Has the COVID-19 Pandemic Affected Community-Acquired Urinary Tract Infections in Children?

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Purpose: To evaluate whether there were any changes in the rates of urinary tract infection (UTI) and antibiotic resistance in pediatric patients during the pandemic period.

Materials and Methods: Urine culture samples collected due to suspected UTI were searched retrospectively from our hospital database, and the patients with growth in urine culture were identified. They were divided into 2 groups as Group A (before COVID-19, March 11, 2019- March 11, 2020) and Group B (COVID-19 period, March 11, 2020- March 11, 2021). Also, COVID-19 period was divided into 3 subgroups (March 2020– June 2020: first epidemic peak, July 2020 – November 2020: normalization process, December 2020– March 2021: second epidemic peak). We adjusted the patient age as <1, 1-6 and 7-18 years. Age, gender, microorganism strain types, and their antibiotic resistance patterns were compared between the 2 groups

Results: This cross-sectional study included 250 eligible patients (Group A, n=182 and Group B, n=68) with a mean age of 10.91 ± 5.58 years. The male/female ratio was higher in Group B than in Group A (p = .004). Incidence of UTIs was lower in the curfew and restriction periods due to epidemic peaks than normalization process (p = .001). The proportion of E.coli decreased from 80.2% to 61.8% during the pandemic period when compared to pre-pandemic period (p = .001). Group B had lower rates of resistance to ampicillin, fosfomycin and nitrofurantoin for E.coli than Group A (p = .001, p = .012 and p = .001, respectively). Also, Group B had higher rate of uncommon microorganisms and lower rate of resistance to nitrofurantoin for E.coli than Group A in patients aged 7-18 years (p = .003 and p = .023, respectively).

Conclusion: Our study demonstrates that the ongoing COVID-19 pandemic process has caused alterations in community-acquired UTIs in children. More hygienic lifestyle may be considered as the main factor in this change.

Keywords: coronavirus; covid-19; pediatrics; urinary tract infection

INTRODUCTION

The urinary tract infection (UTI) is the most common bacterial infection in children(1). Escherichia coli (E. coli) is the most common type of the produced species[(1)]. Early diagnosis and treatment of UTIs in children is essential to prevent the development of renal scarring.

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS COV-2), a single-stranded RNA virus with positive polarity that caused Coronavirus disease (COVID), was discovered for the first time in November 2019 in Wuhan, China. It has influenced all of humanity since that day and has resulted in a complete change in our daily routine. The first coronavirus case in Turkey was reported on March 11, 2020. Following this date, the schools were closed and quarantine practices began. Curfews was also declared for the entire society, lasting several days or weeks on specific dates, including weekends and holidays.

During the pandemic, hospital admissions for non-COVID reasons decreased in the pediatric age group, as well as in all age groups[(2)]. Postponing elective procedures in hospitals, closing the polyclinics or reducing the number of those, and patients' avoidance of coming to the hospital are several factors that contribute to a lower rate of hospital admission. Along with a decrease in hospital admissions, there was a decrease in the rate of some diseases transmitted through contact as a result of protective measures such as mask use, social distance considerations, and adherence to hygiene rules. Although this decrease has been observed in diseases such as viral upper respiratory tract infections and asthma[(3, 4)], studies on urinary tract infections have revealed contradictory results[(5-7)].

The purpose of this study was to evaluate whether the COVID-19 period affects the rates of community-acquired UTI in children, the distribution of causative bacteria, and the resistance of these bacteria.

MATERIALS AND METHODS

Study Design

Ethical approval was granted by the University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital Ethics Committee with reference number 2011/KAEK-25 2021/11-19. One year period prior to March 11, 2020, the date of the first COVID-19 case in Turkey, was defined as the pre-COVID-19 period, and the one year period following this date was defined as the post-COVID-19 period. Also, we divided the

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Received February 2022 & Accepted June 2022

Table 1. Demographic data of the cohorts

Data	n=250
Age, years	10.91 ± 5.58
Gender, n (%)	
Female	199 (79.6)
Male	51
Urine microscopy, n (%)	
< 5 HPF	85 (34)
>5 HPF	165
Isolatedmicroorganisms, n (%)	
Escherichia coli	188 (75.2)
Klebsiella pneumonia	25 (10)
Proteus mirabilis	10 (4)
Others	27 (10.8)

HPF: High power field

post-COVID-19 era into 3 periods based on the intervals when the restrictions began (March-June 2020), the restrictions partially decreased (July-November 2020) and the second epidemic peak (December 2020-March 2021). Similarly, the pre-COVID-19 period was divided into 3 intervals for comparative analysis.

Inclusion and exclusion criteria

This cross-sectional study included the patients under the age of 18 who presented to the Urology polyclinic with suspected UTI symptoms and had bacterial growth in their urine cultures for the first time within one-year intervals (March 11, 2019 - March 11, 2020, and March 11, 2020 - March 11, 2021). We divided the patients into 3 groups according to their age: <1, 1-6, and 7-18. The study excluded the patients with vesicoureteral reflux, posterior urethral valves, urolithiasis, bladder bowel dysfunction, urogenital tract abnormalities, immune system disorders and uncircumcised boys. Also, all of the cohort evaluated in our study were sexually naive.

Evaluation of urine samples

After anamnesis and a thorough physical examination, microscopic findings of centrifuged urine samples from suspicious patients were recorded, in order to make a diagnosis. Urine samples were obtained by transurethral bladder catheter in children who had not been toilet trained. Midstream urine samples were collected from older children. These samples were incubated overnight at 37°C with a standard loop of Blood agar and MacConkey agar media. In catheterization and midstream urine samples, 103-104 CFU/mL growth was considered significant, while leukocytes in spot urine tests with >5 leukocytes in each field in centrifuged urine were considered significant. Antimicrobial susceptibility testing was performed using a panel of antimicrobial agents based on the causative organism in cultures with significant bacteriuria using the disc diffusion method. Until the antibiogram results were available, prophylactic empirical antibiotics based on the local susceptibility patterns were prescribed to the patients. Following that, the treatment was scheduled in accordance with the antibiogram results.

The patients were divided into 2 groups as Group A (before COVID-19, March 11, 2019- March 11, 2020) and Group B (COVID-19 period, March 11, 2020- March 11, 2021). The difference in UTI rates, distribution of bacteria grown in culture, and antibiotic resistance between two groups were analyzed.

Statistical Analysis

The normal distribution of data was evaluated using the Kolmogorov-Smirnov test and graphical method via Q-Q plot. The data were presented as median, interquartile range, number and percentage. Groups were analyzed using the Mann Whitney *U* test for quantitative data and the Chi-square test or Fisher's exact test for categorical data as appropriate. Also, we used logistic regression model to identify possible confounding factors. $p < 0.05$ was considered as statistically significant. SPSS 21.0 program was used.

RESULTS

After 49 patients met exclusion criteria were removed from the study, a total of 250 patients (182 in group A and 68 in group B) were evaluated. During the COVID-19 period, there was a huge decrease in the number of patients when compared to pre-pandemic period (variation: -62.64%). The mean age of the patients was 10.91 ± 5.58 (range: 6 months - 18 years). The initial characteristics of the patients are presented in **Table 1**. Of the patients, 225 had cystitis and 25 had pyelonephritis. Seven patients (5 in Group A and 2 in Group B) with a clinical pyelonephritis and impaired oral intake were hospitalized. It was comparable between the groups in terms of hospitalization ($p = .967$).

While E.coli (75.2%), Klebsiella pneumoniae (10%), and Proteus mirabilis (4%) were the most commonly isolated bacteria, bacteria such as P. aeroginosa, Enterococcus and streptococcus spp. were observed at a rate of 10.8%. The distribution patterns of the bacteria by gender are shown in **Table 2**.

While no significantly difference in median age was observed between the two groups, there was a significantly increase in the male/female ratio in group B (p= .004). The hospital admission rates for UTI in the first and second epidemic peak periods were higher than in Group A ($p = .001$). Despite the fact that E.coli was the most commonly isolated microorganism in both groups, it was significantly less isolated in group B than in group A (61.8% vs 80.2%) ($p = .001$). Ampicillin resistance for E.coli was also found to be statistically lower in group B than in group A (27.9% vs 58.2%) ($p = .001$). Furthermore, there was significantly less resistance to fosfomycin and nitrofurantoin for E.coli in group B ($p = .012$ and $p = .001$, respectively) (**Table 3**). There was no difference in UTI rates between the two groups according to age groups and infection type (p= .515 and $p = .925$, respectively) (**Table 3**). In the subgroup analysis of the patients according to age groups in terms of microorganism strain types and antibiotic resistance patterns, there was no difference in the periods including the patients aged <1 and 1-6 years, while a significant increase was observed at the uncommon microorganisms rate in the group aged 7-18 years during the COVID-19 period (**Table 4**). In addition, only the rate of nitrofurantoin resistance for E.coli decreased significantly during the COVID period in the same group ($p = .023$). Patient' age did not influence the UTI rate according to the regression analysis (95%CI: 0.842- 1.146, OR: 0.988, $p = .874$)

DISCUSSION

COVID-19 has increasingly led to radical lifestyle changes all over the world since its breakthrough. People have begun to avoid crowded places in order to prevent transmission. Furthermore, as a result of social regulations in which governments play a role, patients'

Table 2. Distribution of the bacteria by gender between the groups

	E.coli	K. pneumoniae	P. mirabilis	Others
Before COVID-19, n (%)				
Male	16 (6.4)	8 (3.2)	4 (1.6)	1 (0.4)
Female	130 (52)	10 (4)	4 (1.6)	9 (3.6)
COVID-19 period, n (%)				
Male	8 (3.2)	1 (0.4)	1 (0.4)	12 (4.8)
Female	34 (13.6)	6 (2.4)	1 (0.4)	5 (2)
p value	0.166	0.158	0.990	0.002

non-emergency hospital admissions have been reduced, and home health services have begun to be used more effectively. Both the reduction in hospital admissions and the emphasis on social distance have resulted in a reduction in some diseases for which crowded environments are risk factors[4]. In our study, hospital admissions due to UTIs in children decreased during this period, and the gender predominance along with antibiotic resistance patterns changed.

There are some studies in the literature evaluating the changes in UTI rates in children during the pandemic. Pines et al. reported in their study that the number of patients admitted to the hospital with UTI diagnosis decreased by 47% during the pandemic period compared to the pre-COVID-19 period[6]. Similarly, according to the results of a study reported from Scotland, the rate of admission to hospital due to UTI in children decreased by 55.3% in 2020 when compared to 2018 and 2019[8]. In the study by Wilder et al., a decrease in hospitalizations due to asthma, bronchiolitis, and pneumonia, which are more clearly related to social distance and viruses, was observed in the pediatric patient group during the COVID-19 period compared to the pre-COVID-19 period, while hospitalizations rates for cellulite, gastroesophageal reflux, and UTI did not change[7]. Similarly, according to the results of a multicenter study conducted in Japan, the number of children who required hospitalization due to UTI during the COVID-19 period did not differ significantly from the pre-COVID-19 period(5). Kuitunen et al. found a significant decrease in the incidence of cystitis and pyelonephritis, especially in patients aged 1-6 years during the pandemic period[9]. In their national study, similar to our study, a significantly decrease was found in the incidence of UTIs during the periods of restriction-due to epidemic peak intervals. In our study, while there was no difference in the incidence of UTI according to age subgroups between the groups, patients aged 7-18 years in COVID-19 period had higher rate of uncommon microorganisms than those in pre-pandemic period. The reason for this difference may be that day-care centers where have worse hygienic condition than homes are kept open for day-care aged children whose caregiver parents have to work during the period of restriction in our country, and elementa-

Table 3. Comparison of pre-COVID-19 (Group A) and COVID-19 period (Group B) data

Variables	Group A (n=182)	Group B (n=68)	*p* value
Age (years)	11 (IQR: 7-16)	12.5 (IQR: 5.25-16.75)	0.558
Age groups, n (%)			0.515
<1 year	3 (1.6)	1 (1.4)	
1-6 years	41 (22.6)	20 (29.4)	
7-18 years	138 (75.8)	47 (69.2)	
Infection type, n (%)			0.925
Cystitis	164 (90.1)	61 (89.7)	
Pyelonephritis	18	7	
Infection period, n (%)			0.01
March-June	46 (25.3)	11 (16.1)	
July- November	79 (43.4)	44 (64.7)	
December- February	57 (31.3)	13 (19.2)	
Gender, n (%)			0.004
Male	29 (15.89)	22 (32.35)	
Female	153	46	
Microorganism, n (%)			0.001
E. coli	146 (80.2)	42 (61.8)	
K. pneumoniae	18 (9.9)	7 (10.3)	
P. mirabilis	8 (4.4)	2 (2.9)	
Others	10 (5.5)	17 (25)	
Antibiotic resistance for E. coli, %			
Ampicillin	58.2	27.9	0.001
Piperacillin-tazobactam	18.1	22	0.483
Gentamicin	8.8	7.3	0.715
Amikacin	7.1	1.5	0.083
Ceftriaxone	37.3	35.3	0.763
Cefuroxime	42.8	38.2	0.509
Ceftazidime	39.5	38.2	0.849
Ciprofloxacin	17.5	23.5	0.288
Meropenem	1.6	1.4	0.921
Ertapenem	2.7	1.4	0.557
Fosfomycin	11.5	1.4	0.012
Nitrofurantoin	19.7	2.9	0.001
Trimethoprim-sulfamethoxazole	34.1	29.4	0.485

Table 4. Analysis of microorganism strain types and their antibiotic resistance patterns according to age groups

Variables	Group A	Group B	*p* value
The patients aged < 1 year			
Microorganism, n			0.500
E. coli	2	0	
K. pneumoniae	1	0	
P. mirabilis	0	0	
Others	0	1	
The patients aged 1-6 years			
Microorganism, n			0.175
E. coli	30	10	
K. pneumoniae	6	4	
P. mirabilis	3	2	
Others	2	4	
Antibiotic resistance for E. coli, %			
Ampicillin	63.3	50	0.482
Piperacillin-tazobactam	23.3	40	0.418
Gentamicin	13.3	20	0.629
Amikacin	3.3	10	0.442
Ceftriaxone	53.3	70	0.471
Cefuroxime	53.3	60	0.734
Ceftazidime	50	60	0.721
Ciprofloxacin	20	30	0.665
Meropenem	6.6	0	0.615
Ertapenem	10	0	0.560
Fosfomycin	16.6	0	0.306
Nitrofurantoin	16.6	0	0.306
Trimethoprim-sulfamethoxazole	43.3	30	0.485
The patients aged 7-18 years			
Microorganism, n			0.003
E. coli	114	32	
K. pneumoniae	11	3	
P. mirabilis	5	0	
Others	8	12	
Antibiotic resistance for E. coli, %			
Ampicillin	50.8	34.4	0.098
Piperacillin-tazobactam	14.9	15.6	0.921
Gentamicin	3.5	6.2	0.612
Amikacin	0.8	0	0.781
Ceftriaxone	31.5	25	0.474
Cefuroxime	39.4	34.4	0.600
Ceftazidime	34.2	31.2	0.754
Ciprofloxacin	18.4	18.7	0.573
Meropenem	0.8	0	0.781
Ertapenem	0.8	0	0.781
Fosfomycin	8.7	3.1	0.457
Nitrofurantoin	14.1	0	0.023
Trimethoprim-sulfamethoxazole	28.9	28.1	0.559

ry, middle and high schools interrupt their education. Kruizinga et al. compared the pediatric emergency department admissions between 2016-2019 and 2020[10]. A significant decrease in admissions was observed in February 2020 along with the highest decrease in April 2020. However, in the group of non-communicable diseases including UTI in their study, no significant change was observed between the periods. Similar to the results of study mentioned above, we observed significantly decrease in the incidence of UTI during the first and second epidemic peak periods in our study.

Several hypotheses can explain the decrease in the number of pediatric patients diagnosed with UTI. The first reason could be that schools were closed during this period[11]. It is a well-known fact that schools and common areas have usually worse hygienic conditions than homes in our country. The second reason might be that more attention was paid to personal hygiene during this period and interpersonal contact was minimized. Although UTI is not classified as a communicable disease, societal outbreaks have been reported[12]. Since E.coli is found in normal intestinal flora, hand and food hygiene appear to play a role in contamination. It is known to be transferred between sexual partners and people living in the same household[13]. Third, during the pandemic, parents may have preferred to take their children to branch hospitals where only children can be treated, rather than general hospitals where adults are more numerous. According to the study of Goldmann et al., the decrease in the rate of pediatric admissions to the general hospital emergency department during the pandemic period was 70%, while the fall in the rate of admissions to the pediatric hospital emergency department was determined as 57%[2].

Public health measures against COVID-19 are also known to cause a decrease in other infectious diseases. According to a study conducted in Taiwan, the incidence of Kawasaki disease reduced by 30% in 2020 when compared to 2018[14]. However, it was mentioned that this decline, according to the study's authors, may be a result of both the precautions taken and the decrease in patients' admission to the hospital. During the pandemic period, a new type of phobia, known as "COVID phobia," emerged[15]. Lin et al. reported in their study that as a result of this "COVID phobia," the incidence of emergency department admissions due to respiratory tract infections dropped by nearly 50% in Taiwan[16]. However, no similar decrease in rates of UTI

was seen. According to the findings of Roongpisuthipong et al., there was a change in the pattern of skin diseases during the COVID-19 period[17].

Another result of our research was that the male/female ratio in UTI increased throughout the pandemic period. While female patients used public toilets in schools and playgrounds prior to the pandemic, they met these needs at home since schools were closed and social areas were restricted during the pandemic. Considering that anatomical factors are one of the leading causes of UTI in girls, since houses has better hygienic conditions, it is reasonable to predict that the reduction rate of UTI in girls would be more compared to boys. This relative decrease might account for the rise in the male/female ratio for bacterial growth. Another finding was that the rate of E. coli decreased during the pandemic period when compared to other uncommon causative microorganisms. This might be attributed to a rise in the male/female ratio. In the COVID-19 period, male predomination was observed in the other causative microorganism species in our study. Edlin et al. reported in their research, which involved 24,815 pediatric patients, that microorganisms without E. coli were seen at a higher rate in men than in women[18].

In our study, the highest antibiotic resistance for E. coli was observed in ampicillin (50%). It was followed by cephalosporins[cefuroxime (41.6%), ceftazidime (39.2%), ceftriaxone (36.8%)] and trimethoprim-sulfamethoxazole (32.8%). According to Edlin et al., the highest resistance rates were seen in ampicillin (45%) and trimethoprim-sulfamethoxazole (24%) in their investigation[18]. Another finding of our study is the change in antibiotic resistance patterns during the COVID-19 period. Resistance for *E.coli* has declined dramatically, particularly to ampicillin, fosfomycin and nitrofurantoin. There may be several reasons for this change. In general, lockdown, restriction or less personal interaction with the peers might be the main reasons for this situation. As it is known, pathogen resistance in UTI varies according to time as well as geographical and regional location. For example, in their 6-year study on the change of antibiotic resistance, Erol et al. discovered that resistance to ampicillin, trimethoprim-sulfamethoxazole and nitrofurantoin increased whereas cephalosporin resistance remained steady[19]. Saperston et al. discovered that E.coli resistance to trimethoprim-sulfamethoxazole, ampicillin, cephalosporins, and ciprofloxacin differed significantly between inpatients and outpatients[20]. Another reason could be that antibiotic use has dropped throughout the pandemic. Unless a bacterial agent superinfected, the Ministry of Health did not recommend routinely antibiotic treatment for COVID-19 patients in Turkey during the COVID-19 period, but only Favipiravir was utilized. Antibiotic use in other countries has fallen dramatically in both inpatient and outpatient groups[21,22]. Travel limitations abroad might have reduced the transfer of regional antibiotic resistance genes during this period[23]. According to a study conducted in Belgium, the use of amoxicillin, which is commonly used to treat respiratory tract infections, declined dramatically during the pandemic period, while the use of nitrofurantoin did not change[24]. Based on this information, the decrease in ampicillin resistance may be related to a reduction in the use of this antibiotic group in upper respiratory tract infections during the pandemic. It is believed that the drop in other antibiotic resistances is related to a general decrease in antibiotic use[21,22].

Although our study reveals that the proportion of UTI in children has decreased and antibiotic resistance patterns have changed during the COVID-19 period, but it also has some limitations. First, our study population consisted of relatively small number of patient groups, and the data were analyzed retrospectively. Second, our study population was limited to our region only and consisted of patients who applied to the general urology polyclinic. As the measures taken during the pandemic period differ between countries, results of our study cannot be generalized and cannot represent to the all regions of the world.

CONCLUSIONS

As a result, hospital admission rate for community-acquired UTI in the patients aged ≤18 years has decreased substantially during the pandemic period. Furthermore, male predominance and uncommon microorganism species have increased, and antibiotic resistance patterns have changed. Therefore, we think that it would be more appropriate for clinicians to manage the disease by taking into account the changes in the distribution of microorganism agents under pandemic conditions. Further studies with larger sample size are needed to support the findings of our study.

SUMMARY

The COVID 19 pandemic has led to lifestyle changes all over the world. All these changes have led to changes in the incidence of microorganisms. In our study, we showed that there was a decrease in urinary tract infection rates in children, changes in gender predominance and antibiotic resistance during the pandemic period.

CONFLICT OF INTEREST

The authors declared no conflict of interest.

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