Original Article

A Study on Antibiotic Sensitivity Pattern in Children Hospitalized for Urinary Tract Infection in a Tertiary Care Hospital in South India

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ABSTRACT

Background: The etiology of urinary tract infection (UTI) and their antibiotic sensitivity pattern vary from time to time and across different areas in India. This study is designed to analyse the resistance of uropathogens to commonly used antibiotics. **Aim:** To study antibiotic resistance trends of uropathogens and assess the antimicrobial utilization pattern according to the antimicrobial susceptibility test in the paediatric department of a tertiary care hospital. **Materials and Methods:** It was an ambispective observational cohort study conducted in 144 patients admitted with UTI for a period of one year and observed for recurrent UTI for the next one year. **Results:** *E. coli* (50%) was found to be the most common cause of UTI followed by *Klebsiella* (22.22%). *E. coli* and other isolates were more sensitive to Meropenem and Amikacin compared to other antibiotics tested. These isolates show increasing resistance to commonly used antibiotics. Most (74.31%) children were given single antimicrobial agent. Majority of the children were prescribed with Cephalosporins (60.41%), followed by Penicillin derivatives (29.17%) and Carbapenems (11.11%). Out of 144 children, antibiotics were prescribed according to culture sensitivity report in only 31.94%. Among children whose antibiotics were not selected based on the culture report, 40 had recurrent UTI in the following year. **Conclusion:** Recurrent UTI can occur if adequate antimicrobial therapy based on antimicrobial susceptibility test is not administered during the initial UTI episode. Close cooperation between physicians, microbiologists and pharmacists is essential to ensure that UTI patients receive antimicrobial therapy, if required based on local susceptibility data.

Key words: UTI, Uropathogens, Antimicrobials, Pediatrics, Antibiotic resistance.

INTRODUCTION

UTI can occur in all age group starting with neonates.[1] Incidence of UTI varies with age of the child. UTI is primarily due to the ascending infection from the urethra. Most UTIs are caused by Gram-negative bacteria, among them the most common pathogen is *Escherichia coli*.[2,3] Other bacteria causing UTIs include *Proteus, Klebsiella, Enterobacter, Citrobacter, Enterococcus* and *Staphylococcus saprophyticus*. Fungal UTIs, like *Candida albicans* infections, often happens in patients with recent antibiotic treatment, immunosuppression or urinary catheterisation. Symptomatic viral UTIs are uncommon.[4] In the pediatric population UTI is a reason of acute morbidity and chronic medical conditions, like hypertension and renal scarring in later life. Early diagnosis and appropriate treatment of UTI in young children is essential as it can significantly decrease late serious complications. Diagnosis of UTI is difficult based on clinical characteristics because of the diverse non-specific clinical characteristics. In children, more practical method is to classify UTI as a primary infection versus recurrent infection. The initial UTI documented by a proper urine culture is the first infection. Recurrent infections can be further subdivided into unresolved bacteriuria, bacterial persistence and reinfection.[5] Unresolved bacteriuria is usually caused by resistant uropathogens. Generally appropriate antimicrobial treatment based on antibiotic sensitivity pattern can resolve infections of the urinary tract in most children.[6,7] Anatomic defects of the urinary tract should be suspected if recurrent infections occur at short intervals

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with the same organism. Such defects must be corrected otherwise it can become a bacterial focus within the urinary tract.[8]

It is well known that, there may be marked differences in pathogens found and antibiotic sensitivity pattern between various geographic areas within the same country. There are very few reports on resistance pattern of community acquired UTI from India especially in children.[9,10] Comparison of the antibiogram trends in different studies suggested, an increasing resistance amongst uropathogens to antibiotics over the last few years. There is a need to gain knowledge about the types of uropathogens and their resistance patterns for rational use of antimicrobials. Moreover, there is a need to know whether antimicrobial is selected based on antimicrobial susceptibility test to prevent recurrent infections. With this background the present study aims to assess the antimicrobial utilization pattern and resistance trends of uropathogens isolated in community acquired UTI in children in South India.

MATERIALS AND METHODS

This was an ambispective observational study carried out in the department of paediatrics of a 1250 bed tertiary care hospital, teaching and super specialty referral hospital located in south India over a period of 2 year from Nov 2017 to Nov 2019. Isolates included were those of children aged ≤ 18 years with culture - proven UTI. The standard laboratory test used for diagnosis of UTI was growth of single uropathogenic bacteria in a urine culture from a properly collected urine sample as per institutional guidelines. Ethical clearance was obtained from the Institutional Ethics Committee of the hospital before starting the study. We included 144 patients in our study based on the inclusion and exclusion criteria from Nov 2017 to Nov 2018 and observed for recurrent UTI in the cohort for the next 1 year. Data like patient's demographic characters, antibiotics prescribed, dose, route of drug administration, frequency and duration of treatment were collected from patient records. All data were recorded in data collection form and analysed to answer the objectives of this research. Data was analysed using descriptive analysis and results were presented using tables.

RESULTS

Out of 2187 patients admitted in the paediatrics department during the study period, 144 children had culture positive UTI, making the prevalence of 6.58 %. The most affected age group was 1-5 years (n = 94; 65.28%), followed by children < 1 year (n = 24; 16.67%). Males (n = 15; 10.42%) outnumbered females (n = 9; 6.25%) in < 1 year age group but females (n = 63; 43.75%) were more than males (n= 57; 39.58%) in 1- 5 year age group. Age distribution of patients included in our study is the Table 1. Results indicated that *E. coli* (n = 72; 50%) and *Klebsiella* (n = 32; 22.22%) are the commonest pathogens for causing UTI among paediatric patients in our hospital. Table 2 relates the uropathogens isolated from the paediatric patients during the study period. Comparison of sensitivity and resistance patterns in percentage of *E. coli* and *Klebsiella* for various antimicrobials in urinary tract infection is shown in the Table 3.

Cephalosporins was prescribed to majority of the children (n = 87; 60.41%), followed by Penicillin derivatives (n = 42; 29.17%) and Carbapenems (n= 16; 11.11%), which comprised of Ceftriaxone (n = 55; 38.19%), Cefotaxime (n = 11; 7.64%), Ceftazidime (n = 8; 5.56%), Cefoperazone (n = 6; 4.17%), Cefixime (n = 3; 2.08%), Cefpodoxime (n = 2; 1.38%), Cefuroxime (n = 2; 1.38%), Piperacillin/ tazobactum (n = 17; 11.81%), Amoxicillin/clavulanate (n = 15; 10.42%), Benzyl penicillin (n = 8; 5.56%), Ampicillin/cloxacillin (n = 2; 1.39%) and Meropenem (n = 16; 11.11%) respectively. Among Cephalosporins, third generation Cephalosporins were antibiotics of choice for paediatric patients, which accounts for 59.02% (n = 85). A high percentage of patients 74.31% (n =107) were prescribed on at least one antibiotic, two antibiotics were prescribed in 18.75% (n = 27) and three antibiotics were prescribed in only

Table 1: Age distribution of patients observed in our study.

Age distribution	Number (%) of patients
Less than 1 year	24 (16.67%)
1-5 years	94 (65.28%)
5-10 years	17 (11.81%)
10-15 years	3 (2.08%)
15-18 years	6 (4.17%)
Total number of patients	144 (100%)

Table 2: Isolated uropathogens during study period.

Pathogens	Number (%)
Escherichia coli	72 (50%)
Klebsiella species	32 (22.22%)
Proteus species	4 (2.78%)
Pseudomonas	8 (5.56%)
Enterococcus species	20 (13.89%)
Others	8 (5.56%)
Total	144

Table 3: Comparison of sensitivity and resistance patterns in percentage of *E. coli* and *Klebsiella* for various antimicrobials in urinary tract infection.

Drug	*E. coli*		*Klebsiella*	
	Sensitive n (%)	Resistant (%)	Sensitive (%)	Resistant (%)
Amikacin	124 (86.11)	20 (13.89)	103 (71.53)	41 (28.47)
Gentamycin	86 (59.72)	58 (40.28)	85 (59.03)	59 (40.97)
Tobramycin	94 (65.28)	50 (34.72)	99 (68.75)	45 (31.25)
Ceftriaxone	28 (19.44)	116 (80.56)	58 (40.28)	86 (59.72)
Cefotaxim	20 (13.89)	124 (86.11)	50 (34.72)	94 (65.28)
Ceftazidime	24 (16.67)	120 (83.33)	54 (37.5)	90 (62.5)
Cefoperazone/Sulbactam	98 (68.06)	46 (31.94)	90 (62.5)	54 (37.5)
Cefixime	2 (1.39)	142 (98.61)	0 (0)	100 (100)
Cefuroxime	22 (15.28)	122 (84.72)	36 (25)	108 (75)
Cefazolin	22 (15.28)	122 (84.72)	36 (25)	108 (75)
Ampicillin/Sulbactam	2 (1.39)	142 (98.61)	0 (0)	100(100)
Ampicillin/Amoxicillin	10 (6.94)	134 (93.06)	0 (0)	100(100)
Amoxicillin/Clavulanic acid	12 (8.33)	132 (91.67)	13 (9.03)	131 (90.97)
Piperacillin/Tazobactam	96 (66.67)	48 (33.33)	77 (53.47)	67 (46.52)
Ticarcillin/Clavulanic acid	36 (25)	108 (75)	18 (12.5)	126 (87.5)
Meropenem	138 (95.83)	6 (4.17)	117 (81.25)	27 (18.75)
Nitrofurantoin	122 (84.72)	22 (15.28)	40 (27.78)	104 (72.22)
Co-trimoxazole	34 (23.61)	110 (76.39)	81 (56.25)	63 (43.75)
Ofloxacin	50 (34.72)	94 (65.28)	76 (52.78)	68 (47.22)

6.94% cases (n = 10). Majority of the children were prescribed with antibiotics for duration of 1-5 days in 67 children (46.53%), 6-10 days in 64 children (44.44%) and more than 10 days in 13 children (9.03%). Antibiotics were administered through parenteral route in 114 cases (79.17%), oral route in 22 cases (15.28%) and 8 cases (5.55%) received both oral and parenteral antibiotics.

Out of 144 children, antibiotic was not given for 21 children (14.58%) and was not given based on culture sensitivity pattern in 77 children (53.47%) during first UTI. Among them 40 children (27.77%) had recurrent UTI, in which same organism was isolated in 19 children (13.19%) and different organism was noticed in 21 children (14.58%) during subsequent UTI episodes.

DISCUSSION

The prevalence of UTI in our study population was lower; this might be because our study was conducted at a tertiary care hospital and included only children with positive urine culture test. Children within the age group of 1-5 years were most affected. Our findings were similar to the study conducted by Rad LV *et al*. where they observed that the majority of the patients belonged to the age group of less than 5 years.[11] The main reason may be because of immature immune system in early childhood. Children of this age group are also at risk of developing recurrent UTI due to certain anatomic and physiologic factors like vesicoureteric reflux (VUR). Males were more than females in < 1 year age group but females were more than males in 1-5 year age group. This was similar to the findings of Gupta P *et al*. and Kiran *et al*. in which UTI was more common in males in the first year of life and beyond 1 year with female predominance.[12,13] UTI is more frequent in females as they have short urethra which is near to the anus, therefore aid easy ascent of bacterial pathogens from the gastro intestinal tract to the urinary tract. UTI is less frequent in males due to longer course of urethra and bacteriostatic secretion by prostate gland.

The commonest pathogen found in our hospital was *E. coli* followed by *Klebsiella*. This was in accordance with other studies done by Nisha KV *et al*. Kiran *et al*. Gupta P *et al*. Jitendranath A *et al*. and Gidabayda *et al*. in which *E. coli* was isolated from 46.2% to 69% followed by *Klebsiella* in 15.2% to 30.8% of cases.[12-16] *E. coli* and *Klebsiella* was found to be more sensitive to Meropenem

followed by Amikacin. The isolated organisms showed high level of resistance to commonly used antibiotics like penicillin derivatives, cephalosporins, quinolones and co-trimoxazole. In all cases the patients were found to be resistant to more than 5 antibiotics. This is similar to other studies on community acquired UTI by Nisha KV *et al.* in which *E. coli* showed high level of resistance to commonly used antibiotics like ampicillin, cephalosporins (cefixime, cefotaxime), fluoroquinolones (ciprofloxacin, norfloxacin) and co-trimoxazole.[14] In the study by Taneja N *et al.* consisting of 558 isolates, 32.7% and 75.5% were resistant to ampicillin and cephalosporin respectively.[17] Ghadage DP *et al.* have documented 98% and 87% resistance to ampicillin and cephalosporin in their 390 culture positive samples.[18] Similarly, Rao SP *et al.* in their 857 culture positive urine samples show 89% resistance to cephalosporins.[19] Indiscriminate prescription and high frequency of extended spectrum beta-lactamases (ESBL) producing organism may be the reason for high resistance of *E. coli* to usually used antibiotics resulting in complicated UTI.[20]

Cephalosporins were prescribed to majority of the children followed by Penicillin derivatives and Carbapenems. Among Cephalosporins, third generation Cephalosporins were antibiotics of choice for paediatric patients. In this study Piperacillin/tazobactum and Amoxicillin/clavulanate were mostly prescribed drugs among penicillin derivatives. Among Carbapenems, Meropenem was the only drug which was prescribed for the paediatric patients in this study. Similar study conducted by Rad LV *et al.* assessed that Cephalosporins (58.06%), followed by beta lactamase inhibitors (19.35%) were choice of antimicrobial agents for paediatric patients, which was similar to our study and Ceftriaxone (67.77%) was the most commonly prescribed Cephalosporin.[11] This study also recognized that in case of UTIs, a considerable increase in the use of third generation cephalosporins. This is similar to the study conducted by Copp HL *et al.* and Prabahar K *et al.* in which approximately one third of the UTI patients were treated with broad spectrum antibiotics for empirical therapy which is an example of overprescribing broad spectrum antibiotics in paediatrics.[21,22] Berild D *et al.* showed that modifying antibiotic therapy according to the blood culture results guides to a narrowing of antibiotic therapy.[23] Thus, antibiotic resistance can be avoided or delayed. Kumar R *et al.* reported that among the patient related features, 1-10 year age group received antibiotics significantly more commonly than patients beyond 60 years of age suggesting the over prescription of antibiotics in paediatrics.[24] Gandra S *et al.* concluded that 61.5% of the hospitalized children were on at least one antimicrobial agent with excessive use of third-generation cephalosporins.[25]

Majority of patients were prescribed with single antimicrobial in our study. Similar study conducted by Shankar PR *et al.* assessed that, 98% of patients were prescribed a single antimicrobial which was similar to our study.[26] Another study conducted by Palikhe N *et al.* assessed that two antibiotics were prescribed in more cases (37%), which was differ from that of our study.[27] Majority of the children were prescribed with antibiotics for duration of 1-5 days. The most preferred dosage form was injectables. The excessive use of injectable is common in many developing countries.[28] Injectables are given more compared to oral route for rapid control of infections, to reduce morbidity and to avoid incompliance issues. Another study conducted by Ramesh L *et al.* on analysis of antimicrobial prescriptions in pediatric patients in a teaching hospital had proven that injections were the commonest route of administration by 58.25% followed by oral route 38.20%.[29]

There are chances for physicians to miss the results of urine culture when it is available. The frequency of antibiotic prescription or modification based on urine culture result was low in our study. Because the patients are doing well on empirical therapy often the results of urine cultures are ignored. Relapse UTI is the major problem that can occur due to this ignorance. Inadequate antimicrobial therapy usually results in unresolved bacteriuria. Sometimes the uropathogen resides in a site that is secured from antimicrobial therapy. These shielded sites are usually anatomic abnormalities. Detection of the anatomic defect is also important as surgical intervention may be essential to eliminate the cause of infection.[30]

Limitations of the study

The study was restricted to a single centre. The clinical condition of the patient was not taken into consideration during the study while ensuring the agreement between the empirical therapy and definitive therapy. We recommend further interventional studies by clinical pharmacists on rational use of antibiotics in paediatrics department.

CONCLUSION

The prevalence of UTI with multi-drug resistance is increasing in the hospitalized pediatric population. *E. coli* and *Klebsiella* were more sensitive to Meropenem and Amikacin compared to other antibiotics tested. But Cephalosporins was prescribed to majority of the children, followed by Penicillin derivatives. In all cases the patients were found to be resistant to more than 5 antibiotics. The study helps to obtain information on the antibiotic usage pattern in the pediatric population,

focusing on prevalence of antibiotic misuse in our set-up. Recurrent UTI can occur if adequate antimicrobial therapy based on antimicrobial susceptibility test is not given during initial UTI. This shows the requirement for rational use of antimicrobials and judicious prescribing.

Clinical pharmacists have a key responsibility in monitoring adherence to antimicrobial susceptibility of uropathogens while selecting antibiotics for treatment of UTI. Close co-operation between clinicians, microbiologists and pharmacists is essential to monitor the use of reserved antibiotics. This study helps to encourage proper antibiotic practice and provide as a check mark to the health-care professionals. There is a continued need for monitoring of antimicrobial susceptibility of uropathogens and based on that it is important to generate regional data on antibiogram pattern to guide therapy with periodic assessment of the clinical pharmacist in the study area to monitor the clinical use of these medications.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

UTI: Urinary tract infection; **VUR:** Vesicoureteric reflux; **ESBL:** Extended spectrum beta-lactamases.

SUMMARY

An ambispective observational study was carried out in the paediatrics department to study the antibiotic resistance trends of uropathogens. The study also evaluated the antibiotic utilization pattern and identified the need for close cooperation between clinicians, microbiologists and pharmacists for the rational use of antimicrobials.

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