Available online at **www.ijmrhs.com**

ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2016, 5, 10:166-169

High prevalence of multiple drug resistance among pediatric *Escherichia Coli* infections

Chaudhary Vigi[1], *Sharma Gaurav[1], Chaudhary Naveen[2] and Raghuvanshi R. K.[3]

[1]Department of Applied and Bio-Sciences, Suresh Gyan Vihar University, Mahal, Jagatpura, Jaipur, Rajasthan, India
[2]Smile and Dental Care, Nandpuri Main Market, Hawa Sadak, Jaipur, Rajasthan, India
[3]Department of Botany, University of Rajasthan, Jaipur, Rajasthan, India
**Corresponding Email:jai_gaurav06@rediffmail.com*

ABSTRACT

Antimicrobial resistance is a serious health menace. Infections caused by multiple drug resistant organisms are on rise making community acquired infections a physicians' nightmare. A survey was conducted to evaluate the prevalence of multiple drug resistant urinary tract pathogens affecting children in Jaipur. Urine samples were collected from children below five years of age. The urine samples were defined as positive culture when a single bacterial species was grown with colony count of $>10^5$ CFU/mL. A total of 240 urine samples were collected out of which only 67 were culture positive. It was found that 67% and 18% of infection was produced by E. coli and Staphylococcal species respectively. Other bacteria which produced urinary tract infection included Klebsiella, Citrobacter and Pseudomonas. The antimicrobial sensitivity pattern of E. coli isolates were tested against 10 commonly prescribed antimicrobial drugs for urinary tract infection as E. coli was the most predominant uropathogen. About 66 percent isolates showed resistance to 3 or more drugs. 46 percent E. coli isolates were resistant to 5 antibiotics tested. The highest resistance was shown to Augmentin (64%). Resistance shown by E. coli to Norfloxacin and Cefuroxime was 60%. About 94% isolates were sensitive to Netilmycin. None of the drugs tested was effective against all E. coli isolates. This type of surveys can act as guidelines for initiating empirical treatment of community acquired urinary tract infections until culture reports are generated.

Keywords: Multiple drug resistance, *E. coli*, Urinary Tract Infection, Children, Paediatric

INTRODUCTION

The second most common infectious disease presentation in community medical practice is urinary tract infection (UTI) [1]. UTI accounts for a majority of causes of unexplained fever in children below 3 years of age [2]. The risk of UTI is greatest in the first year of life. Approximately 1% of boys and 3% of girls usually experience UTI before they are eleven and recurrence of UTI is common in childhood. According to available community studies boys younger than 1 year and girls younger than 5 years of age are most at risk for UTI [3]. The prevalence of UTI in febrile children ranges up to 20%. The vast majority of febrile young children with UTI have pyelonephritis which may lead to renal scarring and in long term renal failure. Unfortunately, in the toddler or young child the classic signs of UTI and pyelonephritis are not present or easily discerned as in the case of older children and adults. The most common symptom of UTI in the infant is fever. *Echerichia coli* is the primary etiologic agent associated with UTI in children [2].

The antimicrobial susceptibility of urinary pathogens have been changing over the years; both in the community and hospital settings. Factors such as unregulated antibiotic use in developing countries, extensive use and misuse of antimicrobial agents could all contribute to changes in the microbial profile of uropathogens. In the hospital setting most cases of UTI are initially treated empirically [4]. Empirical treatment is based on the local antimicrobial resistance rates and illness severity. In an infant or acutely symptomatic child with pyelonephritis treatment will have to be started before the results of urine culture and sensitivity as delay in treatment can result in permanent renal damage. The antibiotic sensitivity pattern of uropathogens in a population is essential to determine the

empirical treatment as the use of inappropriate empirical treatment was found to be a predictor of mortality in patients who had septicaemia originating from a urinary tract source. In India, the resistance pattern of community acquired uropathogens has not been extensively studied [5]. This study was conducted to determine antibiotic resistance patterns among uropathogens affecting children in Jaipur to help formulate local guidelines on empirical antibiotic treatment of community acquired UTI.

MATERIALS AND METHODS

Urine samples were collected from patients visiting clinical microbiology laboratory at Jaipur. Only samples collected from children under the age of 5 years (both male and female) were included in the study. All patients had clinical evidence of a urinary tract infection as determined by the treating physician. Only a single positive culture per patient was included in the analysis. Patients without clinical evidence of infection and multiple pathogens in urine culture were excluded from the study. Semi-quantitative urine culture was done using a calibrated loop. Samples were inoculated on blood agar, Mac Conkey agar and nutrient agar plates. Plates were read after overnight incubation at 37ºC. Significant monomicrobic bacteriuria was defined as culture of a single bacterial species from the urine sample at a concentration of $>10^5$ cfu/mL. The significant pathogens were identified by standard biochemical procedures.

Antimicrobial susceptibility testing was performed using the disc diffusion method as described by Clinical Laboratory Standard Institute (CLSI) [6]. Antimicrobial agents (disks) tested and reported were obtained from Pathoteq Biological Laboratories, Gujarat. Sensitivity testing was done for Ampicillin+Sulbactum (AM; 10+10=20mcg), Augmentin (AG; 20+10= 30mcg), Ceftriaxone (RP; 30mcg), Cefoperazone (CP; 75mcg), Cefuroxime (CB; 30mcg), Ciprofloxacin (RC; 5mcg), Doxycycline (DX; 30mcg), Gentamicin (GM; 10mcg), Netilmycin (NT; 30mcg) and Norfloxacin (NX; 10mcg).

RESULTS

Of the 240 urine samples processed, 173 (72%) were sterile and 67(28%) gave significant monomicrobic growth. Data of prevalence of uropathogens (Table 1) revealed that *E. coli* (45) is the single most commonly occurring urinary tract pathogen among children. Gram negative bacilli accounted for 87.6 % while Gram positive cocci accounted for the remaining 19.4 % of the total uropathogens (Figure 1).

Table: 1. Frequency and Distribution of Uropathogens

Serial No.	Microorganism Identified	No. Of Isolates
1	*Escherichia coli*	45
2	*Staphylococci* (coagulase positive)	06
3	*Staphylococci* (coagulase negative)	06
4	*Klebsiella sp.*	04
5	*Citrobacter*	02
6	Non-hemolytic *Streptococci*	01
7	*Proteus*	01
8	*Pseudomonas*	01
9	*Enterobacter*	01

Table: 2. Percentage of *E. coli* resistant to various antimicrobial agents

Serial No.	Antibiotic	No. of resistant strains	Percentage resistance
1	Ampicillin + Sulbactum	17	37.7
2	Augmentin (Amoxicillin + Clavulanic acid)	29	64
3	Ceftriaxone	21	47
4	Cefoperazone	16	35.5
5	Cefuroxime	27	60
6	Ciprofloxacin	25	55.5
7	Doxycycline	18	40
8	Gentamicin	5	11
9	Netilmicin	3	6
10	Norfloxacin	27	60

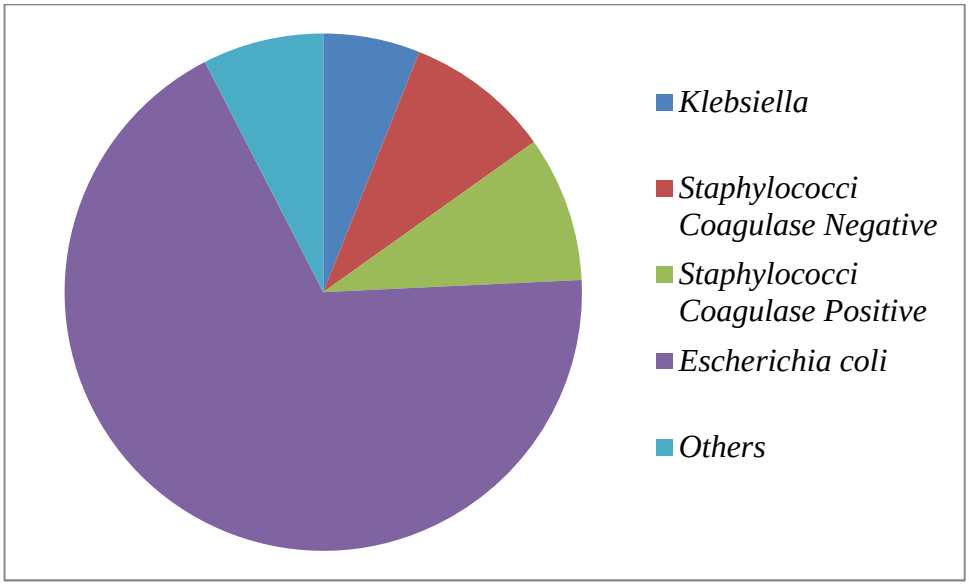

Fig. 1: Relative distribution of uropathogens isolated from children

Table: 3. Class of Antibiotics used in this study

Serial No.	Antibiotic	Classification
1	Augmentin (Amoxycillin + Potassium clavulanate)	Penicillin (Pen)
2	Ampicillin + Sulbactam	First Generation Cephalosporin (Cep^1)
3	Cefuroxime	Second Generation Cephalosporin (Cep^2)
4	Cefoperazone	Third Generation Cephalosporin (Cep^3)
5	Ceftriaxone	Third Generation Cephalosporin (Cep^3)
6	Doxycycline	Tetracycline (Tet)
7	Norfloxacin	Fluoroquinolone (Fqn)
8	Ciprofloxacin	Fluoroquinolone (Fqn)
9	Gentamicin	Aminoglycoside(Amn)
10	Netilmicin	Aminoglycoside(Amn)

The antimicrobial agents with highest levels of activity against *E. coli* isolates were netilmicin and gentamicin. The highest resistance was shown to Augmentin (64%; Table: 2.). Only 40% of *E. coli* isolates were susceptible to Norfloxacin and Cefuroxime. About 94% isolates were sensitive to Netilmycin. None of the drugs tested was effective against all *E. coli* isolates. About 66.6 % *E. coli* isolates showed resistance to 3 or more drugs. 46.6 % and 26.6 % *E. coli* isolates were resistant to 5 and 6 antibiotics tested respectively. Lowest degree of resistance was against aminoglycosides. Surprisingly more that 50 percent of *E. coli* isolated from pediatric patients were resistant to both floroquinolone antibiotics used in this study. 22 isolates were resistant to Penicillins and Cephalosporins combinations as well as Cephalosporins and Fluoroquinolone combinations. About 38 % isolates were resistant to three major classes of antibiotics namely Penicillins, Cephalosporins and Fluroquinolones. *5 isolates showed combined resistance to at least one of the antibiotics of all the five classes of antibiotics tested which in itself is of great concern.*

DISCUSSION

The most commonly isolated uropathogen in community acquired urinary tract infection among paediatric outpatients in our study was *E. coli.* This corresponds with the data obtained by other investigators [7-11]. The antimicrobial susceptibility pattern of uropathogens varies widely by region. We demonstrate a high level of resistance to Augmentin, Norfloxacin, Cefuroxime and Ciprofloxacin. This is similar to previous studies in India on community acquired urinary tract infection [5]. The most widely used antibiotics for the treatment of urinary tract infections are fluoroquinolones [12]. The high prevalence of resistance to both the fluoroquinolones tested may be attributed to its frequent use as antimicrobial agent for treating urinary tract infections in the community. The high degree of resistance to β-lactam antibiotics observed in our study corresponds to earlier reports [11]. A similar study of antimicrobial resistance trends in *E.coli* uropathogen isolated from pediatric patients in Kerala also found high combined resistance to most commonly used antimicrobials including β-lactams, quinolones, tetracyclines and aminoglycosides [13].With widespread non prescription use of antibiotics in India, leading to huge selection pressure the multiple drug resistance problems are likely to get substantially worse in the near future. With few new antibiotics in the pharmaceutical pipeline, this scenario is of great concern [14]. The lack of a national networking

system for the monitoring of antimicrobial resistance in India has compounded to the menace of multiple drug resistant microorganisms [15].

CONCLUSION

Elevated resistance of *E. coli* uropathogens to Ceftriaxone among pediatric patients is very alarming as it is one of the life saving drugs for pediatric patients suffering from septicaemia. High resistance rates to oral antibiotics in our study may be due to the uncontrolled consumption of these antibiotics in the Indian population in the past decades. On the other hand resistance to Netilmicin, Gentamicin and Cefoperazone are low, likely reflecting lower usages of these drugs. The higher number of resistant strains to Norfloxacin and Ciprofloxacin observed was predictable owing to its easy availability as over the counter drugs which are commonly used against all intestinal infections. A systematic and judicious action is necessary to curb the evolution of antibiotic resistance in India. To maintain the useful life of antimicrobial drugs in India, improved surveillance of the emergence of resistance, better regulation of antibiotic use and better education of the public [16], doctors and veterinarians in the appropriate use of the drugs are essential.

Acknowledgements
The authors are grateful to Mr. Firoz for technical support and Dr. Zafar Rafique for his generous support in procuring samples and using the facilities at Meditech Clinical Laboratory, Jaipur.

REFERENCES

[1] Akram M, Shahid M and Khan AU. Etiology and antibiotic resistance patterns of community acquired urinary tract infections in JNMC Hospital Aligarh, India. Ann of Clin Micro and Antimicrob. 2007; 6:4:1-7. doi: 10.1186/1476-0711-6-4
[2] Gulati S and Kher V. Urinary tract infection. Indian Pediatrics. 1994; 33: 211-217.
[3] Shaw KN, Gorelick M, McGowan KL, Yakscoe NM and Schwartz JS. Prevalence of urinary tract infection in febrile young children in the emergency department. Pediatrics. 1998; 102:2:1-5.
[4] Gales AC, Jones RN, Gordon KA, Sader HS, et al. Activity and spectrum of 22 antimicrobial agents tested against urinary tract infection pathogens in hospitalized patients in Latin America: report from second year of the SENTRY Antimicrobial Surveillance Program (1998). J Antimicro Chemo. 2000; 45: 295-303.
[5] Kothari A and Sagar V. Antibiotic resistance in pathogens causing community-acquired urinary tract infections in India: a multicenter study. J Infect Developing Countries. 2008; 2(5): 354-58.
[6] Clinical Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing, document M100-S17. Clinical Laboratory Standards Institute, Wayne, PA. 2007.
[7] Barrett SP, Savage MA, Rebec MP, Guyot A, Andrews N and Shrimpton SB. Antibiotic sensitivity of bacteria associated with community- acquired urinary tract infection in Britan. J Antimicrob Chemo. 1999; 44:359-65.
[8] Daza R, Gutierrez J and Piedrola G. Antibiotic susceptibility of bacterial strains isolated from patients with community-acquired urinary tract infections. Int J Antimicrobial Agents. 2001; 18: 211-15.
[9] Karlowsky JA, Kelly LJ, Thornsberry C, Jones ME and Sahm DF. Trends in antimicrobial resistance among urinary tract infection isolates of Escherichia coli from female outpatients in the United States. Antimicrob Agents and Chemo. 2002; 46:8: 2540-45.
[10] Kahlmeter G. An international survey of the antimicrobial susceptibility of pathogens from uncomplicated urinary tract infections: the ECO.SENS Project. J Antimicrob Chemo. 2003; 51: 69-76. doi: 10.1093/jac/dkg028
[11] Hawser SP, Bouchillon SK, Hoban DJ, Badal RE, Hsueh P and Paterson DL. Emergence of high elevels of extended spectrum β-lactamase producing Gram negative bacilli in the Asia-Pacific region: Data from the study for monitoring antimicrobial resistance trends (SMART) program, 2007. Antimicrob Agents and Chemo. 2009; 53:8: 3280-84.
[12] Lindgren PK, Karlsson A and Hughes D. Mutation rate and evolution of fluoroquinolone resistance in Escherichia coli isolates from patients with urinary tract infections. Antimicrob Agents and Chemo. 2003; 47:18: 3222-32.
[13] Nisha KV, Shenoy RD, Shetty AV, Shenoy VM and Shetty AK. Trends in antimicrobial resistance among uropathogens with special reference to E. coli in community acquired pediatric urinary tract infections from Kerala. J Evol Medical and Dental Sci. 2015;4(54):9313-20. doi: 10.14260/jemds/2015/1354
[14] Kumaraswamy KK, Toleman MA, Bagaria J, Butt F, et al. Emergence of a new antibiotic mechanism in India, Pakistan and the UK: a molecular, biological and epidemiological study. Lancet Infect Dis. 2010; 10(9): 597-602.
[15] Rahal K, Wang F, Schindler J, Rowe B, et al. Reports on surveillance of antimicrobial resistance in individual countries. Clinical Infect Dis. 1997; 24: S169-75.
[16] Jain A, Dhir SK, Batta M and Singh G. Knowledge and practices in community regarding antibiotic usage. Int J Res Med Sci. 2016; 4(20):610-14. doi:10.18203/2320-6012.ijrms20160325