

Research Article

J Ped. Nephrology 2017;5(3)
http://journals.sbmu.ac.ir/jpn

Etiologies of Urinary Tract Infections in Children Considering Differences in Gender and Type of Infection

How to Cite This Article: Naseri M, Tafazoli N. Etiologies of Urinary Tract Infections in Children Considering Differences in Gender and Type of Infection. J Ped. Nephrology 2017;5(3)

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Received: June-2017
Revised: June-2017
Accepted: Sept-2017

Introduction

Urinary tract infections (UTIs) are among the most frequent community-acquired infections worldwide [1]. They are the second most common infectious presentation in community medical practice [2], and are responsible for an estimated 9.6 million doctor visits in the United States each year [3].

Introduction: Urinary tract infection is a common health problem in children. Gram negative enteric bacteria, mainly E-coli, are responsible uropathogens. We aimed to define the main etiologies of urinary tract infection in children considering gender and type of infection (febrile versus afebrile).

Materials and Methods: We assessed the infections etiology of 648 episodes. Type of infection and etiology were compared between genders. Also, for every uropathogen, a comparison was done between febrile and afebrile infections. Chi square was used for data analysis and P values ≤ 0.05 were considered as a significant difference.

Results: The majority of the infections by Proteus and Enterococcus species were febrile, in contrast to Citrobacter infections which were mostly afebrile. E-coli infections were significantly more prevalent in girls ($P=0.0001$). Proteus and Kelebsiella infections were more common in boys ($P=0.115$ and 0.154 respectively), whereas all Enterobacter infections were seen in girls ($P=0.129$). A comparison was done between females and males based on the type of infection. Although febrile infections were more frequent in boys, the difference was not statistically significant ($P=0.059$).

Conclusions: E-coli, Kelebsiella, Enterobacter and Citrobacter species (90.5%) were the main uropathogens. Infections caused by E-coli were significantly more prevalent in girls. Proteus and Kelebsiella infections were more common in boys, whereas Enterobacter species were more prevalent in girls. The majority of Proteus and Enterococcus infections ($>2/3$) presented as pyelonephritis, while the frequency of febrile and afebrile infections was similar for E-coli, Kelebsiella, Enterobacter and Staphylococcus species.

Keywords: UTIs; Etiology; Gender; Pyelonephritis; Cystitis.

Running Title: Etiologies of Urinary Tract Infections in Children

E-coli is the most common UTI pathogen, although underlying host factors such as the patient's age and gender may influence the prevalence of causative agents [1]. As the prevalence of pathogens may vary with time and geographical area, surveillance of local etiologies of UTI is useful to guide empirical therapy [4]. Acute UTIs

are relatively common in children. The cumulative incidence of UTI in children by 6 years of age is 3%–7% in girls and 1%-2% in boys. It is estimated that 70,000 – 180,000 children develop UTI in the United States annually [5]. Although most cases of infections are bacterial, viruses, fungi, and mycobacterial organisms can also cause UTI [5-7].

Objective: The objective of this study was to assess the most frequent pathogens responsible for UTIs, determine the influence of gender on the prevalence of uropathogens, and assess differences in the type of infection (febrile versus afebrile) based on the etiology

Materials and Methods

In this cross-sectional retrospective study, the results of urine cultures were assessed in children who were referred to the nephrology clinic of an academic children hospital during a five-year period (2004-2008). Urine samples were obtained using the mid-stream method in toilet trained children and urine bags in infants. Urinary tract infection (UTI) was defined as the growth of an organism with a colony forming unit $\geq 100,000$ or $\geq 10,000$ in symptomatic cases. For samples obtained by urine bags, the presence of leukocyturia was necessary for diagnosis. UTI was categorized into 2 types: febrile [UTI with a body temperature $\geq 38.5^{\circ}\text{C}$ (axillary temperatures were recorded in patients)], and afebrile infections (without fever or a body temperature $< 38.5^{\circ}\text{C}$). The type of infection and etiology were compared between genders. Moreover, for every uropathogen, a comparison was made between febrile and afebrile infections. Chi square was used for data analysis and P values ≤ 0.05 were considered significant. The Vice Chancellor of Research Affairs of Mashhad University of Medical Sciences supported this study financially. The ethic code of the research was IR.MUMS.REC.1393.762.

Results

A total of 420 cases, including 367 (89.9%) girls and 53 (10.1%) boys, were enrolled in the study and 648 episodes of infections were used for evaluation. The age range of the patients was 3 days to 17 years and 9 months (median: 20 months, mean \pm SD: 33.5 ± 34.2 months). 75% of cases were in less than 48 months old. Our cases included a heterogeneous group of children with uncomplicated and complicated UTIs. Complicated UTIs were those associated with urological

anomalies, such as vesicoureteral reflux (VUR) [125 cases; 29.8%] and urinary obstruction (10 patients; 2.4%), or dysfunctional voiding including neurogenic bladder (32 cases; 7.6%) and voiding dysfunction (25 subjects; 5.95%). Interestingly, urinary stone was a common finding and 64 (15.2%) cases had nephrolithiasis (stones ≥ 3 mm) or microlithiasis (stones < 3 mm) at presentation. Only 2 cases (0.3%) had hospital acquired UTI which occurred during hospital admission. Totally, the number of infections was 1-13 episodes (mean 1.5 episodes), with 1-13(1.5) episodes in girls and 1-5(1.3) episodes in boys. Eight girls (2.2% of girls) experienced ≥ 10 episodes of infection, 23 girls (6.3%) had 6-9 episodes, and the remaining (91.5%) had 1-5 episodes. In boys, of 53 cases, only 19 (35.8%) patients had > 2 episodes of infection during the follow up (Table 1).

Table I. Number of infection episodes by gender

| Number of episode of infections | Girls (N/%) | Boys (N/%) | Total cases (N) |
|---------------------------------|-------------|------------|-----------------|
| One episode | 367(87.4) | 53(12.6) | 420 |
| Two episodes | 107(90.6) | 11(9.4) | 118 |
| Three episodes | 34(91.9) | 3(8.1) | 37 |
| Four episodes | 19(86.4) | 3(13.6) | 22 |
| Five episodes | 13(86.6) | 2(13.4) | 15 |
| Six episodes | 10(100) | 0 | 10 |
| Seven episodes | 5(100) | 0 | 5 |
| Eight episodes | 4(100) | 0 | 4 |
| Nine episodes | 4(100) | 0 | 4 |
| Ten episodes | 2(100) | 0 | 2 |
| Eleven episodes | 2(100) | 0 | 2 |
| Twelve episodes | 2(100) | 0 | 2 |
| Thirteen episodes | 2(100) | 0 | 2 |

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Of 420 cases, 273 patients (65%) were followed up for 1-147 (24.15±27.94) months. The duration of follow up was 25.64±32.8 months in boys and 22.7±24.96 months in girls (P=0.54). Thirty-four boys (66%) and 239 girls (65%) had repeated visits and were followed up for recurrence of UTI. Twenty-four (5.7%) patients needed surgical interventions for repair of urological abnormalities. Figure 1 presents the most common uropathogens responsible for UTI in our cases, and Tables 2 shows the prevalence of each microorganism based on gender.

Table 2. Prevalence of each uropathogen in girls and boys

| Type of microorganism | Girls (N/%) | Boys (N/%) | Number of episodes |
|------------------------------------------------|------------------|-----------------|--------------------|
| E-coli | 469(91.8) | 42(8.2) | 511 |
| Kelebsiella | 39(83) | 8(17) | 47 |
| Proteus | 10(76.9) | 3(23.1) | 13 |
| Enterobacter | 20(100) | 0 | 20 |
| Enterococcus | 9(81.8) | 2(18.2) | 11 |
| Pseudomonas aeruginosa | 4(66.6) | 2(33.4) | 6 |
| Staphylococcus epidermis | 6(85.7) | 1(14.3) | 7 |
| Staphylococcus coagulase negative ¹ | 4(80) | 1(20) | 5 |
| Staphylococcus coagulase positive | 7(77.8) | 2(22.2) | 9 |
| Citrobacter | 4(44.4) | 5(55.6) | 9 |
| Staphylococcus Saprophyticus | 2(66.6) | 1(33.4) | 3 |
| Candida albicans | 0 | 1(100) | 1 |
| Morganella morganii | 0 | 1(100) | 1 |
| Shigella | 1(100) | 0 | 1 |
| Acinetobacter | 1(100) | 0 | 1 |
| Group B streptococcus | 1(50) | 1(50) | 2 |
| Group A streptococcus | 1(100) | 0 | 1 |
| Total episodes of infections | 578(89.2) | 70(10.8) | 648 |

The type of infection was evaluated for each microorganism (Table 3). The majority of the infections by Proteus (69.2%) and Enterococcus (72.7%) species were febrile, in contrast to Citrobacter infections which were mostly afebrile (66.6%).

The prevalence of febrile and afebrile UTIs was similar for E-coli, Kelebsiella, Enterobacter, and Staphylococcus species. E-coli infections were significantly more prevalent in girls (P=0.0001).

Table 3. Type of infection according to responsible microorganism

| Type of microorganism | Febrile infections (N/%) | Afebrile infections (N/%) | Total infections (Number of episodes) |
|-------------------------------------|--------------------------|---------------------------|---------------------------------------|
| E-coli | 274(53.6) | 237(46.4) | 511 |
| Kelebsiella | 24(51) | 23(49) | 47 |
| Proteus | 9(69.2) | 4(30.8) | 13 |
| Enterobacter | 9(45) | 11(55) | 20 |
| Enterococcus | 8(72.7) | 3(27.3) | 11 |
| Pseudomonas | 4(66.6) | 2(33.4) | 6 |
| Staphylococcus epidermis | 3(42.8) | 4(57.2) | 7 |
| Staphylococcus coagulase negative | 3(60) | 2(40) | 5 |
| Staphylococcus coagulase positive | 5(55.5) | 4(44.5) | 9 |
| Citrobacter | 3(33.4) | 6(66.6) | 9 |
| Staphylococcus Saprophyticus | 0 | 3(100) | 3 |
| Candida albicans | 1(100) | 0 | 1 |
| Morganella morganii | 0 | 1(100) | 1 |
| Shigella | 0 | 1(100) | 1 |
| Acinetobacter | 0 | 1(100) | 1 |
| Group B streptococcus | 0 | 2(100) | 2 |
| Group A streptococcus | 0 | 1(100) | 1 |
| Total episodes of infections | 343(52.9) | 305(47.1) | 648 |

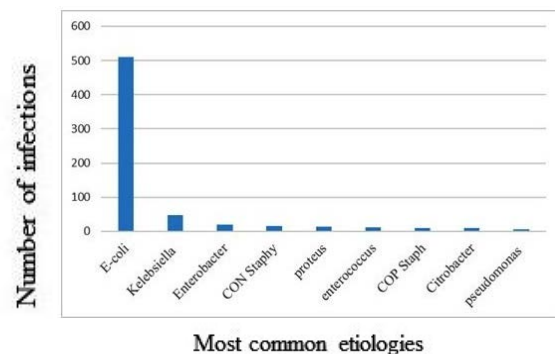


Figure 1. The most common uropathogens responsible for UTI in our cases

Proteus and Kelebsiella infections were more common in boys than girls (P=0.115 and 0.154 respectively), whereas all Enterobacter infections were seen in girls (P=0.129) (Table 4). Of 578 episodes of UTI in girls, 219 (40%) and 347 (60%) episodes were febrile and afebrile respectively, while 33 out of 70 episodes of infection (47.2%) were febrile in boys. The type of infection was not

Table 4. Comparison of the most common etiologies of infections in boys versus girls¹

| Microorganism | Girls (N/% of total infections in girls) | Boys (N/% of total infections in boys) | P value |
|------------------------------------------------------|-------------------------------------------------------|-----------------------------------------------------|---------------|
| E-coli | 469(82) | 42(63.63) | 0.0001 |
| Kelebsiella | 39(6.8) | 8(12.12) | 0.154 |
| Proteus | 10(1.7) | 3(4.54) | 0.15 |
| Enterobacter | 20(3.5) | 0 | 0.114 |
| Enterococcus | 9(1.6) | 2(3.03) | 0.426 |
| Pseudomonas | 4(0.7) | 2(3.03) | ----- |
| Staphylococcus epidermis | 6(1.1) | 1(1.51) | ----- |
| Staphylococcus coagulase negative² | 4(0.7) | 1(1.51) | ----- |
| Staphylococcus coagulase positive | 7(1.2) | 2(3.03) | ----- |
| Citrobacter | 4(0.7) | 5(7.6) | ----- |
| Total episodes of infections | 572 (100) | 66 (100) | ----- |

1. Total episodes of infection which were compared were 638 episodes

defined in 12 boys (22.6%). A comparison was done between females and males based on the type of infection. Although febrile infections were more frequent in boys, the difference was not statistically significant (P=0.059).

In patients with nephrolithiasis at presentation, only 2 cases had infection with urease positive microorganisms (mainly Proteus), and the rest of Proteus infections were seen in cases without stone diseases. Figure 2 illustrates the type of infection (febrile versus afebrile) based on the most common UTI etiology. One case of morganella morganii infection was reported in a 5- month boy with different urological anomalies (vesicoureteral reflux, ureterocele) immediately after surgical intervention for repair of ureterocele. Shigella infection was seen in an infant with imperforated anus and recto-vesical fistula probably due to bladder contamination via fistula and a febrile UTI caused by Candida albicans was documented in a 4.5-month boy with unilateral VUR. All three episodes of infections

with Streptococcus species were reported in girls <9 months (aged 2.5, 5, and 8.5 months).

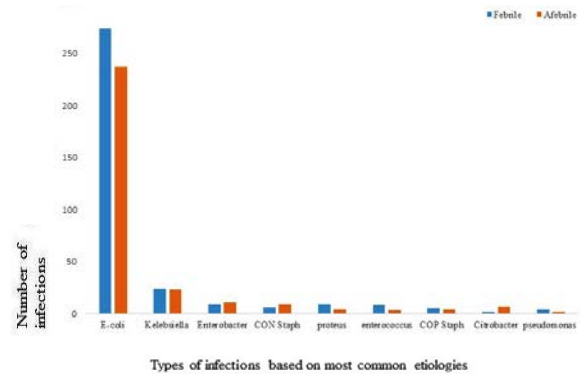


Figure 2. Type of infection (febrile versus afebrile) based on the most common UTI etiology.

Discussion

A review of 12 studies conducted in children aged ≤18 years with a total of 8,837 participants by Shaikh et al. [8] showed that the most common uropathogens responsible for UTI in children are E-coli (85%) followed by Klebsiella, Proteus, Enterobacter, Citrobacter, Staphylococcus Saprophyticus, and enterococcus species. In an extended study including children and adults with UTI, the results of urine cultures in 13820 episodes of UTIS were assessed [1]. E-coli, Klebsiella, Enterococcus, Proteus, and Pseudomonas accounted for 67.6%, 8.8%, 6.3%, 5.2%, and 2.5% of the infections, respectively. Data analysis by age and gender showed that E. coli isolation rates were lower in males aged ≥60 years (52.2%), while Enterococcus and Pseudomonas were more prevalent (11.6% and 7.8%, respectively). In those aged ≤14 years, the prevalence of E-coli infections was lower (51.3%) while the prevalence of Proteus infections was higher (21.2%). Infection due to Streptococcus agalactiae was twice as common in women aged 15 -5 9 years than all enrolled cases (4.1% versus 2.3%). In our subjects, E-coli infections were significantly more frequent in girls than boys (82% versus 63.63%, P=0.0001). Although Klebsiella, Proteus, and Enterococcus infections were more prevalent in boys, the difference were not significant (P>0.05 for all; Table 4).

Qureshi et al. evaluated 100 children with UTI aged ≤ 15 years. In their series, the most common infectious etiologies were E-coli (71%), Klebsiella (13%), Proteus (11%), Staphylococcus (4%), and Pseudomonas (1%). In contrast to our cases, they

found *Proteus* infections only in boys [9]. International studies have identified *E. coli* as the main etiologic agent of UTI with a prevalence of 60- 90% depending on the region where the study is carried out and the age range of the enrolled subjects [9-22]. Less common uropathogens include *Staphylococcus*, *Klebsiella*, *Serratia*, *Enterococcus*, and *Proteus* species [23-26]. In one study, urine culture in 50 patients aged <1 year to 94 years (median: 56 years) with uncomplicated UTI showed *E-coli* (70%) followed by *Pseudomonas aeruginosa* (10%). *E-coli* infections were most often reported in younger females [20]. In our cases, *E-coli* infections were significantly more common in girls than boys. Roy et al. [21] reported the most common etiologies after *E-coli* are *Proteus*, *Klebsiella*, *Enterococcus* and *Pseudomonas*. In our series, the most common pathogens were those reported by Shaikh et al. [8]. In contrast to the study by Roy et al. [21], *Pseudomonas* was a very uncommon pathogen in our cases (0.9%).

Proteus is reported to be a common pathogen in boys [26]. UTI secondary to group B streptococci is more common in neonates than older populations [27]. Common bacteria for pediatric UTI are gram-negative species (*Escherichia coli*, *Klebsiella*, *Proteus*, *Enterobacter*, *Pseudomonas*, and *Serratia*), and gram-positive organisms (group B streptococci, *Enterococcus*, and *Staphylococcus aureus*) [28]. In our cases, 94.1% of infections were caused by gram negative organisms, and gram positive bacteria were responsible for 38 (5.9%) infection episodes. We found that *Staphylococcus* species was the most common gram positive bacteria in our patients (24 episode; 63% of the UTIs were caused by gram-positive organisms). In our series, no episode of *Serratia* infection was reported. Analysis of UTI etiology in 299 children [22] showed *Escherichia coli* was the most common pathogen (62.9 %), followed by *Klebsiella* (23%), *Proteus* (7%), *Citrobacter* (5.4%), *Staphylococcus Saprophyticus* (1.4%), and *Candida Albicans* (0.33%). Like our cases, in this study, *Klebsiella* was the second most common uropathogen. Farajnia et al. [23] reported the results of urine culture in 676 UTI episodes. *Escherichia coli* was the most common etiology (74.6%), followed by *Klebsiella* (11.7%), *Staphylococcus Saprophyticus* (6.4%), and *Pseudomonas* (2.2%). Interestingly, although *Enterobacter aerogenes* is not reported as a common etiology of UTI in pediatric groups in the literature [22], it was the fourth most common

pathogen after *E-coli*, *Klebsiella*, and *Staphylococcus* species in our subjects; it was detected in 20 cases (3.1%) who were all female patients. Lo et al [29] studied 291 UTI proven cases aged 11 days to 14.99 years (median age: 2.6 years). They reported that *E. coli* was the most prevalent community-acquired uropathogen and showed a high prevalence for *Staphylococcus Saprophyticus* in patients > 10 years and *Proteus mirabilis* in males. Similar to their findings, *Proteus* infections were 2.5 times more common in boys, but this microorganism was not uncommon in girls in our cases (Table 2). An extended study (using the results of 37,261 urine samples) by Kiffer et al. [30] which included children and adults found gram negative enteric bacteria in 87.3% and gram positive cocci in 6.9% of UTIs. They categorized patients into 4 age subgroups: < 4 years, 4-13 years, 13-60 years, and >60 years. *E-coli* was the most common pathogen in all age groups followed by *Klebsiella* (6.4%), *Proteus* (6.1%), *Enterococcus* (4.8%), *Pseudomonas* (1.8%), *Staphylococcus Saprophyticus* (1.6%), and *Enterobacter* species (2.7%). *Klebsiella* was significantly more common in the population ≥ 13 years, whereas *Proteus* infections were significant more prevalent in the age groups ≥ 13 and < 4 years. Similar to our study, infection with *Enterobacter* species was not uncommon in their cases (3.1% of total infections in our cases and 2.7 % in their subjects were due to *Enterobacter* species).

A study was performed in two towns of Cameroon [31] to define regional variations in the etiology of community-acquired urinary tract infection (CAUTI). The participants were 2-80 years old. The results were completely different from the literature review. Predominant pathogens were *E-coli* (31.4%), *Klebsiella* (25.5%), and *Staphylococcus* species (24.1%). The authors concluded that there are some geographic variations in the distribution of uropathogens. Farrell et al. [32] assessed 1291 episodes of UTI including 394 (30.5%) hospital acquired infections. They categorized patients to 4 subgroups (CAUTI in age groups ≤65 and >65 years, hospital acquired UTI and pyelonephritis). *E-coli* infections were responsible for 56.3-77.3% of UTIs in different subgroups. The next 3 more important uropathogens were *Enterococcus*, *Klebsiella*, and *Proteus*. In addition to CAUTI which was mostly caused by *E-coli*, *E. coli* was reported as the most common pathogen (81%) in hospital admitted children (aged ≤18 years) followed by *Klebsiella* (6.5%),

Enterococcus (6%), and Proteus (3.5%) [33]. In our cases including CAUTI, the most common uropathogens were E. coli (78.85%), Klebsiella (7.25%), Staphylococcus species (3.7%), Enterobacter (3.1%), Proteus (2%) and Enterococcus (1.7%). The most common gram positive organisms in their cases were Enterococcus species, whereas Staphylococcus species were the most prevalent gram positive bacteria causing UTI in our cases.

Few studies suggest Enterobacter species as a common etiology of UTI in children. A Study by Mishra et al. [34] which included inpatient and outpatient children showed that E-coli (21.4%) was the most common etiology of UTI in children followed by Klebsiella (18.6%), Enterococcus (16%), Staphylococcus Aureus (12.7%), Enterobacter (12.5%), Pseudomonas (6.3%) and Proteus (4.3%). This study is one of the few studies showing a low prevalence (21.4%) of UTIs caused by E-coli. Yoon et al also reported that Enterobacter infections are one of the most prevalent etiologies of UTI in a study performed in Korea [35]. They found E- coli (81.4%), Klebsiella (8.4%), Enterobacter (1.7%), and Proteus (0.4%) are the most common etiologies of UTI. Moreover, Yasemi et al. [36] showed that Enterobacter is the third most common uropathogen responsible for 15% of UTIs. The prevalence of infections caused by E. coli (44.5%) in their cases was much lower than our patients (78.85%), while Klebsiella infections (18.6%) were more common compared with our cases (7.25%). A study by Rezaee et al [37] in 940 children with a mean age of 4.5 years and 4.2 months suffering from UTI showed that E-coli (71.4%) was the most frequent uropathogen, followed by Klebsiella (9.6%), Enterococcus (6.4%), Pseudomonas (4.2%), Serratia (4.2%), and Enterobacter (4.2%). Contrary to our results indicating that Pseudomonas was an unusual etiology, it was not unusual in their series. We did not find any infection with Serratia species, whereas Serratia was not uncommon in their cases and as it was the fifth most prevalent pathogen.

Community surveillance for uropathogens in a rural setting in India showed E- coli (66%) as the most common uropathogen species and Staphylococcus in 12.6%, Klebsiella in 5.8%, Streptococcus in 5.2%, Enterococcus in 2.6% and Proteus in 2.26% [36]. In this study, the prevalence of E- coli infection was lower and the frequency of infection with gram positive uropathogens was higher than previous reports and our findings. Staphylococcus saprophyticus

has been reported to be an important cause of UTI by European investigators. It is the second most common cause of UTI in young adults (mean age, 20 years), sexually active females, and those with preceding manipulation of the urinary tract in whom it mostly presents as acute cystitis [38].

In our series, gram positive uropathogens were responsible for 5.8% of the infections whereas these microorganisms were found in 20.4% of the cases in previous researches.

Assessment of CAUTI in infants <2 months admitted to the hospital [39] showed that single and mixed pathogens were responsible for 88.1% and 11.9% of UTIs, respectively. The most prevalent uropathogens in the first group (UTIs due to a single pathogen) were E-coli (56.3%), Klebsiella (10.6%), Enterococcus (5.2%), Morganella morganii (5.2%), Proteus (4.5%), and Enterobacter (3.9%). The authors found that E. coli was responsible for the majority of first and recurrent urinary tract infections.

Jordan et al. [40] found that this organism was rarely found as a contaminant in urine cultures, and should be accepted as an important urinary tract pathogen in young females. In our series of 24 cases with UTI due to Staphylococcus species, 19 cases (79%) were girls and 5 (21%) were boys. The age range of the patients was 2.5 months to 10 years (median: 23 months, mean: 43.8 months).

There are reports of gender differences in the etiology of UTI. Magliano et al.[1] reported E. coli, Klebsiella, and Serratia were the most frequent uropathogens in females, whereas Enterococcus, Proteus, and Pseudomonas were the most common pathogens in males. They found that the prevalence of infections caused by E-coli was lower in men ≥ 60 years while Enterococcus and Pseudomonas were more frequent in this age group. Infection with Proteus had the highest frequency in boys ≤ 14 years. We also noted gender differences in the etiology of UTI. E-coli and Enterobacter infections were more common in girls while Proteus and Klebsiella infections were more prevalent in boys.

The present retrospective study showed the distribution of different uropathogens isolated from a large number of urine samples during a 5-year period. Although E-coli has been reported to be the main uropathogen responsible for UTI all around the world, the frequency of E-coli infection is different from 47.6% to 85.9% based on geographic distribution of the cases [16,22,29,30,39-43]. WU [41] and Modarres [42] reported Proteus as a common cause of UTI in

boys, but this finding has not been confirmed by other studies in children suffering from UTI [43,44]. In our series, *Proteus* infections were 2.5 times more common in boys than girls (it was responsible for 4.5% of infections in boys and 1.7% of UTIs in girls). This pathogen is an important uropathogen in young females [1].

Few studies have addressed the form of UTI based on the uropathogen responsible for infection. We searched the literature using keywords UTI, type of infection, cystitis (afebrile infection), pyelonephritis (febrile infection) and etiology, but we could not find any related papers.

In our series, the prevalence of febrile and afebrile infection caused by *E-coli*, *Klebsiella*, *Enterobacter*, and *Staphylococcus* species was similar, whereas more than two-thirds of infections caused by *Proteus* and *Enterococcus* species presented as pyelonephritis.

Conclusions

Gram negative and gram positive bacteria were responsible for 94.1% and 5.9% of infections. The four most prevalent uropathogens were *E-coli*, *Klebsiella*, *Enterobacter*, and *Citrobacter* (90.5%). The main gram positive microorganisms were *Staphylococcus* (24 cases), *Enterococcus* (9 cases), and *Streptococcus* group A and B (3 cases). Infections caused by *E-coli* were significantly more prevalent in girls than boys. *Proteus* and *Klebsiella* infections were more common in boys, whereas infections with *Enterobacter* species were more prevalent in girls. The majority of *Proteus* and *Enterococcus* infections (>2/3) presented as pyelonephritis, while the frequency of febrile and afebrile infections was similar for *E-coli*, *Klebsiella*, *Enterobacter*, and *Staphylococcus* species.

Acknowledgement

The authors would like to appreciate Dr. Simin Hiradfar for advocated help.

Author's contribution: Mitra Naseri was involved in study concept and design, analysis and interpretation of data, drafting of the manuscript, revision of the manuscript and statistical analysis. Niayesh Taffazoli was actively involved in data acquisition.

Conflict of Interest

The authors declared any

Financial Support

This study was supported by a research grant from Research and Development Section of Mashhad University of Medical Sciences. The ethic code of the research is IR.MUMS.REC.1393.762

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