



Prevalence of Urinary Tract Infection and Drug Resistance among Infants and Children in Pakistan

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Authors' contributions

This work was carried out in collaboration among all authors. Author MS designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors MAS, KS, MA, QA, and Author SA managed the analyses of the study. Authors YJ, MAR, QA and MMH managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

In infancy most common and a serious disease is known as Urinary tract infection (UTI). The aim of the current study is to evaluate the frequency and antibiotic resistant among infant presenting with UTI in Lahore General hospital, Lahore-Pakistan. The current observational study comprised 100 (n=100) cases diagnosed with UTI. The study was conducted at Lahore General Hospital, Pakistan, between March 2019 and January 2020. Data were collected and recorded on specified proformas that had information on demographics, biochemical analysis, and complaints, as well as the antibiotic used and blood cultures. The most common gram-negative bacilli (GNB) causing UTI was *E. coli* constitute about 72% followed by *Klebsiella* (11%), *Enterobacter* (7%) and *Enterococcus*

(4%). Most of the isolated pathogens are highly resistant to ampicillin, cotrimoxazole, and cephalixin (72%–95%), have intermediate sensitivity to third- generation cephalosporins, and high sensitivity to amikacin, nitrofurantoin and ciprofloxacin. Similarly, the other pathogens showed different degree of occurrence and resistance against empirically used antibiotics. The most prevalent UTI causative organism among children was *E. coli*. The insulated microorganisms were highly resistant to ampicillin, and highly sensitive to amikacin.

Keywords: Antibiotic; *Escherichia coli*; resistance; sensitivity; UTI.

1. INTRODUCTION

In infancy Urinary tract infection (UTI) is one of the critical illnesses. It is a bacterial infection mostly seen in admitting infant and a leading cause of hospitalization in children. Untreated UTI leads to life threatening conditions like renal failure and other complications. UTI occurs mainly in the first year of life for boys, much more often among uncircumcised boys. The prevalence of UTI differs by age. In the first year of life, the relationship between males and females is between 2.8 and 5.4, respectively. Over the age of 1 to 2, there is a striking female predominance with a male-female ratio of 1:10.

Escherichia coli (*E. coli*) representation 78%-88% of all UTIs, following *Klebsiella* and *Proteus* species in females, but earlier reports have shown that *Potenus* species is as common as *E. coli* in UTIs of males aged 1 year. Others report the disposition of Gram-positive organisms in male UTI. *Staphylococcus saprophyticus* and *Enterococcus* are infective agents triggering urinary tract infection in both genders. Urinary tract infections are the most frequent infections among infants, children and adults [1]. The worldwide prevalence of the disease is about 1500,000, in which hospital acquired infection, constitute about 4% [2-5]. It is a common complication of cauterization and may cause serious problems like abortion, high blood pressure or even renal disfunction if not treated accurately. Urinary tract infections are the most frequent infections among infants, children, and adults [6-8]. This is a common practice, particularly in children, who have received empirical treatment without knowing the causal agent. Most of these children receive empirical antibiotic therapy before revealing the causative pathogen through antimicrobial sensitivity and resistance. Recently, Farrell et al have demonstrated extremely high resistance to trimethoprim, ampicillin and cephalosporin, making them inappropriate for empirical use. The increasing resistance of pathogenic bacteria is a global concern that varies from region to region.

These reports indicate a continued need to monitor and explore new oral agents for UTI treatment in the community [9-11]. A recent study by Mortazavi and Shahin from Azerbaijan showed that the incidence of the bacterial source of UTI and resistance to antibacterial regimens transformed rapidly. The aim of this study was to assess clinical presentations and outcomes, and in particular antimicrobial resistance in infants and children hospitalized with UTI at the Lahore General Hospital, Pakistan.

2. MATERIALS AND METHODS

The current descriptive study included total of one hundred participant admitted with urinary tract infection in the nursery of Lahore General Hospital between March 2019 and January 2020. The study was approved by the institutional review board and informed consent was taken from the parents before including the participant in the study. Chief presenting complains, biochemical analysis and urine culture and sensitivity reports were collected from Hospital records for the further analysis. Infant ages from 1 to 2.5 years and children of both ages were included in the study whose documentations were found complete. Change of diagnosis, genitourinary reflex and loss of any variable was considered the exclusion criteria. Different methods were used to collect the urine sample according to the age. For the neonate suprapubic approach was used, while from infant and children's sample was taken from urine bag or midstream urine collect. The statistical analysis was done by using the SPSS software version 23. Quantitative data was presented in the form of a mean, standard deviation, while qualitative data was presented in the form of frequency and percentage. The statistical comparison tests were the chi-square test, the independent t-sample test. A P-value less than 0.05 was judged to be statistically significant.

3. RESULTS

The data extracted from the record analyzed thoroughly which showed mean age of infant was

9.11 ± 6.65 months, similarly the mean age of children calculated as 5.98 ± 4.69 years. Male to female ratio was 31:69. Age group wise ratio, aged below one year, between one to two years, and above 2 years was 11:31, 6:10 and 10:30 respectively. There were thirty-six patients had the history of hospitalization. The mean body weight of the study population was 12.68 ± 6.69 kg and mean period of hospital stay were 6.66 ± 4.91 days (Table 1). Table 2 showed the comparison of population, clinical and laboratory outcomes by cause of UTI.

The most common feature at the time of presentation was fever (mean temperature 37.69 ± 0.88). the mean WBC count noted ranged from 4100-29000/mm³. Fifty-four percent patients had

leukocytosis noted from reports. The average body temperature at the time of admission was 37.88°C ± 0.98°C (range 36.10°C to 41.7°C). 36 percent of the patients had a fever. The average white blood cell count was 12900 ± 5226/mm³ (4100 to 29000/mm³). 66 percent of patients had leukocytosis. The CRP was negative in 53%; +1 in 21%, +2 in 16%, +3 in 8% and +4 in 2%. The mean ESR level for the first hour was 36.45 mm/hour (range 2 to 120 mm/hour). Eighty-nine patients (89%) were tested for active urine infection (more than five WBC per field). The most isolated pathogen was *E. coli* (72%), followed by *Klebsiella* (11%), *Enterobacter* (7%) and *Enterococcus* (4%). Antibiotic resistance is reported in Table 3.

Table 1. Comparison of demographic, clinical, and laboratory findings according to cause of UTI

variables	<i>E.coli</i> (N = 77)	<i>Klebsiella</i> (N = 10)	<i>Enterobacter</i> (N = 9)	<i>Enterococcus</i> (N = 4)	P*
Male to female ratio (31:69)	14:63	3:7	3:6	1:3	0.62
Infant to child ratio	42:35	9:1	5:4	4:0	0.09
Infant age (months)	9.8 ± 6.6	7.16 ± 5.50	7.70 ± 4.99	10.25 ± 6.34	0.50
Child age (years)	6.4 ± 3.9	4 (1 case)	4.75 ± 2.06	–	0.45
Weight (kg)	12.7 ± 7.9	6.33 ± 2.97	11.82 ± 7.03	8.57 ± 2.23	0.09
Body temperature (°C)	37.7 ± 0.9	37.67 ± 0.76	38.61 ± 1.45	37.87 ± 0.62	0.09
Fever (N)	24	3	6	1	0.19
WBCs (/mm ³)	13,250 ± 5702	11,960 ± 2825	11,944 ± 3437	10,675 ± 2601	0.64
Leukocytosis (N)	49	5	6	2	0.75
First-hour ESR (mm/hour)	41.03 ± 30.71	22.30 ± 19.81	45.44 ± 39.83	20.75 ± 20.83	0.17
Duration of hospitalization (days)	7.71 ± 4.60	8.50 ± 3.65	8.87 ± 3.11	7.75 ± 4.50	0.87

*p-value is insignificant that showed the groups were comparable with each other

Table 2. The main complain leads to the admission

Symptoms	Percent
Fever	36%
Dysuria	24%
Crying at time of urination	11%
Failure to thrive	9%
Diarrhea	8%
Anorexia	8%
Flank pain	7%
Frequency	7%
Vomiting	6%
Hematuria	5%
Malodorous urine	5%
Poor feeding	5%
Abdominal pain	4%

Table 3. Antibiotic resistance of isolated pathogens

Antibiotic	Resistance (%)			
	<i>E.coli</i>	<i>Klebsiella</i>	<i>Enterobacter</i>	<i>Enterococcus</i>
Ampicillin	93.7%	95%	98%	100%
Cotrimoxazole	70.1%	95%	67.7%	75%
Cephalexin	67.3%	85%	76.8%	–
Gentamicin	35.1%	65%	37.5%	100%
Nalidixic acid	32.2%	40%	28.2%	75%
Ceftazidime	26.5%	70%	0%	–
Ceftizoxime	25.3%	65%	22.2%	–
Ceftriaxone	21.3%	65%	33.3%	–
Cefotaxime	22.5%	55%	22.2%	–
Cefixime	22.9%	55%	22.2%	–
Nitrofurantoin	14.7%	40%	11.1%	25%
Amikacin	10.5%	10%	22.2%	–
Ciprofloxacin	15.5%	10%	0%	75%

4. DISCUSSION

UTI is one of the emerging causes of fever in young children. Although fever is a common presentation of every infection but in our study the fever was the most common presentation of UTI, which indicate that every clinician should consider and pay attention to towards the UTI when a children present with fever. This approach can save many lives as untreated UTI may lead the many complications even progressive renal failure. Other clinical symptoms of UTI can be lower abdominal pain, flanks tenderness, nausea, vomiting generalized body pain and in some cases with diarrhea [12-15]. In children the abovementioned feature can be find but in neonate or in infant the most common presentation of UTI is poor feeding, irritability or weight loss that can be dure to deceased feeding. In our study the sequence of clinical present was from most common being the fever, followed by painful and cry during micturition, deprived growth, loose motion, anorexia and flank or abdominal pain. In our study the frequency of diarrhea and abdominal pain was not as frequent as reported before.

If we discuss the demographic variable with earlier studies our finding were the consistent with the previous findings such as frequency of UTI in male to female as compared to the age groups. Similarly, the female predominance after the age of one year is a common finding all studies conducted on UTI, specifically in children [16-18]. In the current analysis the most common isolate pathogen was the *E. coli* being the 72 percent, followed by the *Klebsiella* (11%),

Enterobacter (7%) and *Enterococcus* (4%). Bacterial are constant being resistant to many available chemotherapies and creating significant interference in treatment. In Japan *E. coli* resistant to the fluoroquinolones created serious problems as for as the treatment and complication concerned [19].

Antibiotic resistant showed by the *E. coli* in our study was the maximum against the most used penicillin group (ampicillin 93.7%). Other antibiotics also showed high values of resistance such as 70.1% clotrimazole and 67.3% cephalexin. Most of the countries around the globe facing the same problem [20-22]. The best sensitivity against the *E. coli* was achieved with amikacin, ciprofloxacin and nitrofurans. Thirst generation cephalosporine was also showed good sensitivity, secondary to the amikacin and ciprofloxacin [23]. *Klebsiella* showed varying degree of antibiotic resistance. Highest resistance noted against the ampicillin that was 95% in our study. Intermediate resistance was calculated with ceftriaxone (65%) and minimum resistance with amikacin (10.5%). Here our results are consistent with the finding of previous studies. The most common reason to the resistance is uncontrol empirical usage of antibiotics. *Enterobacter* showed lowest prevalence in the case of UTI. But it had the highest resistance against the ampicillin (100%), first generation cephalosporins and mild resistance against the third generation cephalosporines. The rate of antibiotic resistance of *Enterobacter* to ciprofloxacin is low in children because of the scarcity of its administration. Contrary to findings from Caksen *et al.*, [24], unfortunately, 100% of isolated *Enterobacter*

were resistant to ciprofloxacin in this study. In that study, 4% of the UTI pathogens were *Enterococcus*; its prevalence was like that of the Muratani and Matsumoto reports [25]. The results of this study revealed the presence of single *Enterococcus* were exceedingly resistant (100%) to ampicillin and gentamicin. Such high resistance to these antibiotics has already been reported by others. The susceptibility of *Enterococcus* spp to vancomycin and nitrofurantoin was 100% and 75%, respectively, consistent with the findings of Turnidge et al. [26]. By comparing the current study with a recent study by Mortazavi and Shahin [27] in Eastern Azerbaijan, the demographic characteristics and frequency of bacteria causing UTI have not altered. Comparison of antibacterial strength of *E. coli* study of Mortazavi and Shahin, ampicillin resistance, enhanced and resistance to gentamicin, nalidixic acid, ceftazidime and Cefixime decreased, but remained unchanged compared to other antibiotics. In addition, *Klebsiella* showed increased antibacterial resistance toward nalidixic acid, and cotrimoxazole, and decreased resistance to amikacin and nitrofurantoin. Finally, the present study was a small, regional retrospective study and results show that there is a need for large longitudinal national studies to figure out prevalence, demographic characteristics, etiology, and antibiotic resistance [27-31]. The present study has also evaluated the pattern of antibiotic resistance among hospitalized children with diagnosis of UTI, which provides valuable information concerning this region.

5. CONCLUSION

E. coli is the most prevalent isolated bacterium in hospitalized children with a preliminary diagnosis of UTI. Most of the isolated pathogens are highly resistant to ampicillin, cotrimoxazole, and cephalexin (72%–95%), have intermediate sensitivity to third- generation cephalosporins, and high sensitivity to amikacin, nitrofurantoin, and ciprofloxacin.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by

the producing company rather it was funded by personal efforts of the authors.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author.

ETHICAL APPROVAL

Ethical approval for the study has been taken from the institutional review board and ethical committee of Lahore General Hospital, Lahore (LGH/Uro/10135)

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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