HAYDARPAŞA NUMUNE MEDICAL JOURNAL

DOI: 10.14744/hnhj.2019.61580
Haydarpasa Numune Med J 2021;61(2):149–154

hnhtipdergisi.com

ORIGINAL ARTICLE

Evaluation of Clinical and Laboratory Findings of Patients Hospitalized for Urinary Tract Infection

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Abstract

Introduction: Urinary tract infections (UTIs) are common and important because of their long-term consequences in childhood. The treatment of UTI consists mainly of antimicrobial agents to eliminate the symptoms, to prevent urosepsis, and to reduce the likelihood of renal damage. Here, we aimed to evaluate the clinical, laboratory findings of children hospitalized for UTI, in a 3-year period.

Methods: Hospital records of the patients were investigated retrospectively. Data about demographic features, past and family history, clinical and laboratory findings, urine sampling methods, microorganisms isolated from urine culture, treatment duration, and recurrent hospitalization data were collected. Urinary system imaging (USG), dimercaptosuccinic acid scintigraphy, and voiding cystourethrography findings were obtained.

Results: We enrolled 201 children aged between 1 month and 18 years (median age: 10 months) to our study. About 45.8% of children had urinary tract anomalies. The presence of recurrent UTI, congenital anomaly, and vesicoureteral reflux was 26.4%, 8.5%, and 8.5%, respectively. The most common symptoms were fever (54.2%), vomiting (22.9%), and dysuria (12.4%). Upper urinary tract involvement rate was 45.3%. Fever was observed in children with upper UTI significantly (p=0.0001) more than in children with lower UTI, while jaundice (p=0.004) and restlessness (p=0.039) were observed more in lower UTI than in upper UTI. *Escherichia coli* was the most isolated agent from urine cultures (74.6%). About 26.9% of cases (n=54) had pathologic urinary sonography (USG) findings. About 53.7% and 55.2% of cases had 99m Tc-DMSA scintigraphy and VCUG, respectively. Thirty-one cases with DMSA and 32 cases with VCUG had pathologic findings. Mean duration of treatment was 8.48±1.94 days.

Discussion and Conclusion: Urinary tract infections should be in differential diagnosis of infants with fever and vomiting. Appropriate antimicrobial and supportive treatment, urinary tract imaging studies, in relevant cases, multidisciplinary treatment, and follow-up are the main steps of UTI management. Treatment should be aimed according to resistant microorganisms in cases with urinary tract anomalies. Before initialization of treatment, urine culture should be done. Cases with renal scarring should be followed up for long-term complications.

Keywords: Fever; pediatrics; urinary tract infections.

Urinary tract infections (UTIs) are the most common infections after upper respiratory tract infections in childhood. Recurrent UTIs are common, especially in children with urinary tract abnormalities or known renal disease. In children with recurrent UTIs, voiding disorders, and/or urinary system anomalies, complications such as

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Submitted Date (Başvuru Tarihi): 04.02.2019 **Accepted Date (Kabul Tarihi):** 05.05.2019

renal scarring, progressive deterioration in renal functions, renal failure, and hypertension may occur[1].

Vesicoureteral reflux (VUR) and renal scarring leading to chronic kidney disease are known to be in association. For this reason, in 2010, the American Urological Association recommended that the condition of the kidney, growth parameters, and blood pressure should be evaluated first in a child with VUR[2]. As laboratory tests, complete urinalysis, presence of pyuria and proteinuria, and serum creatinine level should be checked. The condition of the kidney should be examined with renal imaging. Congenital conditions that may cause hydronephrosis are excluded with renal USG. Dimercaptosuccinic acid (DMSA) scan is more useful in detecting renal cortical anomalies, and USG is more useful in patients with renal parenchyma loss or risk of renal scarring, than other imaging methods. VUR is a risk factor for recurrent pyelonephritis and possible renal scarring. The higher the degree of reflux, the higher the risk of renal scarring. For this reason, voiding cystourethrography (VCUG) is recommended for children at risk with febrile UTI[3].

UTIs and reflux nephropathy are the most common causes of renal failure in our country[4]. It is aimed to eliminate the symptoms, prevent urosepsis, and minimize the possibility of renal damage with appropriate treatment in UTIs. When starting the treatment, it is started empirically considering the clinical and laboratory findings of the patient, possible microorganisms according to the age group, antibiotic resistance in the community and patient compliance[5].

In our study, we aimed to examine the clinical, laboratory, and imaging findings of patients who were hospitalized with the diagnosis of UTI in a 3-year period.

Materials and Methods

All children (1 month–18 years old) who were hospitalized with a pre-diagnosis of UTI and had growth in their urine cultures between January 2009 and January 2012 in Zeynep Kamil Women and Child Diseases Training and Research Hospital Pediatric Clinic were included in the study. Newborns, patients with suspicion of nosocomial infection, patients who were followed up for spina bifida or neurogenic bladder, patients who were followed up in an outpatient clinic, and patients with mixed growth or contamination with more than 1 bacteria in their urine cultures were not included in the study.

The files of the cases were analyzed retrospectively from the hospital records. Age, gender, weight percentiles of the cases, admission complaints, personal and family history, complete blood count, C-reactive protein (CRP), renal and liver function tests, electrolyte levels, complete urinalysis, urine culture result, method of collecting urine for culture, microorganism isolated from urine culture, duration of treatment, and history of recurrent hospitalization due to UTI data were collected. Urinary system imaging results were examined; USG, 99m Tc-DMSA scintigraphy scan, if available, and voiding cystourethrography (VCUG) findings were recorded.

Urine cultures were taken under sterile conditions with catheterization, suprapubic aspiration, or in children who gained voiding control, as midstream urine sampling. UTI was defined according to the American Academy of Pediatrics guidelines. Growth of $>10^5$ cfu/ml Gram-positive bacteria in culture obtained from midstream urine, of $>10^4$ cfu/ml in culture obtained by urinary catheterization, and of $>10^3$ cfu/mL in cultures obtained by suprapubic aspiration, and Gram-negative growth of 1 cfu/mL was considered significant. Samples in which more than 1 microorganism was isolated were not included in the study. Five or more leukocytes in each microscope field at 40× of the centrifuged urine were considered as "pyuria" and 5 or more erythrocytes as "hematuria[3]".

Infants and children with fever of 38°C and above, flank pain/costovertebral angle tenderness, and the presence of bacteriuria were considered acute pyelonephritis/upper UTI[6] and the diagnosis was supported by the high level of markers such as leukocytosis, CRP/procalcitonin. A blood leukocyte value of >14.000/mm^3 in 1–23 months old children, >12.000/mm^3 in children aged 2–9 years, and >10.500/mm^3 in children aged 10–17 years was evaluated as leukocytosis. Serum CRP value of >1 mg/dL was considered pathological.

Recurrent UTI was considered as two or more pyelonephritis/upper UTI or one pyelonephritis/upper UTI + one or more cystitis/lower UTIs, or three or more cystitis/lower UTIs[6].

SPSS (Statistical Package for the Social Sciences Version 15.0 for Windows, SPSS ® Inc., Chicago, IL, USA) was used for the statistical evaluation of the data obtained in the study. In addition to descriptive statistical methods (such as minimum, maximum, and median), Chi-square test and Fisher's exact test were used for categorical variables in analyzes comparing two groups. The results were evaluated within a 95% confidence interval and a significance level of $p<0.05$. Approval was obtained from the ethics committee of our hospital for the study.

Results

A total of 201 patients, 51.7% (n=104) of whom were female, were included in the study. The age of the patients ranged from 1 month to 18 years, and the median age was 10 months. The number of patients under the age of 1 was 110 (75.5% male). Male gender was at the forefront in the 1st year of age and female after the age of 1 (p=0.001).

There was urinary system pathology in the history of 45.8% (n=92) of the patients and in the family history of 1.5% (n=3). Urinary system anomaly was not found in 54.2% of the cases. The rate of recurrent UTIs was 26.4%, and the rate of congenital anomalies and VUR was 8.5% for each.

The proportion of those whose weight was below the 25th percentile was 21.4% (n=43) and the proportion of those above the 75th percentile was 38.3% (n=77). When compared with cases above the 75th percentile, the presence of urinary system pathology was found to be significantly higher in cases below the 25th percentile and between the 25th and 50th percentile (p<0.05).

While the most common complaints were fever (54.2%), vomiting (22.9%), and dysuria (12.4%), 8.5% of the patients had no symptoms. Only 5.5% (n=11) of the patients had UTI findings in their physical examination findings. In terms of the location of the UTI, the upper urinary system was affected in 45.3% (n=91) of the patients and the lower urinary system was affected in 54.7% (n=110). In Table 1, the admission complaints of the patients according to the location of the UTI are presented.

When the whole blood leukocyte count, serum BUN, creatinine, and CRP values of the patients were examined, 23.4% (n=47) of the patients had leukocytosis, 4% (n=8) had electrolyte disturbance, 1.5% (n=3) had high serum BUN levels, 2% (n=4) had high serum creatinine, 55.7% (n=112) had high CRP levels, and 2.5% (n=5) had serum liver function tests disorders. Concomitant urinary system pathology was present in two of three patients with high serum BUN levels and three of four patients with high serum creatinine values.

The ratio of those with normal results in complete urinalysis (TIT) was 27.9% (n=56). Urine pH varied between 5 and 8 (mean 6.02±0.66) and urine density between 1000 and 1033 (mean 1012±7). Leukocyte esterase positivity was found in 30.3% (n=61) of the patients and protein positivity in 30.8% (n=62). In microscopic examination, the rate of pyuria and hematuria in urine at 40× was found to be 62.2% and 32.8%, respectively. Nitrite positivity was detected in urine in 23.9% of the patients (n=48). When nitrite positivity in urine was examined by age groups, the rate of those with nitrite 2+ in the age group >60 months was found to be significantly higher than the other age groups (p=0.007).

Growth was detected in the urine culture of 71.1% (n=143) patients during hospitalization. Urine samples were obtained by ureteral catheterization in 59.2% of the patients, by midstream urine sampling in 32.3%, and by suprapubic aspiration in 8.5%. There was no statistical relationship between urine collection method and growing microorganisms. *Escherichia coli* was the most common agent (74.6%) isolated in the urine culture. Microorganisms grown in urine culture and their frequencies are presented in Table 2.

The relationship between microorganisms isolated in urine cultures and complaints of patients hospitalized with UTI was examined. While fever was observed in all groups, it was significantly less in those who were infected with *group D hemolytic streptococci*, compared to those who were not infected and abdominal bloating was found to be more.

Table 1. Complaints at admission of patients according to the location of the urinary tract infection (upper/lower)

Complaint at admission	Upper urinary tract infection (n=91)	Lower urinary tract infection (n=110)	p
Fever	88	21	0.0001
Vomiting	21	25	0.953
Abdominal pain	11	10	0.489
Jaundice	0	9	0.004
Restlessness	4	14	0.039
Urinary problems	21	35	0.891
Constipation	1	0	0.453
Growth retardation	0	2	0.502
Flank pain	6	3	0.305
Anorexia	7	2	0.082
No symptom	1	16	0.001

Table 2. Microorganisms isolated from urine culture

Microorganism grown	Number of patients (n=201)	%
E. coli	150	74.6
Klebsiella spp.	14	7.0
Enterobacteriaceae spp.	8	4.0
Proteus spp.	7	3.5
Group D beta-hemolytic Streptococcus	7	3.5
Pseudomonas spp.	4	2.0
Other	11	5.5

Jaundice was significantly less in those infected with *E. coli* than in those who were not infected, growth retardation was significantly higher in those who were infected with *Pseudomonas*, and color abnormalities in urine were significantly higher in those who were infected with *Proteus* than in those who were not infected (p<0.05).

All patients were evaluated with urinary tract USG. Urinary tract USG findings were pathological in 26.9% (n=54) of the patients, hydronephrosis accompanying pelviectasis was found in 8% and diffuse thickening of the bladder wall was found in 8.5% of the patients. In 10.4% of the cases, other USG findings such as increased echogenicity in the renal parenchyma, solitary kidney, atrophic kidney, and extrarenal pelvis were observed.

DMSA could not be performed in 46.3% of the patients and VCUG in 44.8% of the patients. The result was pathological in DMSA scintigraphy in 31 patients and in VCUG in 32 patients (Grade 1 and 2 VUR 7.2% each; Grade 3 VUR 9%; and Grade 4 and 5 VUR 2.7% each). The rate of patients with normal USG results and pathological DMSA results was 9.3% (n=10), the rate of patients with normal USG results and abnormal VCUG results was 12.6% (n=14), and the rate of those with normal USG and DMSA findings and impaired VCUG findings was 6.5% (n=7) (Fig. 1).

Forty-four cases (21.9%) were hospitalized due to recurrent UTI. Urinary system pathology and VUR were found with a significantly higher rate in these patients compared to patients without rehospitalization (p=0.0001 and p=0.0001, respectively). The duration of treatment of the patients ranged from 4 to 17 days, and the mean duration was 8.48±1.94 (median=8) days.

Discussion

UTIs are important in terms of long-term problems such as renal scarring, hypertension, and kidney failure. Therefore, knowing the facilitating causes, symptoms and signs of UTIs in all age groups will help in early diagnosis and treatment. The frequency of UTIs in young children with fever is around 7%. This frequency may vary depending on gender, age, and circumcision status in male gender.

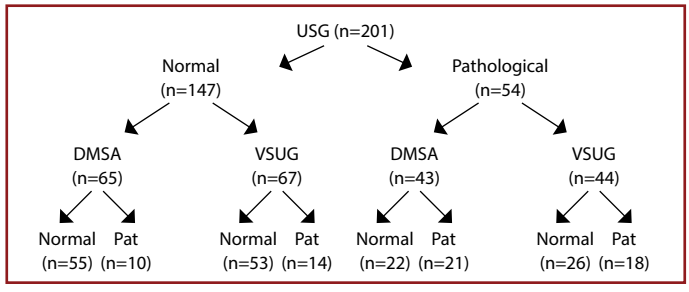

Figure 1. Urinary sonography, dimercaptosuccinic acid, and voiding cystourethrography results of the patients.

UTI is more common in boys in the neonatal period. The reason for this is the high frequency of congenital anomalies of the urinary system in boys[7-9]. Arıkan et al.[10] showed that UTIs are more common in girls outside the neonatal period and the risk of recurrence is higher (p<0.05). In our study, while female patients were in majority in the group with age over 12 months, and 75.5% of the patients in the 1–12 months of age range group were male. The presence of urinary system pathology in patients with 1–12 months of age was higher than in patients older than 60 months of age (p<0.0001). Compared to boys, girls had higher UTI findings on physical examination, presence of urinary system pathology, frequent UTI rates, and need for rehospitalization (p<0.05). Considering all age groups, we think that this situation is due to the fact that the infection is more common in girls.

UTIs can cause nonspecific signs and symptoms, especially in infants and young children. In a meta-analysis examining the accuracy of the diagnosis of UTI symptoms and findings in children under 2 years of age, the presence of UTI in the history, fever >40°C, suprapubic tenderness, absence of circumcision, and fever lasting longer than 24 h were found to be significant. In young children, fever can sometimes be the only finding. In children under 2 years of age, the rate of UTI in the presence of fever of >39°C was 4%, whereas it was found to be 2% at fever of <39°C. The absence of a source that can cause fever does not lead to a diagnosis of UTI, and the finding of the source of fever does not exclude the diagnosis of UTI. Prolonged jaundice, restlessness, feeding difficulties, and growth retardation in young children are among other symptoms and signs[11]. In older children, symptoms such as fever, urinary symptoms (dysuria, urgency, frequent urination, urinary incontinence, and macroscopic hematuria), and abdominal pain can be observed. Fever, chills, and flank pain suggest pyelonephritis. In a meta-analysis study, symptoms and signs of abdominal pain, back pain, dysuria and frequent urination, and new-onset urinary incontinence have been shown to be useful in the diagnosis in older children with self-expression[12].

The most common complaint in our study was fever (54.2%). Vomiting (22.9%) and dysuria (12.4%) were the other admission complaint frequently observed. In a study conducted in our hospital in 2008, the admission complaints of children with UTI were fever (62.7%), vomiting

(46%), abdominal pain (48.4%), and dysuria (49.2%)[13]. In another study, it was determined that UTI was found in 5.3% of infants with fever who applied to the emergency outpatient clinic, fever, nausea, and vomiting which were observed more frequently in patients younger than 2 years of age, and this was statistically significant (p<0.05)[14]. Although restlessness was common under the age of 1 year (p<0.05)[10], we could not obtain a similar result in our study. This difference may be due to the fact that we only examined patients who were hospitalized, outpatient UTI patients were not included in our study.

Physical examination in children with UTIs is usually normal[15]. In our study, only 5.5% of the patients had physical examination findings such as suprapubic tenderness and costovertebral angle tenderness associated with UTI.

Urine culture is the standard test in the diagnosis of UTI. Urine sample for culture should be collected by ureteral catheterization or suprapubic aspiration method in young children without toilet training. Clean midstream urine sample is suitable for culture in children who had toilet training[3]. We collected urine samples as ureteral catheterization (59.2%), suprapubic aspiration (8.5%), and midstream urine sample (32.3%). Urine samples obtained with bags in hospitalized patients are not preferred for culture due to the risk of contamination.

Nitrite positivity in urine is important in the diagnosis of UTI, but urine must wait for at least 4 h in the bladder for positivity. For this reason, urine nitrite is usually negative in UTIs, especially in young children where voiding is more frequent. In our study, we found that nitrite positivity was significantly higher in children over 60 months of age, compared to other younger age groups (p<0.007)[16]. In another study, it was observed that the rate of positivity in the nitrite test increased as the age of the children increased (p<0.05)[10].

Markers showing acute inflammation such as erythrocyte sedimentation rate, C-reactive protein (CRP), and procalcitonin are used in the diagnosis of upper urinary tract infection. In a meta-analysis conducted in 2015, the sensitivity of these markers was found to be 86–95% and specificity 38–71% in the diagnosis of culture-proven UTI and DMSA-confirmed pyelonephritis, between 0 and 18 years of age[17]. In our study, there was leukocytosis with a rate of 23.4% and CRP positivity with a rate of 55.7%. We evaluated 45.3% (n: 91) of our patients as upper UTI and 54.7% (n=110) as lower UTI.

The most common cause of UTI in the childhood age group is Gram (–) enteric bacilli and *E. coli* (84.8–92%) takes the first place. Other factors are *Klebsiella, Enterobacter, Proteus, Staphylococcus, Pseudomonas, Citrobacter, Serratia, and Providencia*[18-20]. In studies conducted in our country and in different countries, *E. coli* is significantly higher in urine cultures in girls than in boys (p<0.001)[18,21].

In our study, the most common isolated agent was *E. coli* (74.6%) in urine culture. There was no significant relationship between *E. coli* isolation and gender. *E. coli* (81.3%) was found with a significantly higher rate in those with upper UTI than in those with lower UTI (69.1%) (p<0.05). Other common agents seen in our study were Klebsiella (7%), *Enterobacter* (4%), and *Proteus* (3.5%). Salduz et al.[18] found the frequency of *Enterobacter spp*. in UTIs as 6.1%. In another study, it was stated that the prevalence of *Enterobacter spp.* was the lowest among pathogens causing UTI[22].

In our study, *E. coli* was significantly lower in patients with VUR (p=0.042), and *Pseudomonas* (p=0.037) and *group D β hemolytic* streptococcus (p=0.014) were significantly higher than those without VUR. *Proteus*, *Pseudomonas*, and *Candida spp*. are more frequently isolated in patients with underlying urinary tract pathology (p<0.001)[23]. Similarly, in our study, we isolated *Proteus* and *Pseudomonas spp.* agents from urine cultures more frequently in patients with urinary system pathology (p<0.05).

VUR and recurrent UTIs are known to be associated[24]. Forty-four patients (21.9%) were hospitalized with recurrent UTIs. Urinary system pathology and VUR were found with a significantly higher rate in these patients compared to patients without rehospitalization (p<0.001). There was no rehospitalization in patients without urinary system pathology (n=102). In our study, we found pathology in 28.7% and 28.8% after DMSA scintigraphy and VCUG, respectively (Grades 1 and 2 VUR 7.2% each; Grade 3 VUR: 9%; and Grades 4 and 5 VUR: 2.7% each).

Conclusions

The diagnosis of UTI should definitely be considered in the complaints of fever and vomiting in infancy. Appropriate antibiotic and supportive treatment of the infection, application of imaging methods, and multidisciplinary follow-up and treatment when necessary are important steps of UTI management. Considering that patients with underlying urinary system pathology may be infected with more resistant microorganisms, the treatment should be planned, and urine culture should be taken with an appropriate method beforehand. Patients with renal parenchymal damage and scarring should be followed up in terms of long-term complications (hypertension, renal failure, etc.).

Ethics Committee Approval: Scientific Research Board of Zeynep Kamil Women and Child Diseases Training and Research Hospital (5599/30.03.2011).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: D.M., A.B.; Design: D.M., A.B., R.G.B.; Data Collection or Processing: D.M., N.U.K.; Analysis or Interpretation: N.U.K., R.G.B.; Literature Search: D.M., N.U.K.; Writing: D.M., N.U.K., R.G.S., A.B.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study received no financial support.

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