

Original Research Article

Prevalence and antibiotic susceptibility pattern of pathogens in children with urinary tract infection in a tertiary care hospital

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ABSTRACT

Background: The changing pattern of antimicrobial susceptibility of bacterial pathogens causing acute UTI is a growing problem. Hence, the knowledge of the local pattern of urinary pathogens and their susceptibility to various antimicrobials is of utmost importance for selection of the appropriate empiric therapy for children with acute UTI.

Methods: This retrospective cross-sectional study was conducted in 208 children of 1-18 years age group with suspected UTI infection who were admitted in KIMS hospital, Bangalore from January to December 2018. The data of all samples were collected from medical record.

Results: Overall 208 children between 1-18 years with suspected UTI were screened. Out of which 48 were culture positive, with a prevalence of 23%. Culture positive UTI was predominantly found in males in 1-5 years age group as against female predominance in 6-18 years age group. *E. coli* (45.83%) was the commonest organism isolated in our study, followed by *Enterococcus* (31.25%), *Klebsiella* (16.67%), *Proteus* (4.17%) and *Acinetobacter* (4.17%). Antibiotics with highest sensitivity to *E. coli* are Amikacin (91%) and Gentamicin (77%). *Klebsiella* is most sensitive to Gentamicin (87.5%) and piperacillin (75%). *Enterococcus* has highest sensitivity to Vancomycin (67%) and Linezolid (60%).

Conclusions: It requires regular monitoring to determine the current status of resistance against antimicrobial agents. The use of antimicrobials must be restricted in order to decline the resistance and we suggest that empirical antibiotic selection should be based on the knowledge of local pattern of bacterial organisms and their susceptibility to various antimicrobials rather than on universal guidelines.

Keywords: Antibiotic susceptibility, Urinary tract infections, Uropathogens

INTRODUCTION

Urinary tract infections (UTIs) are a common cause of acute bacterial illness in infants and children.¹ Urinary Tract Infection is defined as invasion of any of the tissue of the urinary tract extending from the renal cortex to the urethral meatus with pathogens and associated with significant bacteriuria. Significant bacteriuria means colony count 10^5 colony forming units (CFU)/ml of single species on clean catch specimen and $>50,000$ CFU/ml in transurethral specimens.² UTI is often missed

in infants and children, as urinary symptoms are nonspecific and very minimal. Timely diagnosis and adequate, appropriate antibiotic treatment is necessary to prevent renal damage in the form of renal scarring, hypertension and subsequent renal parenchymal damage.

The incidence of UTI varies with the age and sex of the children. Approximately 5% of all children under 2 years of age with fever experience UTI. In the first year of life, UTI was mostly found in boys, which is about 3.7% compared to girls of about 2%. However, this incidence

changes mainly in school-age children, decreased in boys and increased in girls.³ Common uro-pathogens include *Escherichia coli* (accounting for approximately 85 percent of UTIs in children), *Klebsiella*, *Proteus*, *Enterobacter*, *Citrobacter*, *Staphylococcus saprophyticus*, and *Enterococcus*.⁴

The changing pattern of antibiotic susceptibility of bacterial pathogens causing acute UTI is a growing problem. The pattern of bacteria causing UTI in children varies based on geographical variability. Many organisms not known to be common in causing acute UTI may emerge as important causative pathogens because of injudicious use of antibiotics by few medical practitioners. Adequate knowledge of the local pattern of urinary pathogens and their susceptibility to various antimicrobials are essential for selection of the appropriate empiric therapy for children with acute UTI.^{5,6} Therefore, periodic evaluation of causative uropathogens and antibiotic susceptibility is very essential for their appropriate management.

Therefore, this study was taken up to know the causative organisms and their antibiotic susceptibility in children admitted in KIMS hospital, Bangalore.

Objective was to study the prevalence of culture positive urinary tract infection in children of 1-18 years age and its bacteriological profile with antibiotic sensitivity pattern over one-year period.

METHODS

This retrospective cross-sectional study was done in 208 children of 1-18 years age group with suspected UTI infection who were admitted in KIMS hospital, Bangalore from January 2018 to December 2018. The data of all samples were collected from medical record like brief clinical history obtained from each patient and their parents to find out if there was any risk factor predisposing to UTI.

Inclusion criteria

Children between 1-18 years with diagnosis of suspected urinary tract infection. Children with age <1 year and if the data was not completed in medical record were excluded from the study. Institutional Ethical approval was taken before starting this study.

Urinalysis

To get a clean uncontaminated urine sample, precautions were taken. In girls, labia was separated and introitus was washed with plain water. In boys, the prepuce was retracted and glans cleaned beforehand. Only midstream urine was collected. And urine sample was sent for routine urine examination and culture sensitivity testing immediately after collection. Urine collected in a sterile container, was examined grossly for turbidity, colour and

sediments, pH, sugar and protein (albumin). About 10 ml sample was centrifuged at 5000 RPM and the supernatant discarded. The remaining 0.5 ml was placed on a slide and examined under high power (X 100) objective of microscope to find out pus cells, casts, debris, epithelial cells, RBCs, crystals and microbes.

Urine culture and sensitivity

Uncentrifuged sample was subjected to culture and sensitivity. The culture was done as early as possible (within 2 hours of collection) on 5% blood agar, nutrient agar and MacConkey agar. Inoculated culture plates were incubated in aerobic atmosphere at 37-degree Celsius for 24 hours. A positive urine culture was defined as colony count 10^5 CFU/ml for midstream urine. All positive cultures were further identified by their colony characteristics. Gram staining was done to identify gram positives and gram negative pathogens.

Antibiotic susceptibility testing

Antibiotic susceptibility testing was done by modified Kirby-Bauer disc diffusion method as per the National Committee recommendations.^{5,6} As per the protocol followed by Microbiology Department, a set of antibiotic discs was used, depending on the gram staining nature of bacterial grown. At least 10 antibiotic discs were used for finding antibiotic susceptibility.

Other tests done were routine blood investigations, abdominal ultrasound to delineate anatomical details of urinary system. MCU and DMSA scans were performed in certain cases if required.

Analysis

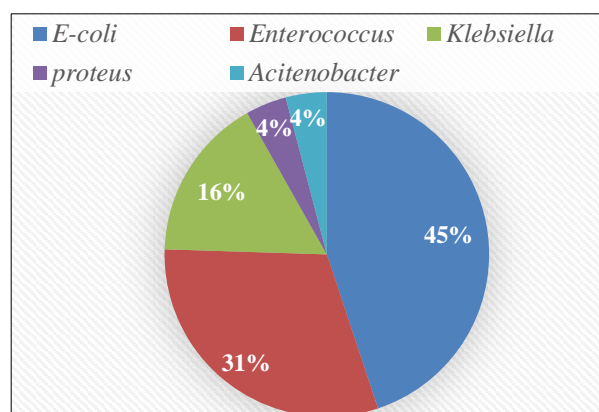
Data were collected and entered in Microsoft excel 2010. It was analysed using frequency distribution in number and percentage.

RESULTS

Overall, 208 children between 1-18 years with suspected UTI were screened. 46.2% were males as against 53.8% of females in our study group. Out of which 48 were culture positive, with a prevalence of 23%. More prevalence among 1-5 years age (32.4%) as compared to 6-18 years age (18.2%). Prevalence of culture positive UTI in the age group of 1 to 5 years were 41.4% males and 19% females, whereas between 6 to 18 years, it was 16.4% males and 20% females. Culture positive UTI was predominantly found in males in 1-5 years age group as against female predominance in 6-18 years age group (Table 1). *E. coli* (45.83%) was the commonest organism isolated in our study. *Enterococcus* was second most common which was isolated in 31.25%. *Klebsiella* was isolated in 16.67% cases followed by *Proteus* and *Acinetobacter* which was isolated in 4.17% cases each (Figure 1).

Table 1: Age and sex distribution in relation to positive urine culture.

	Total number of patients	Male	Female	Total culture positive	Culture positive males	Culture positive females
1-5 years	71 (34.1%)	29 (41%)	42 (59%)	20 (28%)	12 (41.4%)	8 (19%)
6-18 years	137 (65.9%)	67 (49%)	70 (51%)	28 (20%)	11 (16.4%)	17 (24%)

**Figure 1: Bacteriological profile of urinary tract infections.**

E. coli had sex predilection of male in 1-5 years age as compared to Female predilection in 6-18 years age group (Table 2). *Klebsiella* and *Enterococcus* were more common in females as compared to *proteus* which is more common in males.

Sensitivity pattern of these urinary pathogens to antimicrobials like Aminoglycosides, Cephalosporins, Fluoroquinolones and other commonly used antibiotics is shown in Table 3,4,5,6. Table 3 shows the sensitivity pattern of pathogens to Aminoglycosides. *E. coli* shows highest sensitivity to amikacin (91%), followed by gentamicin (77%) and Netilmicin (68%). *Klebsiella* and *Proteus* is more sensitive to gentamicin, *Acinetobacter* to both amikacin and tobramycin. But *Enterococcus* is resistant to most of Aminoglycosides.

Table 2: Age and sex wise distribution of pathogenic organisms.

Age	<i>E. coli</i>		<i>Klebsiella</i>		<i>Enterococcus</i>		<i>Proteus</i>		<i>Acinetobacter</i>	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
1-5 years	7	5	0	5	3	0	2	0	0	1
6-18 years	5	5	2	1	4	8	0	0	1	0
total	12	10	2	6	7	8	2	0	1	1

Table 3: Sensitivity patterns of the pathogens to aminoglycosides.

Antibiotic	<i>E. coli</i>		<i>Klebsiella</i>		<i>Enterococcus</i>		<i>Proteus</i>		<i>Acinetobacter</i>	
	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)
Amikacin	20 (91)	2 (9)	3 (38)	5 (62)	3 (20)	12 (80)	1 (50)	1 (50)	2 (100)	0 (0)
Gentamicin	17 (77)	5 (23)	7 (88)	1 (12)	6 (40)	9 (60)	2 (100)	0 (0)	1 (50)	1 (50)
Netilmicin	15 (68)	7 (32)	5 (63)	3 (37)	5 (33)	10 (67)	1 (50)	1 (50)	1 (50)	1 (50)
Tobramycin	10 (45)	12 (55)	3 (38)	5 (62)	4 (27)	11 (73)	1 (50)	1 (50)	2 (100)	0 (0)

Table 4 shows sensitivity pattern of uro pathogens to commonly used cephalosporins. *E. coli* and *Klebsiella* shows resistance to most of cephalosporins like cefixime, cefoperazone and ceftiofene. *Enterococcus* and *proteus* is partly sensitive to cefepime and ceftriaxone but resistant to most of other cephalosporins. *Acinetobacter* is resistant to most of cephalosporins.

Table 5 shows sensitivity pattern of pathogens to commonly used Fluoroquinolones. *E. coli*, *Klebsiella* and *Enterococcus* shows resistant to most of the

fluoroquinolones but *Proteus* and *Acinetobacter* are sensitive to fluoroquinolones like Norflox and ciproflox.

Table 6 shows the sensitivity pattern of the pathogens to commonly used antibiotics. *E. coli* and *Klebsiella* is partially sensitive to Piperacillin and Nitrofurantoin but resistant to Ampicillin, Linezolid and Vancomycin. *Enterococcus* is most sensitive to Linezolid and vancomycin. *Proteus* and *Acinetobacter* is highly sensitive to Amoxyclav and resistant to most of other antibiotics.

Table 4: Sensitivity patterns of the pathogens to cephalosporins.

Antibiotic	<i>E. coli</i>	<i>Klebsiella</i>	<i>Enterococcus</i>	<i>Proteus</i>	<i>Acinetobacter</i>
	S (%) R (%)	S (%) R (%)	S (%) R (%)	S (%) R (%)	S (%) R (%)
Cefepime	9 (41) 13 (59)	5 (63) 3 (37)	6 (40) 9 (60)	1 (50) 1 (50)	0 (0) 2 (100)
Cefixime	1 (5) 21 (95)	0 (0) 8 (100)	4 (27) 11 (73)	1 (50) 1 (50)	0 (0) 2 (100)
Cefoperazone	0 (0) 22 (100)	0 (0) 8 (100)	3 (20) 12 (80)	0 (0) 2 (100)	0 (0) 2 (100)
Ceftazidime	4 (18) 18 (82)	3 (38) 5 (62)	3 (20) 12 (80)	2 (100) 0 (0)	1 (50) 1 (50)
Ceftriaxone	11 (50) 11 (50)	5 (63) 3 (37)	7 (47) 8 (53)	2 (100) 0 (0)	1 (50) 1 (50)
Cefoxitin	0 (0) 22 (100)	1 (13) 7 (87)	0 (0) 15 (100)	0 (0) 2 (100)	0 (0) 2 (100)

Table 5: Sensitivity patterns of the pathogens to fluoroquinolones.

Antibiotic	<i>E. coli</i>	<i>Klebsiella</i>	<i>Enterococcus</i>	<i>Proteus</i>	<i>Acinetobacter</i>
	S (%) R (%)	S (%) R (%)	S (%) R (%)	S (%) R (%)	S (%) R (%)
Norflox	4 (18) 18 (82)	1 (13) 7 (87)	7 (47) 8 (53)	2 (100) 0 (0)	1 (50) 1 (50)
Ciproflox	3 (14) 19 (86)	5 (63) 3 (37)	4 (27) 11 (73)	2 (100) 0 (0)	2 (100) 0 (0)
Oflox	2 (9) 20 (91)	1 (13) 7 (87)	0 (0) 15 (100)	1 (50) 1 (50)	0 (0) 2 (100)
Nalidix acid	2 (9) 20 (91)	0 (0) 8 (100)	3 (20) 12 (80)	1 (50) 1 (50)	0 (0) 2 (100)

Table 6: Sensitivity patterns of the pathogens to other antibiotics.

Antibiotic	<i>E. coli</i>	<i>Klebsiella</i>	<i>Enterococcus</i>	<i>Proteus</i>	<i>Acinetobacter</i>
	S (%) R (%)	S (%) R (%)	S (%) R (%)	S (%) R (%)	S (%) R (%)
Ampicillin	1 (5) 21 (95)	2 (25) 6 (75)	4 (27) 11 (73)	0 (0) 2 (100)	1 (50) 1 (50)
Amoxyclav	4 (18) 18 (82)	2 (25) 6 (75)	7 (47) 8 (53)	2 (100) 0 (0)	2 (100) 0 (0)
Linezolid	1 (5) 21 (95)	1 (13) 7 (87)	9 (60) 6 (40)	0 (0) 2 (100)	0 (0) 2 (100)
Piperacillin	12 (55) 10 (45)	6 (75) 2 (25)	4 (27) 11 (73)	0 (0) 2 (100)	1 (50) 1 (50)
Vancomycin	1 (5) 21 (95)	1 (13) 7 (87)	10 (67) 5 (33)	0 (0) 2 (100)	0 (0) 2 (100)
Co-trimoxazole	4 (18) 18 (82)	3 (38) 5 (62)	5 (33) 10 (67)	1 (50) 1 (50)	1 (50) 1 (50)
Nitrofurantoin	13 (59) 9 (41)	6 (75) 2 (25)	7 (47) 8 (53)	0 (0) 2 (100)	0 (0) 2 (100)

Overall, *E. coli* has highest sensitivity to Amikacin (91%), Gentamicin (77%), and Netilmicin (68%). *Klebsiella* is most sensitive to Gentamicin (87.5%) and piperacillin (75%). *Enterococcus* has highest sensitivity to Vancomycin (67%) and Linezolid (60%). *Proteus* has 100% sensitivity for amoxiclav, amikacin, tobramycin, and ciprofloxacin whereas *Acinetobacter* for gentamicin, ceftriaxone, amoxiclav, ampicillin, norfloxacin and ciprofloxacin.

DISCUSSION

Prevalence of culture proven UTI was 23% in our study which was similar to prevalence in other studies by Kaur, Thaddene and Patwardhan in which 15.7%, 26.8% and 18.3% respectively of suspected UTI children had Culture proven UTI respectively.⁷⁻⁹ Other studies done by Palak et al and Iranian study in which 35.4% and 34.2% of suspected UTI children had Culture proven UTI respectively.^{10,11} In age group of 1-5 years males and in 6-18 years females predominantly had prevalence of culture positive UTI similar to other studies. In the age group of 1 to 5 years the prevalence is 32.4% and in the age group of 6 to 18 years it is 18.2%. The results are in

accordance with the study done by Jitendranath A, Radhika R, which showed urinary tract infections tend to occur in smaller children, that is in the age group 1-5 years.¹² This is because smaller children are still not trained properly to urinate and have not been able to maintain proper genital area hygiene. Lower prevalence in 6-18 years age group may be due to improvement in their immunity and personal hygiene.

The most common causes of UTI in children obtained in this study were *Escherichia coli* (45.83%) and *Enterococcus* (31.25%) followed by *Klebsiella* (16.67%). Although *E. coli* is the commonest organism isolated in the present study (45.83%), the prevalence is low as compared to some other studies such as that of Rai et al and Bagga et al, where they found *E. coli* in 93.3% and 90% of cases respectively.^{4,13} However, some studies, such as, Ashtiani H et al (38.6%), Ejaz et al (37%), Akram M et al (21.4%), have shown less prevalence of *E. coli* as compared to the present study.¹⁴⁻¹⁶ In our study *Klebsiella* and *Enterococcus* were more common in females as compared to *Proteus* which is more common in males. Ghedira et al, mentions that *E. coli* and *Klebsiella* predominantly occurs in girls while *Proteus*

mirabilis are likely encountered in boys.¹⁷ The reason why *E. coli* and Enterococcal UTI occurs more commonly in females is due to retrograde movement of bacteria into lower urinary tract because of proximity of the urethra to anal canal with more chances of Use of diapers and faulty toilet training can lead to infection of urinary tract with faecal organisms as *E. coli* and Enterococci.

Antibiotics with highest sensitivity to *E. coli* were Amikacin (91%), Gentamicin (77%), and Netilmicin (68%). Highest resistance is seen for Ampicillin, vancomycin, Linezolid and most of Fluroquinolones. A Study conducted by Rai et al and Saeed et al, showed that amikacin is the most sensitive antibiotic to *E. coli*.^{14,18} In addition, the Oscarson study also mentions that tigecycline and amikacin are the most sensitive antibiotics to *E. coli*.¹⁹ Next common pathogen in our study was Enterococcus which has highest sensitivity to Vancomycin (67%) and Linezolid (60%). According to Subbalaxami et al, and Rekha Thaddanee et al, Enterococcal infection is increasingly reported in hospital settings from India and these isolates are reported to be sensitive to Vancomycin and Linezolid.⁹

Klebsiella has highest sensitivity for Gentamicin (88%) and piperacillin (75%) whereas highly resistant to cefixime, cefoperazone and Nalidixic Acid (100%). This is similar to results of study done by Batabyal B and Himanshu et al which showed *Klebsiella* has highest sensitivity to Amikacin and Gentamicin and resistance to cefixime and Amoxycylav.²⁰

Proteus has 100% sensitivity for amikacin, tobramycin, and ciprofloxacin and resistant to most of the Cephalosporins. The results are similar to study done by Wilotta adamus-bialek et al which showed all strains of *Proteus mirabilis* were susceptible to Amoxicillin and clavulanate, norfloxacin, ciprofloxacin, ofloxacin and cotrimoxazole.⁴

Acinetobacter is 100% susceptible for gentamicin, ceftriaxone, amoxiclav, ampicillin, norfloxacin and ciprofloxacin and resistant to most of the Cephalosporins. Similar results were seen in a study done by Pooja patel et al in which *Acinetobacter* constituted the third most common agent for UTI and was found to be most sensitive to Piperacillin+Tazobactam, Ofloxacin and Amikacin.¹⁹

This study showed that urinary pathogens are still sensitive to commonly used antibiotics, particularly in community infections, but species distribution and their susceptibility to antibiotics are changing. It requires regular monitoring to determine the current status of resistance against antimicrobial agents.

Limitation of the study were this is a retrospective study so chances of missing data will be more, includes small sample size, prior treatment is also likely among children

admitted to hospital which results in false estimation of prevalence. Follow up for complications were not done.

CONCLUSION

The present situation is alarming, because of emergence of resistance for commonly used antibiotics in children with UTI. Different factors are attributable for emergence of resistance like high consumption of antibiotics, irrational use, incomplete course of therapy, and self-medication by patients. If this continues an effective antibiotic would be failed to treat even simple or minor infections.

Hence, to determine the current status of resistance against antimicrobial agents, routine antimicrobial susceptibility testing must be timely performed. Each country or region has epidemiological data on the bacteria that cause UTIs and different antibiotic sensitivity patterns which is important for guidance in UTI therapy. The pattern of bacterial sensitivity to antibiotics is rapidly changing over time, especially in developing countries so knowledge of hospital sensitivity pattern is atmost important for proper selection of antibiotics in UTI therapy.

In order to decline the resistance, the use of antibiotics must be restricted and monitored. We recommend that empirical antibiotic selection should be based on the knowledge of local pattern of bacterial organisms and antibiotic susceptibility rather than on universal guidelines.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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