clearly distinguish between upper or lower urinary tract infections (1). In our survey, approximately one-third of our resident physicians stated that fever would not be observed in lower urinary tract infections, indicating insufficient knowledge regarding UTI symptoms.

The role of urine dipstick examination in diagnosing UTI remains contentious. The specificity of nitrite positivity or positive nitrite results with leukocyte esterase is high enough to diagnose UTI and initiate empirical treatment (16). The National Institute for

Table 3. Incorrect statements directed towards pediatric health and disease assistant physicians to measure their knowledge levels regarding diagnosis, treatment, and prophylaxis of urinary tract infections, and the rate of participants choosing the relevant option

General Informations Regarding Urinary Tract Infection:	**%**
The prevalence is higher in girls within the first year of life.	45.2
Fever is not observed in lower urinary tract infections such as cystitis.	35.5
The presence of pyuria in urine is sufficient for the diagnosis of urinary tract infection.	5.4
Enterococcus feacalis is the causative agent in the majority of cases.	15.1
Having ⩾2 urinary tract infections in the past year is defined as recurrent urinary tract infection.	67.7
Informations Directed for the Definite Diagnosis of Urinary Tract Infection:	
The presence of 100,000 colony-forming units of bacteria per milliliter (mL) in bag urine is one of the definite diagnostic criteria for urinary tract infection.	36.6
Informations Directed for the Treatment of Urinary Tract Infection:	
Asymptomatic bacteriuria should be treated due to the risks it carries.	27.3
In the treatment of uncomplicated lower urinary tract infections, 7-10 days of oral treatment is superior to 3-7 days of oral treatment.	26.9
Informations Directed for Imaging Methods after Urinary Tract Infection:	
The detection of abnormal ultrasound findings after the first pyelonephritis or a history of recurrent febrile urinary tract infections encompasses all indications for voiding cystourethrography (VCUG).	55.9
If a pathogen other than enteropathogenic E.coli is detected, VCUG is not necessary.	4.3
Informations Items Directed for Prophylaxis of Urinary Tract Infection:	
Intermittent clean catheterization due to neurogenic bladder or posterior urethral valves is one of the indications for starting antibiotic prophylaxis.	80.6
Long-term prophylactic antibiotic use reduces the frequency of febrile urinary tract infections more in boys under 2 years of age compared to girls.	54.8
Long-term prophylactic antibiotic use significantly prevents renal scar formation in both sexes.	78.5
Trimethoprim-sulfamethoxazole should be used for antibiotic prophylaxis in the neonatal period.	31.2
Informations Directed for Factors That Can Be Protective against Urinary Tract Infection:	
Reducing fluid intake is protective against urinary tract infection.	5.4

Health and Care Excellence (NICE) guidelines recommend urine culture only for patients at risk of severe illness or with a history of recurrent UTIs, and treatment planning based on nitrite/leukocyte esterase results in other patients (14). Conversely, guidelines from the Italian Society of Pediatric Nephrology (SINePe) and the European Society of Urology/European Association of Pediatric Urology (EAU/ESPU) strongly advise that urine culture should always be performed in the case of nitrite/leukocyte esterase positivity on dipstick (11,12). In our study, 5.4% of the resident physicians stated that pyuria alone was sufficient for the diagnosis of UTI, which may result from the discrepancies in UTI diagnostic criteria among the guidelines that the residents apply.

Urine sampling for urine culture is critical for diagnosing UTI. Different techniques are employed in daily practice. The technique used to obtain urine for urinalysis or culture influences the contamination rate, which may hinder accurate evaluation of the results, especially in early infancy (17). Suprapubic aspiration and bladder catheterization have low contamination rates but are invasive procedures that raise concerns, especially among parents. Consequently, a plastic bag attached to the genital area has become the most commonly used technique for urine collection in daily practice, but despite being simple and noninvasive, it has a high contamination rate of up to 63% and should not be used for culture (18,19). However, in our survey, more than one-third of the physicians stated that growth in urine culture obtained by the bag method was sufficient for the definitive diagnosis of UTI. Recent updates in different guidelines have generally lowered the thresholds for defining a significant positive urine culture. A threshold of 50,000 CFU/mL is typically considered significant, but this threshold varies depending on the urine collection technique. Some guidelines recommend lower thresholds for urine obtained by suprapubic aspiration or urethral catheterization and higher thresholds for the clean capture/midstream method (10,20). More than half of the physicians in our survey reported that they consider 50,000 colonies of bacteria per mL in culture to be significant in the presence of pyuria in midstream urinalysis and 1,000-10,000 colonies of bacteria in urethral catheterization.

Empiric therapy for pediatric UTI is a contentious area, and most guidelines recommend a broad range of molecules as appropriate empiric therapies. Thus, the choice of initial antibiotic often depends on personal experience. The misuse and overuse of antibiotics are the primary causes of the alarming spread of antibiotic resistance in community-acquired pediatric UTIs, which further increases the risk of resistance development by promoting the empirical use of broad-spectrum molecules (1,21). The situation is similar for prophylactic antibiotics used without a real indication. Although pro-

phylactic antibiotics reduce the frequency of recurrent UTI by up to 50%, they are not effective in preventing new renal scar formation (22,23). In our survey, the rate of physicians who believed that antibiotic prophylaxis prevented new renal scar formation was quite high. This finding suggests that resident physicians lack knowledge about the necessity of prophylaxis. In the presence of low-grade VUR, the complications of prophylaxis outweigh the benefits, and prophylaxis is not recommended in patients with low-grade VUR (24). In our survey, almost all participants reported that prophylaxis should be used in patients with high-grade VUR.

Prophylactic non-antibiotic preventive measures classically include increasing fluid intake, ensuring genital hygiene, correction of bladder-bowel dysfunction and voiding dysfunction, and circumcision for male infants younger than 1 year and diagnosed with recurrent UTI (25). In addition, cranberry, vitamin A supplementation, and probiotic/prebiotic use have also been shown to reduce the frequency of UTIs and prevent renal scar formation (26-28). Approximately one-quarter of the resident physicians who participated in our survey were aware of the benefits of cranberry and vitamin A in terms of UTI. The protective properties of probiotic/prebiotic use were known by 40.9% of our physicians.

In conclusion, since UTI is a common problem for primary care pediatricians and a major cause of pediatric emergency department visits, collaboration among pediatricians and agreement on common guidelines are essential for the appropriate management of pediatric UTIs. Although several specific and well-established guidelines have been published in recent years, the management of pediatric UTI remains controversial. UTI may be managed differently depending on the level of knowledge and experience of physicians. In our study, we observed that residents who were in the last year of their residency training and/or had worked in pediatric nephrology units were more knowledgeable about the diagnosis, treatment, and follow-up of UTIs than residents who were at the beginning of their training and had not yet done a pediatric nephrology rotation. In addition to correct answers, incorrect/incomplete answers were also noteworthy in our survey. At some points, it was observed that the awareness and knowledge levels of the participants were low. However, the fact that the resident physicians who participated in the survey were at different stages of their specialty training and that different recommendations regarding UTI management were given in various guidelines should not be ignored. In conclusion, it is thought that updating the knowledge of residents on UTI management in every period of their training with new guidelines is extremely important to eliminate the long-term negative consequences of pediatric UTIs.

Ethics Committee Approval: This study was conducted with the permission of the Gazi University Local Ethics Committee (decision no: 2023-1135, date: 15.10.2023).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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