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Research Article

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Prescribing pattern in complicated urinary tract infections at a tertiary care hospital

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ABSTRACT

A complicated UTI (cUTI) is an infection associated with a condition, such as structural or functional abnormalities of the genitourinary tract or the presence of an underlying disease, which increases the risks of acquiring an infection or of failing therapy. To study the prescribing pattern in cUTI in a tertiary care hospital along with the antimicrobial sensitivity of the causative organisms. This prospective observational study was conducted in Institute of Nephro-urology, Bangalore from January to December 2010. The details of demographics, past medical history, details of the drugs including dose, duration of therapy, route of administration, urine culture and antimicrobial sensitivity were obtained from the case records of the patients. The prescriptions were analysed for the WHO/INRUD indicators. Descriptive statistics was used for the analyses of the results. Mean ± Standard deviation, percentages was used wherever appropriate. A total of 84 patients were included in the study, of which 49 were males and 35 were females. The age of the patients ranged from 16 to 82years, with an average of 48.4years. Mean duration of antimicrobial agents (AMAs) therapy was 11.23±6.1days. Only 34.5% of the patients had Culture and sensitivity of urine done, of which E.coli was detected in about half of them. E.coli was sensitive to Piperacillin & Tazobactum, followed by Cefoperazone & Sulbactum. Most commonly used AMAs include Cephalosporins (29%), Quinolones (26%) and Penicillins (23%). Many patients with cUTI were associated with Type 2 Diabetes mellitus. Average number of drugs per prescription was 6.21 ± 3.36 with number of antibiotics per prescription was 2.1 ±0.78 and number of injections per prescription was 1.9±1.37. The prescription of empirical AMAs were in accordance with EUA guidelines. But, the use of large number of AMAs prescribed after discharge needs to be reduced. The shift from broad spectrum to narrow spectrum AMAs based on laboratory results needs to be improved in our hospital. Tendency towards polypharmacy and intravenous AMAs also should be reduced in our hospital. There is an urgent need for implementing region specific antimicrobial guidelines for the treatment of cUTI.

Key Words: complicated urinary tract infections, E.coli, Broad spectrum antimicrobial agents, narrow spectrum antimicrobial agents.

INTRODUCTION

Urinary tract infections (UTIs) are one of the most common bacterial infections in the general population, with an estimated overall incidence rate of 18 per 1000 person per year [1]. In addition, UTIs are a major cause of hospital admissions and are associated with significant morbidity and mortality as well as a high economic burden [2].

A complicated UTI (cUTI) is an infection associated with structural or functional abnormalities of the genitourinary tract or the presence of an underlying disease, which increases the risks of acquiring an infection or of failing therapy [3]. The microbiology of cUTIs is characterized by a greater variety of organisms and an increased likelihood of antimicrobial resistance as compared with uncomplicated UTIs [4]. Therefore, patients with cUTIs require more diagnostic testing, broad-spectrum empiric antimicrobial therapy, and a longer duration of treatment. Although E coli continues to be one of the most common etiologic agents of cUTIs, other Gram-negative organisms

such as Klebsiella., Proteus, Enterobacter cloacae, Serratia marcescens, and Pseudomonas aeruginosa and Gram-positive organisms such as Enterococci, coagulase-negative staphylococci and Staphylococcus aureus are also commonly isolated [5].

The primary goal of managing cUTIs is optimal administration of appropriate antimicrobial agent and correction of any underlying genitourinary abnormalities. With the increased prevalence of antimicrobial resistance, and the lack of well-designed clinical trials, treatment of cUTIs can be challenging for clinicians. Consideration of an optimal antimicrobial agent (AMA) should be based on local resistance patterns, patient-specific factors, including anatomic site of infection and severity of disease, pharmacokinetic and pharmacodynamic principles, and cost [6]. Intense use of any empirical antimicrobial agent in this group of patients with a high likelihood of recurrent infection, may lead to the emergence of resistant micro-organisms in subsequent infections. Hence, empirical therapy should be replaced by a therapy adjusted for the specific infective organism identified in the urine culture. Though, many AMAs namely, Fluroquinolones, Cephalosporins and Aminoglycosides have proved their efficacy in the management of cUTI, emphasis should be given for rational use of AMAs.

Prescribing pattern studies can provide useful information for the improvement of appropriate and effective use of drugs in a hospital. This will have an enormous impact on patient's quality of life and contribute substantially to the financial cost of patient care. The assessment of the prescription will help to know the attitude of the physicians towards their prescribing and their therapeutic knowledge to ensure rationality in the prescription [7]. As there is limited literature regarding the management of cUTI in India, the present study was undertaken to evaluate the same objective. This data is expected to be helpful in establishing an antibiotic utilisation guideline for the treatment of cUTI.

EXPERIMENTAL SECTION

This prospective observational study was conducted in Institute of Nephro-urology, Bangalore from January to December 2010. Ethics committee approval was obtained before initiating the study. Detail of the study procedure was explained to the patients and informed consent was obtained from them. All the patients satisfying the following selection criteria were involved in the study.

Inclusion criteria

1. Patients with diagnosis of complicated UTI.
2. Patients who voluntarily give informed consent
3. Patients aged > 16years

Exclusion criteria

1. Patients with diagnosis of acute UTI
2. Patients who do not voluntarily give informed consent
3. Patients < 16 years

Definition of cUTI: A cUTI is an infection associated with structural or functional abnormalities of the genitourinary tract or the presence of an underlying disease, which increases the risks of acquiring an infection or of failing therapy

The details of demographic data, past medical history, details of the drugs including dose, duration of therapy, route of administration, urine culture and antimicrobial sensitivity were obtained from the case records of the patients. The prescriptions were analysed for the following WHO/INRUD indicators:

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

Statistics

Descriptive statistics was used for the analyses of the results. Mean ± Standard deviation, percentages was used wherever appropriate.

RESULTS

A total of 84 patients were included in the study, of which 49 were males and 35 were females. The age of the patients ranged from 16 to 82years, with an average of 48.4years. About 38 patients were in the age group of 16-40years, 27 patients in 41-60 years and 19 patients were above 60 years. The stay in the hospital extended from 2 to 30days, with an average of 7days.

Mean duration of AMA therapy was 11.23±6.1days, with majority of the patients receiving AMAs for 5 days (73%), followed by 7 days (13%) and 10 days (5%). On discharge, patients were prescribed AMAs for 5days (20%), followed by 7days (7%) and 10days (6%) patients.

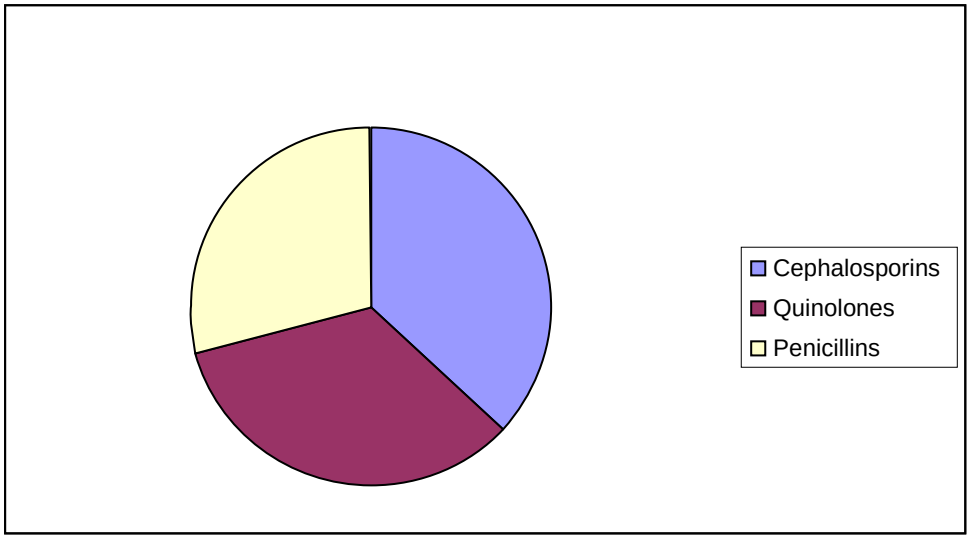
About 75% of patients had ultra-sonography of abdomen done. Only 34.5% of the patients had Culture and sensitivity of urine done. In 48.2% of the positive urine culture, E.coli was detected, followed by Klebsiella in 10.3%. The antimicrobial sensitivity pattern is as shown in table 1. E.coli was sensitive to Piperacillin & Tazobactum, followed by Cefoperazone & Sulbactum.

Table 1: Antimicrobial sensitivity pattern

Micro-organism	Drugs (number of patients)
E.coli	Piperacillin & Tazobactum (7) Cefoperazone & Sulbactum (5) Amikacin (4) Imipenem (2) Ciprofloxacin (2) Amoxicillin (1) Nitrofurantoin (1) Ceftriaxone (1) Gentamycin (1) Ofloxacin (1) Gatifloxacin (1)
Klebsiella	Imipenem (2) Gatiflxacin (1)

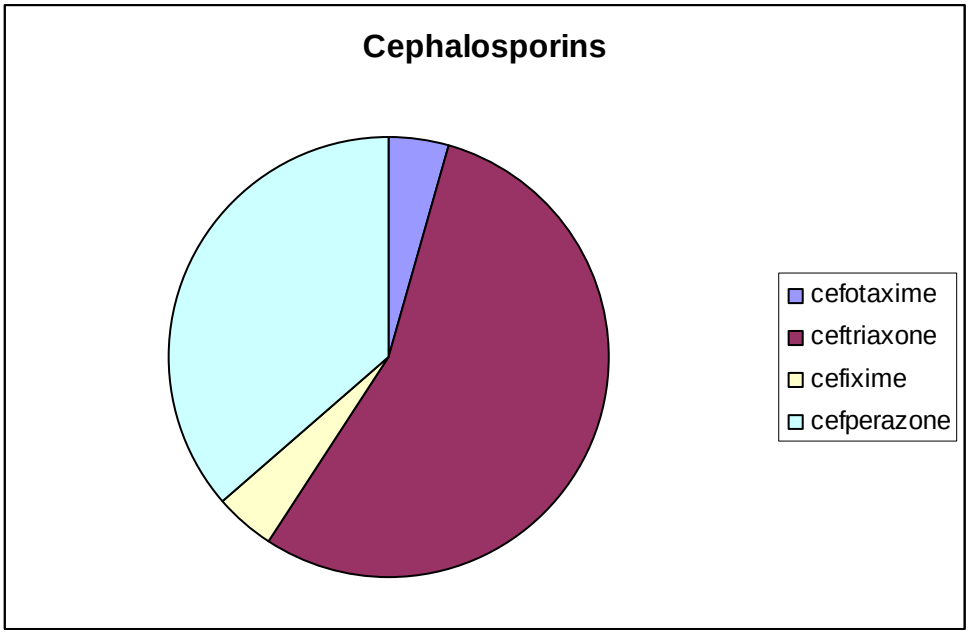
As shown in figure 1, most commonly used AMAs include Cephalosporins (29%), Quinolones (26%) and Penicillins (23%). The commonly prescribed AMAs combinations include Piperacillin & Tazobactum (14%), followed by Cefoperazone & Sulbactum (8%) and Levofloxacin + Ceftriaxone (3.5%). About 96.4% of the patients received AMAs intravenously during hospitalization.

Figure 1: Commonly used AMAs in cUTI



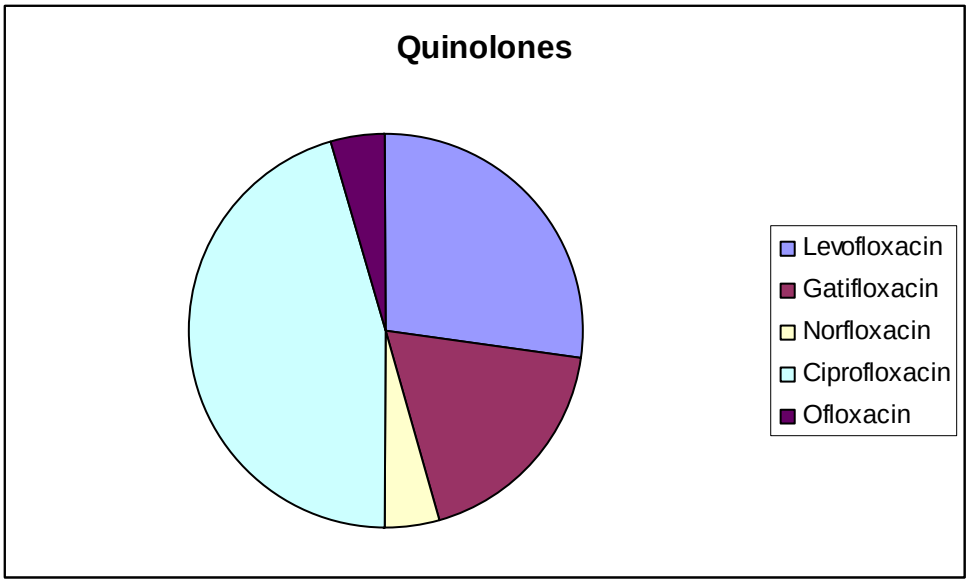
As shown in figure 2, among Cephalosporins, Ceftriaxone (50%) was most commonly prescribed followed by Cefoperazone (34%), Cefixime (8%) and Cefotaxime (8%).

Figure 2: Cephalosporins used in cUTI



As shown in figure 3, among Quinolones, Ciprofloxacin (45%) was most commonly prescribed, followed by Levofloxacin (27%), Gatifloxacin (18%), Norfloxacin (5%) and Ofloxacin (5%).

Figure 3: Quinolones used in cUTI



As shown in figure 4, among Penicillins, piperacillin (84%) was most commonly prescribed, followed by Amoxicillin (5%), Augmentin (5%) and Crystalline penicillin (5%).

Table 2 shows AMAs prescribed on discharge. On discharge, patients initially treated with Cephalosporins in the hospital, were prescribed no AMAs (34%), Cefixime (20%), Ciprofloxacin (17%), Levofloxacin (17%), Cotrimoxazole (8%) and Nitrofurantoin (4%).

Figure 4: Penicillins used in cUTI

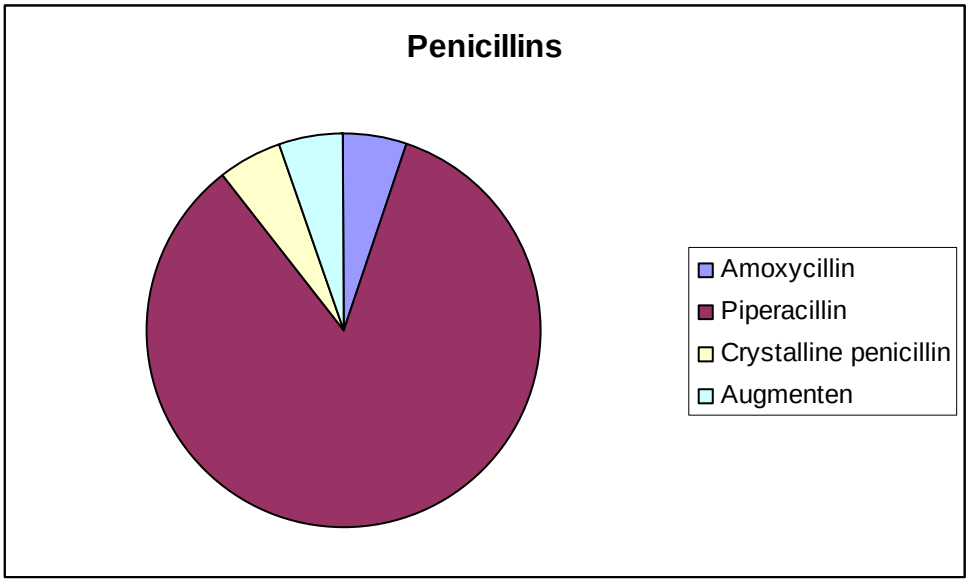


Table 2: AMAs prescribed on discharge

AMA at hospital	AMA on discharge	Percentage of patients
Cephalosporins	Nil	34
	Cefixime	20
	Ciprofloxacin	17
	Levofloxacin	17
	Cotrimoxazole	8
	Nitrofurantoin	4
Quinolones	Ciprofloxacin	36
	Nil	18
	Levofloxacin	14
	Nitrofurantoin	14
	Gatifloxacin	9
	Ofloxacin	9
Penicillins	Nil	43
	Cefixime	16
	Nitrofurantoin	16
	Ofloxacin	5
	Amoxycillin	5
	Ciprofloxacin	5
	Cotrimoxazole	5
	Augmentin	5

On discharge, patients initially treated with Quinolones in the hospital, were prescribed Ciprofloxacin (36%), no AMAs (18%), Levofloxacin (14%), Nitrofurantoin (14%), Gatifloxacin (9%) and Ofloxacin (9%).

On discharge, patients initially treated with Penicillins in the hospital, were prescribed no AMAs (43%), Nitrofurantoin (16%), Cefixime (16%), Amoxicillin (5%), Ofloxacin (5%), Ciprofloxacin (5%), Cotrimoxazole (5%) and Augmentin (5%).

Among 84 patients included in the study, 43% had Type 2 Diabetes mellitus 25% had structural abnormality of genito-urinary tract, 19% had chronic kidney disease and 6% patients had recurrent UTI.

As shown in table 3, in patients with Type 2 Diabetes Mellitus and chronic kidney disease, Piperacillin & Tazobactum (13patients) was prescribed in majority of the patients followed by Cefaperazone & Sulbactum (6patients). In patients with structural abnormality of genito-urinary system, Ciprofloxacin was prescribed in 5 patients, followed by Piperacillin & Tazobactum in 4 patients. Piperacillin and Tazobactum was prescribed in majority of the patients with recurrent UTI (2 patients) and septicaemia (3 patients).

Table 3: AMAs prescribed in hospital and discharge for cUTI associated with other clinical conditions

Clinical Condition (no. of patients)	AMA in hospital(no. of patients)	AMA after discharge
Structural abnormality in Genito-urinary system (21)	Ciprofloxacin*(5)	Ciprofloxacin+
	Piperacillin&Tazobactum*(4)	Nil
	Levofloxacin+ (2)	Levofloxacin+
	Cefotaxime *	Ciprofloxacin+
	Ceftriaxone*& Amikacin*	Nil
	Ceftriaxone*	Cefixime+
	Cefpearazone&Sulbactum*	Cotrimoxazole+
	Piperacillin&Tazobactum*	Augmentin+
	Piperacillin&Tazobactum & Amikacin*	Cefixime+
	Meropenam*	Nitrofurantoin+
	Ciprofloxacin*	Nitrofurantoin+
	Levofloxacin* & Ceftriaxone*	Nitrofurantoin+
	Gatifloxacin+	Nil
Recurrent UTI(5)	Piperacillin & Tazobactum (2)*	Nil, Nitrofurantoin+
	Levofloxacin*	Levofloxacin+
	Gatifloxacin*	Gatifloxacin+
	Meropenam*	Nitrofurantoin+
Septicemia(5)	Piperacillin & Tazobactum*(3)	Nil
	Cefoperazone & Sulbactum*	Cotrimoxazole+
	Ciprofloxacin*	Ciprofloxacin+
Chronic kidney Disease(16)	Piperacillin & Tazobactum*(5)	Nil
	Cefoperazone & Sulbactum(4)*	Nil, Ciprofloxacin+,Cotrimoxazole+
	Gatifloxacin*(2)	Gatifloxacin+
	Gatifloxacin & Amikacin*	Gatifloxacin+
	Levofloxacin*	Cefixime+
	Ofloxacin*	Ofloxacin+
	Ceftriaxone*	Nil
	Meropenam* & Ceftriaxone*	Nil
Type 2 DM(36)	Piperacillin & Tazobactum*(13)	Nil, Cefixime+, Nitrofurantoin+
	Cefoperazone & Sulbactum*(6)	Nil, Levofloxacin+, Cotrimoxazole+
	Gatifloxacin* (4)	Gatifloxacin+
	Levofloxacin * (4)	Levofloxacin+
	Levofloxacin*	Cefixime+
	Levofloxacin * & Ceftriaxone *	Levofloxacin+
	Gatifloxacin & Ceftazidime*	Levofloxacin+
	Norfloxacin+	Nil
	Ciprofloxacin*	Ciprofloxacin+
	Ofloxacin*	Ofloxacin+
	Ceftriaxone*	Cefixime+
	Ceftriaxone & Amikacin *	Nil

**Intravenous administration, + oral administration*

Drugs prescribed other than antimicrobial agents are given in table No. 4. The most commonly prescribed drugs include Ranitidine, followed by Omeprazole, Iron supplements and Ondansetron.

Altogether 522 drugs were prescribed for the patients, with an average of 6.2 ± 3.36 drugs/ patient. The prescriptions analyzed according to the WHO/INRUD prescribing indicators are as follows:

1. Number of drugs per prescription: 6.21 ± 3.36
2. Number of antibiotics per prescription:2.1 ±0.78
3. Number of drugs prescribed by generic name: 19±0.5drugs
4. Number of drugs prescribed from the WHO Model List of Essential Medicines (EML): 395±2.81 (75.8%)
5. Number of injections per prescription: 1.9±1.37

DISCUSSION

The present study showed that the incidence of cUTI was higher in males compared to females. This is in contrary to many other studies [8,9] which reported that females are at higher risk for UTI because of structural and anatomical differences like shorter urethra. This result could be attributed to the fact that many women get treated for UTI in OBG department which was not included in the study.

Patient's age ranged from 16 to 82 years with an average of 48.4years. Majority of the patients were in the younger age group of 16 to 30 years. The same age preponderance was shown in another Indian study by Mohan J et al [9].

The duration of AMA therapy ranged from 5 to 25 days, with an average of 11.23±6.1days, with majority of the patients receiving it for 5 days. The optimal duration of AMA therapy for the treatment of cUTI has not been systematically studied. Because of the wide variation in underlying abnormalities and clinical presentations, a uniform recommendation for treatment duration cannot be provided. Most clinical trials have evaluated seven to 14 days of therapy, but as short as five days and as long as 20 days have also been reported [3].

Table 4: Drugs other than AMAs prescribed in cUTI

Classification	Drug (no. of patients)
Gastro-intestinal system	Omeprazole (14)
	Ranitidine (15)
	Ondansetron (12)
	Pantoprazole(5)
	Domperidone(1)
Analgesics	Paracetamol (6)
	Ibuprofen (1)
	Diclofenac (1)
	Tramadol (2)
	Spasmoproxyvon (1)
	Drotaverin (1)
Calcium supplements	7
Vitamin supplemets	20
Iron supplements	13
Cardiovascular system	Nifedipine (3)
	Carvedilol (1)
	Enalapril (1)
	Amlodipine (8)
	Prazosin (3)
	Clonidine (2)
	Metaprolol (1)
	Frusemide (10)
	Digoxin (1)
	Isosorbide mononitrate (1)
	Aspirin (3)
	Clopidogrel (1)
	LMW Heparin (1)
	Dopamine(1)
Genito-Urinary system	Tamsulosin (3)
	Alfuzosin (1)
	Tolterodine (1)
Hormones	Insulin (10)
	Thyroxine (1)
	prednisolone (1)
Respiratory system	Salbutamol (1)
	Doxyphylline (1)
Antifungal drugs	Fluconazole (2)
Oral Hypoglycemic drugs	Gliclazide (1)
	Glimiperide (1)
	Glipizide (1)
	Glibenclamide (1)
	Pioglitazone (1)
Central Nervous system	Gabapentin (1)
	Sodium Valproate(1)
	Chlorpromazine (1)

About 34.5% of the patients had culture and sensitivity of urine done, of which E.coli was detected in about half of them, followed by Klebsiella. Even though the bacterial spectrum causing cUTI vsries from hospital to hospital, E.coli is detected in about 60-75% of the cultures everywhere[10,11]. Although the likely organism and usual susceptible patterns are sufficient to guide initial empiric therapy of uncomplicated UTI, adequate treatment of complicated UTIs necessitates precise therapy based on isolation of the causative bacterium and its antimicrobial susceptibility. Hence, practice of prescribing AMAs based on antimicrobial sensitivity pattern needs to be improved in our hospital.

Antimicrobial sensitivity pattern showed that E.coli is highly susceptible to Piperacillin/Tazobactum, followed by Cefoperazone/Sulbactum and amikacin. In a similar type of study conducted in Chennai [9], E.coli was reported to be highly susceptible to Amikacin followed by Cephalosporins. This explains the importance of performing the antimicrobial sensitivity patterns in every hospital as it varies from region to region.

Patients with symptomatic infection can usually be treated with oral therapy [12]. Patients who are haemodynamically unstable, unable to tolerate oral medication, or in whom gastrointestinal absorption is impaired, require parenteral therapy. In the present study about 96.4% of the patients received AMA intravenously in the hospital. This can be reduced in our hospital on careful selection of patients making the therapy more economical.

Clinical trials of parenteral therapy for cUTI have reported efficacy for a wide variety of agents, but there are limited comparative studies. Aminoglycosides [13], fluoroquinolones [14], piperacillin/tazobactam [15], ceftazidime [14] and carbapenems [15] have all been reported to achieve high rates of clinical and microbiological cure. Most commonly used empirical AMAs in the present study include Cephalosporins, followed by Quinolones and Penicillins. The commonly prescribed AMAs combinations include Piperacillin & Tazobactum followed by Cefoperazone & Sulbactum. Even in the absence of regional antibiotic policy to guide the treatment of cUTI, prescription of empirical AMAs were in accordance with European Urological Association guidelines [16]. However, use of wide variety of AMAs prescribed for this clinical condition can be reduced by following regional hospital specific AMAguidelines. Consensus regarding AMAs on discharge is very much required in our hospital, as there was higher rate of inappropriate prescription. Hence, there is an urgent need for regional hospital specific AMA guidelines in our hospital to reduce both the emergence of bacterial resistance and treatment expenses.

The common clinical conditions associated with cUTI were Type 2 Diabetes mellitus, followed by structural abnormality of genitourinary tract and chronic kidney disease. Fluoroquiolones are recommended for the treatment of cUTI with structural abnormality of genitourinary tract and chronic kidney disease. In cases of cUTI with chronic kidney diseases, aminoglycosides, nitrofurantoin and tetracyclines are contraindicated. Broad spectrum AMAs like piperacillin/Tazobactum and Cefoperazone/Sulbactum were very widely used in the treatment of cUTI associated with other clinical conditions in our study. It has been reported that, if the patients do not respond, this may lead to change to even broader spectrum agents. Heavy use of broad-spectrum agents will lead to emergence of multi-drug-resistant organisms, as well as significant expenses [17]. Hence, after empirical therapy with broad spectrum AMAs, efforts should be made to introduce narrow spectrum agents based on laboratory and clinical changes within 48 h to 72 h.

The most commonly prescribed drugs other than antimicrobial agents include Ranitidine, followed by Omeprazole. Prescriptions of these drugs are used as a preventive measure of gastric irritation caused by AMAs. If the use of these drugs are restricted to only high risk patients like elderly or history of previous peptic ulcer disease, then polypharmacy and related adverse effects can be reduced. Co-prescription of vitamins, calcium and iron supplements can also be prescribed appropriately.

According to WHO/INRUD indicators, the average drug per prescription was high. As there is tendency towards polypharmacy in our hospital, educational interventions towards improving prescribing practices are required. Although the prescription of AMAs were appropriate, intravenous administration of the same could be reduced in order to prevent spreading of infections and use of scarce technical staff [18]. Prescribing by generic name needs to improve in our hospital to prevent medication errors and further adverse effects due to it.

In conclusion, prescribing pattern in cUTI done in a tertiary care centre for about one year included 84 patients with majority of them in the age group of 16-40years. The incidence of cUTI was seen to be more in males than females. E.coli sensitive to Piperacillin/Tazobactum, was the most common organism isolated from the urine culture and sensitivity test. Though the prescription of empirical AMAs were in accordance with EUA guidelines, use of wide variety of empirical AMAs can be reduced and AMAs prescribed after discharge needs to be more rational. The shift from broad spectrum to narrow spectrum antimicrobial agent based on laboratory results needs to be improved in our hospital. Tendency towards polypharmacy and intravenous AMAs also should be reduced in our hospital. There is an urgent need for implementing region specific antimicrobial guidelines for the treatment of cUTI.

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