Drug Prescribing Patterns in Pediatric Urinary Tract Infections: A Retrospective Drug Utilization Analysis in an Urban Tertiary Care Hospital

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Introduction: A constant update of antibiotic sensitivity of pathogens of the area, country, or institution helps in interventions that would improve the prescribing pattern and rational use of drugs in children. This study aimed to assess prescribing trends for urinary tract infection (UTI), a common distressful pediatric infection in a tertiary care teaching hospital. Materials and Methods: This study was a descriptive, retrospective, cross-sectional, and record-based analysis including pediatric patients aged <18 years of either gender diagnosed with UTI. The case record files retrieved from medical records department based on the International Classification of Diseases, 10th Revision (ICD-10) disease coding were analyzed for demographics, and details of drugs including dose and route of administration, frequency, and duration of treatment with antimicrobial used and other concurrent drugs were recorded. Results: Of 42 patients included in the study, 14 (33.3%) were males and 28 (66.67%) were females. Third-generation cephalosporins were the most commonly used antibiotics (71.4%) followed by aminoglycosides (35.7%), amoxicillin clavulanate (11.9%), fluoroquinolones (7.1%), and miscellaneous (doxycycline, metronidazole, and nitrofurantoin) (9.5%). Ceftriaxone among the cephalosporins and amikacin among the aminoglycosides were the most commonly used drugs. Intravenous route was the most commonly used route of administration followed by patients who received by both intravenous and oral routes. The average duration of therapy was 4.43 ± 1.9 days. Conclusion: This study concludes that third-generation cephalosporin is used as first-line drugs irrespective of the causative agent for UTI which should ideally be reserved for complicated UTIs. Moreover, existing guidelines also indicate that the duration of antimicrobial therapy should be seven to 14 days. These results highlight the necessity for a remedial education program within the health care system designed to improve pharmacotherapy of UTI.

Keywords: Drug utilization, pediatric, prescribing patterns, urinary tract infection

INTRODUCTION

Urinary tract infection (UTI) constitutes one of the most common ailments in children, perturbing to both the child and parents and may also be a forerunner for renal damage, especially in recurrent cases. Expeditious diagnosis coupled with timely and effective treatment of febrile UTI are the cornerstones in the
prevention of discomfort in acute cases and kidney damage in recurrent ones. The incidence of UTI may differ with respect to the age of the child. In children below 2 years, 5% of the children with fever may be infected with UTI. The incidence is more common in boys (3.7%) than in girls (2%) in the first three months of the infant life. Thereafter, it is more often seen in girls (3%) than in boys (1.1%).

Children top the risk category of developing UTI as a consequence of certain factors chief among which is vesicoureteral reflux (VUR). VUR results in recurrent infections including complexities like chronic pyelonephritis with eventual scarring of the kidneys. Therefore, it is of paramount importance to timely diagnose this condition and prevent further consequences more-so-ever as it is a preventable cause. Escherichia coli is commonly found as the most recurrent culprit of bacterial UTI. The drug susceptibility patterns of the bacterial isolates may vary from one place to another and is most commonly employed as a standard for selecting empirical antibiotics. However, the etiology and susceptibility patterns of organisms causing UTI are constantly changing and evolving with drug resistance posing as a significant menace for effective therapy.

Infection of the urinary tract is established by identifying “significant growth of single species organisms in the urine sample, in a symptomatic patient.” Positive urine culture should be the deciding factor in the diagnosis of UTI as it is most relevant in subsequent therapy and follow-up of the patient. Recurrent UTI, defined as “the recurrence of symptoms with significant bacteriuria in patients who have recovered clinically following treatment,” is common among females. Recurrent UTI not only adds on to the anxiety of parents, but it also poses significant medical expenditure and risk of renal parenchymal damage in children. The recently published revised statement on Management of UTIs by the Indian Society of Pediatric Nephrology is a handy reference guide for physicians in managing UTI in children.

Uncomplicated UTI is mostly amenable to treatment with outpatient antibiotics without consequent sequelae. The dramatic rise of antibiotic resistance among uropathogens is indeed causing a significant threat in recent times. Exposure to antibiotics for previous infections for instance otitis media may be associated with subsequent resistance to antimicrobials used for UTI and should be a decisive factor in choosing empiric therapy. Variations in rates of resistance are a norm rather than a chance and hence mandate constant updating of antibiotic sensitivity of uropathogens specific for a particular geographical area, country, or institution. Resistance is clinically significant in uncomplicated UTI albeit less than in systemic infections such as cystitis or pyelonephritis. Development of resistance can significantly be reduced by short duration of therapy as reported earlier.

Medical audit is an important step in elevating the standards of therapeutics. One of the important components of medical audit constitutes the study of prescribing pattern which aims at monitoring, evaluating, and seeking requisite changes in the prescribing habits of the physicians. The main goal of such studies is to achieve rational therapeutics and cost-effective health care. Defining prescribing patterns and identification of irrational prescriptions help to reform and restitute healthcare practices of the prescribers. Drug utilization is defined as “the marketing, distribution, prescription and use of drugs on society with special emphasis on the resulting medical and social consequences.” Drug utilization studies empower rational therapeutics in identification of errors in implementing therapy and find appropriate remedies and solutions to rectify them. Rational drug prescribing is defined as “the use of the least number of drugs to obtain the best possible effect in the shortest period and at a reasonable cost.” Prescription monitoring and drug utilization studies focus on determining the causes and associated problems and also offer actionable feedback to the prescriber so as to increase their perceptions and familiarize them about the irrationality in their use of drugs. These studies ascertain and evaluate the efficacy, safety, convenience, and economic aspects of the use of drugs all levels in the chain of use of drugs. In earlier analyses involving adult patients in India, authors have shown that there were increased irrational prescriptions of antibiotics in the treatment of UTI, which if found in children might lead to increased prevalence of antimicrobial resistance, a physician induced-health hazard. As prescription studies in children have been limited and the consequences of irrational drug use grave, this study was designed to assess prescribing trends and analyze utilization pattern of drugs used for UTI in the pediatric department of a tertiary care teaching hospital. The information is expected to help in interventions that would improve the prescribing trends and promote the judicial use of drugs in children.

**Materials and Methods**

The study was a retrospective, cross-sectional, record-based analysis. The medical case records of pediatric patients (age <18 years of either gender) diagnosed with UTIs admitted in our institution from November 2017 to October 2018 were included in the study. The study
was conducted after the approval of the Institutional Ethics committee.

The case sheets were collected from the medical records department (MRD) based on the International Classification of Diseases, 10th Revision (ICD-10) disease coding (World Health Organization, ICD-10, F00-F99). The demographic data and prescription pattern of each patient were recorded. The relevant investigations (microbiological and hematological) were noted down along with the urine culture report wherever available with the antimicrobial sensitivity testing. Comorbid conditions were noted down. As per the Performa followed, drug details including dose, route of administration, frequency, and duration of treatment with antimicrobial used to treat UTI and other concurrent drugs were analyzed and detailed.

The following WHO/INRUD indicators were used to analyze the prescriptions:[21]

1. Number of drugs per prescription
2. Number of antibiotics per prescription
3. Number of drugs prescribed by generic name
4. Number of drugs prescribed from the WHO Model List of Essential Medicines (EML)
5. Number of injections per prescription

**Statistical analysis**
A descriptive analysis using Microsoft Excel was done.

**RESULTS**
This study showcased the drug utilization pattern of pediatric in-patients treated for UTI. A total of 42 case records of the patients with different presenting symptoms were analyzed. Demographic characteristics showed that UTI was more common in females (66.67%) than in males (33.3%). It was more common in the age group 1-5 years as shown in Table 1. Some of the comorbid conditions noted included bronchial asthma, febrile seizures, thalassemia major, sickle cell anemia, acute tonsillitis, atopic dermatitis, acute gastroenteritis, acute lymphoid leukemia, Ewings sarcoma of sacrum, varicella, iron deficiency anemia, inguinal hernia, and respiratory tract infections.

Culture sensitivity reports were obtained only for 22 patients. Of these, 11 (50%) showed no growth on culture. *Escherichia coli* was the culprit in 10 (45.5%) of the cases and *Klebsiella* was the pathogen involved in only one (4.5%) of the cases.

Third-generation cephalosporins were the most commonly used antibiotics (71.4%) followed by aminoglycosides (35.7%), amoxicillin clavulanate (11.9%), fluoroquinolones (7.1%), and miscellaneous (doxycycline, metronidazole, and nitrofurantoin) (9.5%). Ceftriaxone among the cephalosporins and amikacin among the aminoglycosides were the most commonly used drugs. Intravenous route was the most commonly used route of administration followed by patients who received by both intravenous and oral routes. The average duration of therapy was 4.43 ± 1.9 days.

Data obtained on WHO/INRUD prescribing indicators are as follows:
1. Number of drugs per prescription: 3.95 ± 2.2
2. Number of antibiotics per prescription: 1.4 ± 0.9
3. Number of drugs prescribed by generic name: 37 (22.21%)
4. Number of drugs prescribed from the WHO Model List of EML: 114 (68.3%)
5. Number of injections per prescription: 1.71 ± 1.29

**DISCUSSION**
Drug utilization reviews are the tools that help us to promote rational use of drugs and enable physicians to improve the aptness of their prescriptions. Practice of evidence-based medicine entails judicious use of medicines so as to maximize the benefits to the patients. A retrospective analysis might help reduce errors in future and might also provide evidence for good current clinical practice. Ascertaining rationality of the prescriptions prove to decrease the rates of treatment failure and lessen economic burden on patients and community alike. WHO and the National Health Policy of India advocate use of essential drugs to treat diseases prescribed using generic names. Analyses of prescription patterns form an important link between prudent and rational drug utilization, pharmacovigilance, evidence-based medicine, and pharmacoeconomics.

| Age group (in years) | Males (%) | Females (%) | Total (%) |
|----------------------|-----------|-------------|-----------|
| Less than 1 year     | 3 (60)    | 2 (40)      | 5 (11.9)  |
| 1–5 years            | 6 (23.1)  | 20 (76.9)   | 26 (61.9) |
| 6–10 years           | 3 (42.9)  | 4 (57.1)    | 7 (16.67) |
| Greater than 10 years| 2 (50)    | 2 (50)      | 4 (9.5)   |
In this study, UTI was most commonly observed in the age group of 1–5 years which is concordant with earlier studies,[22] which showed that the children in this age group are more prone to infections. A female preponderance among the patients with UTI was noted in this study as reported earlier too. [23,24] Escherichia coli followed by Klebsiella were the common uropathogens isolated, which has been corroborated by previous research.[21,24,25] However, in this study it was observed that treatment of UTI was mainly empirical as the causative organism was identified in only 26.2% of the cases. This has been reported in an earlier study albeit in adults with UTI.[11]

Third-generation cephalosporins were the most commonly prescribed antibiotics as detailed in Table 2. This finding has been also corroborated by earlier studies.[24] This conforms with the guidelines framed by the Indian Society of Pediatric nephrology.[36] According to the guidelines, “therapy with a single daily dose of an aminoglycoside may be used in children with normal renal function. Once the result of antimicrobial sensitivity is available, the treatment may be modified. Intravenous therapy is given for the first 2–3 days followed by oral antibiotics once the clinical condition improves. Children less than 3 months of age and those with complicated UTI should be hospitalized and treated with parenteral antibiotics (ceftriaxone, cefotaxime, amikacin, gentamicin, coamoxiclav). The choice of antibiotic should be guided by local sensitivity patterns. A third-generation cephalosporin is preferred. Children with simple UTI and those above 3 months of age are treated with oral antibiotics (cefixime, coamoxiclav, ciprofloxacin, ofloxacin, cephalexin).”[26]

Data gathered in this study suggest that the prescribing pattern of UTI in in-patient pediatric patients is largely concordant with the above guidelines. The guideline also states that the duration of therapy is 10–14 days for infants and children with complicated UTI, and 7–10 days for uncomplicated UTI.[38] The average duration of treatment in our study was 4.43 ± 1.9 days indicating that the duration of treatment of the drugs was less than optimum and need to be improvised. The route preferred in our study is intravenous as it deals with the indoor patients as reported in earlier studies.[22,27]

WHO/INRUD prescribing indicators reveal that “the average number of drugs prescribed per encounter should be ≤ 3.” However, in this study, it was 3.95 ± 2.2. An earlier study has indicated that it was 2.42 ± 0.54 which was optimal, whereas another study[21] showed it to be 5.2 ± 2.4, more than the recommended values. The present data on the “Average number of antibiotics per prescription and number of injections per prescription” (1.4 ± 0.9 and 1.71 ± 1.29, respectively) are also concordant with few studies,[24] whereas an earlier study found an increased utilization of antimicrobial including parenterals.[21] A total of 22.21% of the drugs were prescribed using generic names, whereas the study conducted by Adhikary et al.[24] claimed it to be 83.7%; however, according to WHO, it should be 100%. This indicates that the WHO/INRUD prescribing indicators in our institution have yet to be improved upon and there is an urgent need to improve awareness among the physicians.

This study has a few limitations: the time duration studied was for 1 year and the sample size was also small. The study could be further strengthened by studying the prescribing indicators in a larger sample population over a prolonged period of time. The drug costs involved were also not analyzed which could be explored in further studies.

To conclude, regular conduct of drug utilization and prescription monitoring studies is the need of the hour. These studies help us to pinpoint gaps in rational prescribing, streamline drug utilization by generating adequate data relying on evidence-based medicine to fulfill our objective of promoting rational use of medicines.

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**Conflicts of interest**
There are no conflicts of interest.

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Govindarajan and Shenoy: Drug prescribing patterns in pediatric UTI

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