

Original Research Article

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Study of Antibiotic Resistance among Uropathogens and Faecal Commensal *Escherichia coli* in Pediatrics Age Group to Revise the Role of Faecal *Escherichia coli* as a Reservoir of Antibiotic Resistance

Sujatha Karjigi* and R. Karthik

Department of Microbiology, Dr. B. R. Ambedkar Medical College and Hospital
Kadugondanahalli, Bangalore-45 Karnataka, India

*Corresponding author

ABSTRACT

Antibiotic resistance is a growing problem in pediatric urology as nonselective use of prophylaxis, and poor empiric prescribing practices. The faecal reservoir provides optimal conditions for the transmission of resistance genes within and between bacterial species as gut is exposed to large number of bacteria. So, this study was undertaken for the knowledge of drug resistance among uropathogens and also revises the possible role of the intestinal microbiota as a reservoir of drug resistant bacteria. Out of 344 urine samples, from 0-14 age group 124 samples had significant growth yielded 134 isolates. *Escherichia coli* was most predominant isolate 71(53%) Antibiotic resistance of Enterobacteriaceae isolates for cephalosporins was 48%, Ampicillin 62%, amoxiclav 50%, Ciprofloxacin 19%, levofloxacin 10.3%, norfloxacin 43%, Nitrofurantoin 6%, gentamicin 12%, amikacin 2.8%, piperacillin -tazobactam 14% and carbapenems 2.8%. Commensal *E. coli* from same patient showed 56.3% resistance to cephalosporin whereas urinary *E. coli* which was 53.5%. Aminopenicillins resistance was also high in both isolates. Resistance to Norfloxacin 21% in faecal *E. coli* and 53.5% in urinary *E. coli*, which was higher among other fluoroquinolones. Aminoglycoside, Nitrofurantoin, Carbapenems had 0-2% antibiotic resistance. Resistance to some of the most commonly prescribed primary care antibiotics in faecal isolates suggest that one cause of carrying bacterial resistant faecal flora could be previous exposure to antibiotics. So Future research must prioritize understanding resistance in non-pathogenic bacteria, which could allow prescribing guidelines to be updated before it affects patient therapeutic outcomes.

Keywords

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Introduction

Urinary tract infection is common clinical problem occurring upto 10% female, 3% male infants and toddlers (Demuri *et al.*, 2008). UTI accounts for majority of causes of unexplained fever in children below 3 years of age (Vigi *et al.*, 2016). UTI with Significant number of

pathogenic bacteria if not treated have greater risk of recurrent episodes and potentially serious consequences including cystitis, urethritis, pyelonephritis and renal scarring in children with vesico ureteric reflux (VUR). (Coulthard *et al.*, 1997) Antibiotics are frequently prescribed everywhere in both empiric and regular therapy for UTI (Cullen *et*

al., 2012). The etiologic agents of urinary tract infection are generally limited to the patient's own intestinal microbiota, with *Escherichia coli*, *Enterococcus* spp., *Klebsiella-Enterobacter* spp., and *Proteus* spp (Henry D Isenberg 2nd ed 2007). The microbiota in the human gastrointestinal tract (GIT) is highly exposed to antibiotics, and may be an important reservoir of resistant strains and transferable resistance genes. Maternal GIT strains can be transmitted to the offspring, and resistances could be acquired from birth (de Vries *et al.*, (2011). Under normal conditions, the gut "receives" a large number of bacteria from the hands, pharyngeal and nasal secretions, water, food, and beverages. Neonates acquire the environmental flora very quickly after birth (Guarino *et al.*, 2012) and in a few cases develop sepsis after translocation of this new flora (Das *et al.*, 2011).

Antibiotic resistance particularly important in low-income countries, where antibiotics are often available OTC, without the need for a prescription (Planta, 2007).

Misuse of antibiotics in this way can expose harmless or opportunistic bacteria to a plethora of antibiotics to which they develop resistance. The resistant organisms then contaminate the environment via the faces [86]. Cross transmission of the resistant strains can occur relatively easily if strong hygiene measures are not taken

Prior antibiotic therapy has been associated with subsequent infection by resistant organisms this pattern is consistent with UTI as well as other infection paper 1(14-19) and the pattern seems consistent irrespective of age, site of initial infection or whether the subsequent infection with the same or different organisms.

The empirical treatment is based on local antimicrobial resistance rates, illness severity.

The antibiotic sensitivity pattern of uropathogens in a population is essential to determine the empirical treatment, as use of inappropriate empirical treatment is found to be predictor of multidrug resistant uropathogens.

So this study was undertaken for the knowledge of drug resistance among uropathogens and also revises the possible role of the intestinal microbiota as a reservoir of drug resistant bacteria. Since *E. coli* was the predominant bacterial lineage found in the gut of young children, this bacterium was investigated for detailed drug resistance profile and was compared with antibiotic resistance of urinary *E. coli* isolates.

Results and Discussion

Out of 344 urine samples from 0-14 age group 124(36%) sample had significant growth.172 (50%) no growth, 28 (8.1%) insignificant bacteriuria20 (5.8%) isolates had mixed growth of more than 3 types suggestive of improper sample collection (Table 1).

124 (36%) samples with significant growth yielded 134 isolates. Causative agents were *E. coli* (53%), *Klebsiella* species (22.4%), *Proteus* species (4.5%) *Enterobacter* species (4.5%), *Pseudomonas* spices (1.5%), *Staphylococcus aureus* (1.5%), Coagulase negative *Staphylococcus aureus* (CONS) (4.5%), *Enterococcus* species (6.7%) and *Candida* species (1.5%) (Figure 1). *Escherichia coli* was most predominant isolate 71(53%) Antibiotic resistance of *Enterobacteriaceae* isolates for cephalosporins was 48%, Ampicillin 62%, amoxiclav 50%, Ciprofloxacin 19%, levofloxacin 10.3%, norfloxacin43%, Nitrofurantoin 6%, gentamicin 12%, amikacin 2.8%, piperacillin-tazobactam 14% and carbapenems 2.8% (Table 2).

Seventy one *Escherichia coli* isolates from stool samples of patient who had significant bacteriuria were further processed for antibiotic resistance as it is most predominant bacteria (Table 3).

In our study gut commensal *E. coli* showed 56.3% resistance to cephalosporin whereas urinary *E. coli* which was 53.5%. Aminopenicillins resistance was also high in both isolates. Resistance to Norfloxacin 21% in feecal *E. coli* and 53.5% in urinary *E. coli*, which was high among other fluoroquinolones. Aminoglycoside, Nitrofurantoin, Carbapenems had better antibiotic sensitivity.

In another study by Ashley Bryce et al antibiotic resistance of urinary pathogen was compared with *E. coli* from insignificant bacterial counts in urine which were considered as gut contaminants. In this study amoxicillin showed 49.37% resistance for urinary isolates and 37.2% for contaminant isolates but cephalosporin's resistance was only 3.8% compared to our study which was

higher 53.3% in urinary isolates may be due to local prescribing patterns.

Study by Kousalya Prabahar et al showed Over 50% of antibiotic prescriptions were started on a clinical basis, without confirmation of a bacterial infection. 70% prescriptions were for cephalosporins in pediatric in patients which supports our finding of increased cephalosporin resistant isolates.

Study by Karen et al., Characterize the *E. coli* fecal flora of UTI patients and healthy controls who had never had a UTI. *E. coli* colonies from each rectal swab were random amplified polymorphic DNA (RAPD) typed for clonality, dominance in the sample and correlation to the infecting UTI isolate in patients. The conclusion of this study was Feecal-UTI isolates from patients were more often associated with multidrug resistance compared to feecal-only clones, indicating a link between UTI virulence and antimicrobial resistance.

Table.1 Age, Gender and Culture Growth Distribution of urine samples

Age group	Growth	Insignific ant growth	No growth	mixed growth >3 isolates	total	SEX	
						Male	Female
<1year	8(50%)	2(12.5%)	4(25%)	2(12.5%)	16(4.6%)	5(31.3%)	11(68.7%)
1-2years	37(67.3%)	2(3.6%)	12(21.8%)	4(7.2%)	55(16%)	18(32.7%)	37(67.3%)
2-5yrs	33(32.4%)	6(5.8%)	60(58.8%)	3(2.9%)	102(30%)	51(50%)	41(40%)
5-10yrs	30(27.5%)	16(14.6%)	56(51.4%)	7(6.8%)	109(32%)	49(45%)	60(55%)
10-14yrs	16(25.8%)	2(3.2%)	40(64.5%)	4(6.4%)	62(18%)	34(54.8%)	38(61.3%)
Total	124(36%)	28(8.1%)	172(50%)	20(5.8%)	344	157(45.6%)	187(54.4%)

Table.2 Antibiotic resistance profile of urinary isolates

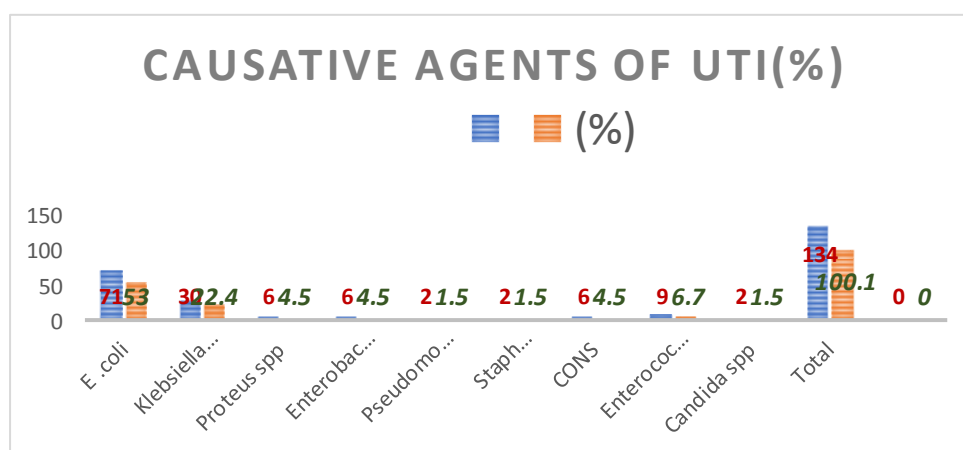
Isolate	AMP	AMC	CZ	CXM	CTR	CTX	CIP	LE	NX	COT	NIT	GEN	AK	PIT	IPM/MRP/ERT
<i>E. COLI - 71</i>	40(56%)	26(36.7%)	38(53.5%)	38(53.5%)	38(53.5%)	38(53.5%)	14(19.7%)	4(5.6%)	38(53.5%)	32(45%)	2(2.8%)	12(17%)	2(2.8%)	12(17%)	2(2.8%)
<i>Klebsiella sp-30</i>	30(100%)	30(100%)	14(46.6%)	14(46.6%)	14(46.6%)	14(46.6%)	4(13.3%)	4(13.3%)	8(26.6%)	6(20%)	2(6.6%)	1(3.3%)	0	2(6.6%)	0
<i>Proteus spp-6</i>	2(33.3%)	2(33.3%)	4(66.6%)	4(66.6%)	4(66.6%)	4(66.6%)	4(66.6%)	4(66.6%)	4(66.6%)	2(33.3%)	3(50%)	2(33.3%)	0	2(33.3%)	0
Total- 116	72(62%)	58(50%)	56(48%)	56(48%)	56(48%)	56(48%)	22(19%)	12(10.3%)	50(43%)	40(34.4%)	7(6%)	15(12%)	2(2.8%)	16(14%)	2(2.8%)

AMP-ampicillin,AMC-amoxyclov,CZ-cephazolin,CXM-Cefuroxime,CTR-ceftriaxone,CTX-Cefotaxime,CIP-Ciprofloxacin,LE-levofloxacin,NX-Norfloxacin,COT-Cotrimoxazole,NIT-Nitrofurantoin,GEN-Gentamicin,AK-Amikacin,PIT-Piperacillin-Tazobactam,IMP-Imipenem,MRP-Meropenem,ERT-Ertapenem

Table.3 Antibiotic resistance of commensal faecal *E. coli* and uropathogen *E. coli* isolates

Isolate	AMPICILLIN-AMP	AMOXYCLAV-AMC	CEPHAZOLIN-CZ	CEFUROXIME-CXM	CEFTRIAZONE-CTR	CEFOTAXIME-CTX	CIPROFLOXACIN-CIP	LEVOFLOXACIN-LE	NORFLOXACIN-NX	COTRIMOXAZOLE-COT	NITROFURANTOIN-NIT	GENTAMICIN-GEN	AMIKACIN-AK	PIP-TAZ-PIT	IPM/ MRP/ ERTA
<i>Faecal E. COLI - 71</i>	45 (63.4%)	30 (42.3%)	40 (56.3%)	40 (56.3%)	40 (56.3%)	40 (56.3%)	12 (17%)	6 (8%)	15 (21%)	29 (40.8%)	0	6(8%)	5 (7%)	5 (7%)	0
<i>Urinary E. COLI - 71</i>	40 (56%)	26 (36.7%)	38 (53.5%)	38 (53.5%)	38 (53.5%)	38 (53.5%)	14 (19.7%)	4 (5.6%)	38 (53.5%)	32 (45%)	2 (2.8%)	12 (17%)	2 (2.8%)	12 (17%)	2 (2.8%)

Figure.1 Causative agents of UTI(%)



The present study isolated showed higher antibiotic resistance to Aminopenicillins, Norfloxacin, cotrimoxazole and Cephalosporin in both faecal and pathogenic

E. coli suggests poor empiric prescribing practices and nonselective use of prophylactic antibiotics this is particularly important in low-income countries, where antibiotics are

often available over the counter, without the need for a prescription (Planta, 2007).

Misuse of antibiotics in this way can expose harmless or opportunistic bacteria to a plethora of antibiotics to which they develop resistance. Which contribute to or cause dysbiosis by directly eliminating the bacterial populations that confer colonization resistance to the intestinal microbiome and exerts selective pressure on both pathogenic and non-pathogenic bacteria which can alter the gut flora and subsequently the urinary tract. This can create an environment where resistant bacteria are able to thrive and persist, and may be an important reservoir of resistant strains and transferable resistance genes. Future research must prioritize understanding resistance in non-pathogenic bacteria, which could allow prescribing guidelines to be updated before it affected patient therapeutic outcomes.

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