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Original Article

Urinary Tract Infection Treatment Pattern of Elderly Patients in a Tertiary Hospital Setup in South India: A Prospective Study

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ABSTRACT

Introduction: Urinary tract infections (UTIs) are more common in geriatrics due to physiological alterations/pathological conditions. The main objective of this study was to analyze the incidence, causative organisms, types of antibiotics used, drug interactions, the antibiotic cost, and its outcome. **Method:** This is across-sectional study conducted in selected medicine units over a period of 18 months. The enrolled patient's therapy pattern spotted from the admission to discharge. The mandatory patients provided with pharmaceutical care services. **Results:** Among 475 observed cases, 106 patients had UTIs (22.31%). The mean number of drug were 7.42 ± 2.31per prescription. Out of 106 prescriptions, 63 prescriptions had drug interactions. The drug interactions degree varied from mild (12.63%), moderate (60.3%) and severe (26.58%) remained managed by spacing intervals, alternate drug use, and close monitoring techniques. Strangely, all comorbid UTI patient outcomes showed improvement. The antibiotic cost of the management ranged from $ 0.21-160.8 with a median of $ 26.30 and the common organisms were *E. coli* (48%), *Enterococcus* (16%). The average length of patient hospital stay was 11.65 ± 8.94 days. **Conclusion:** This study showed that about one-fourth patients have UTIs and half of them were affected by *E. coli*. Hence, this study proposes the paucity and its implication of pharmaceutical care service research studies, on health-hygiene, proper use of antibiotics & its cost minimization; untoward interactions cost prevention, for better outcome in India.

Key words: Urinary tract infection (UTI), Drug interaction (DI), Geriatrics, Hypertension(HTN), Discharge against medical advice (DAMA), Tricyclic antidepressants (TCA), HCT: Hydrocholrothiazide.

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INTRODUCTION

Urinary tract infection (UTI) is one of the most prevailing causes of infectious diseases (shared by bacteria) among the geriatric population in both genders.[1] Due to their anatomy and reproductive physiology, women are more susceptible.[2,3] However, between females and males, the ratio varies from geriatrics (50:1) to younger (2:1) population.[4] Diagnosis and treatment of UTI in elderly varies when compare to younger patients and is quiet difficult due to the non-specific/absence of symptoms and lack of clear clinical history.[5] This lead toits under-diagnosisandlack of treatment.[6]

Previous studies showed that UTI is often erroneously diagnosed, with around 40% of hospitalized elderly admissions due to non-specific symptoms. Even studies reported that the UTI was caused due to urinary incontinence, previous history, urogenital surgery and diabetes mellitus in specific patient populations.[3,4]

Bacteria is the most common causative agent in humans. Even though sometimes viruses and fungi can also be observed, hence this should not be ignored. Common infecting organisms are *Escherichia coli* (80% to 85%) and *Staphylococcus saprophyticus* (10% to 15%), while *Klebsiella pneumonia, Pseudomonas* and *Proteus* species account for the rest of the infections.[7]

Among the two urinary tract infections, Nosocomial UTIs is major, caused by *Escherichia coli, Pseudomonas aeruginosa* and *Proteus sp,* whereas community acquired is caused by *Escherichia coli, Klebsiella pneumonia, Proteus mirabilis and Staphylococcus saprophyticus*.[8]

Previous studies showed that increased mortality associated with bacterial infections, in older UTI patients was more and extensive need for prevention with early diagnosis of UTI is vital to reduce morbidity and mortality.[9]

Antibiotics play a vital role in the treating of bacterial UTIs and in the majority of cases the initial empirical treatment is with broad spectrum antibiotics.[10] Unfortunately, this trend of antibiotic usage leads to antibiotic resistance, the emergence of multi-drug resistant (MDR) strains (*Clostridium difficile* infection) and adverse drug reactions (ADRs).[11] At present, antibiotic resistance (MDR strains) is a global concern which greatly affects the cost of treatment, hospitalization period, morbidity and mortality of patients in healthcare.[12] Hence, the use of broad spectrum antibiotics should be minimized and a more targeted approach to therapy can be devised with narrow spectrum based antibiotic susceptibility patterns of isolated organisms from patients. The antibiotic policy of respective hospitals should be in place to guide the doctors in selecting appropriate antibiotics. Hence, this study conducted in hospitalized elderly patients with the following objectives, namely to understand the treatment pattern, to measure the incidence of UTI, causative organisms, usage of antibiotics, antibiotic susceptibility pattern, drug interactions, the direct cost burden of antibiotic treatment, hospitalization period and its clinical outcome.

METHODOLOGY

A prospective observational study was conducted in selected General medicine units of Kasturba Hospital, Manipal, Karnataka over a period of 18 months (July 2012 to January 2014) after getting Institutional ethical clearance (IEC: 191/2012). The patients were enrolled as per the listed criteria (**Inclusion criteria**: **1.** Patients of either sex of 60 years and above. **2.** A patient, willing to give informed consent form.

Exclusion criteria: Comatose patients, > 2 months, Hospital stay, ≥ 5 co-morbid disease),after getting their informed consent. Patient case records were studied, reviewed and data collected on demographics (age, sex), medical history, diagnosis, co-morbidities, microbiological reports (antibiotic susceptibility), drug treatment chart, and duration of hospitalization and clinical outcome of the patients with well-designed data collection/case report form (CRF). Prescribed drugs were checked for drug interactions by using sources of drug information (Micromedex 2.0, Medscape) and if necessary informed to the clinician. The patients and caretaker were provided with verbal patient counseling on proper use of antibiotic and patient outcomes were assessed based on their laboratory parameter and their satisfaction. The total costs incurred by use of antibiotics in these patients were calculated. A descriptive statistical analysis carried out by using statistical package social sciences (SPSS version 20.0).

RESULTS

Among 475 enrolled subjects, 106 patients had urinary tract infection (22.31%) of which 56males (53%) constituted the majority. Patients with age group between 60-65 years were 52%, out of which males were dominant, followed by 66-70 years of age (Table 1).

Type 2 diabetes mellitus and hypertension are the most common co-morbidities, either alone or combined. The major diagnosis revealed type II diabetes mellitus UTI (43; 40.6%) followed by hypertension UTI (38; 35.8%) and type II diabetes mellitus with hypertension UTI (25; 23.6%). Interestingly, no UTI alone cases were observed in our study population.

Out of 106 patients, the culture sensitivity test was performed in 83 patients for various biological specimens (sputum, broncho-alveolar lavage fluid, blood, pleural fluid, wound swab and endo-tracheal aspirate). Of these, 36 patient specimens were sterile and the rest 47 (44.3%) showed growth of different organisms, wherein 50 organisms are isolated. Out of 50 organisms, 47 organisms were isolated from urine samples (bacteria), followed by one isolate from blood, endotracheal aspirate and sputum (fungi: Candida species) each. The majority (44; 88%) were mono isolates and the rest were multiple (two pathogens) isolates.

Gram negative organisms were more frequently isolated than gram positive (66% vs. 28%). *Escherichia coli* (48%)>*Klebsiella* (*10*%)and *Enterococcus species* (16%) > Methicillin resistant *Staphylococcus aureus* (MRSA)were the most prevalent gram negative and gram positive organisms, respectively. (Table 2).

Sensitivity studies of *E. coli*revealed Amikacin, Netilmicin and Imipenem were 100% sensitive followed by Cefoperazone-Sulbactam (95%) and Piperacillin-Tazobactam (77.2%). Aztreonam, Ticarcillin-Clavulanic acid, Cefazolin or Cefodroxil and Ciprofloxacin or Levofloxacin were completely resistant.

Antibiogram of the remaining isolates are not taken into consideration as the number of organisms isolated was very less.

Table 1: Distribution of patients based on age

Age group (years)	Females	%	Males	%
60-65	23	46	32	57.1
66-70	13	26	12	21.42
71-75	06	12	8	14.2
76-80	06	12	3	5.35
81-85	01	2	0	0
86-90	01	2	0	0
91-95	00	00	1	1.78
Total	50	100	56	100

Table 2: Most prevalent organisms in Urinary tract infections

Type of microbe	Organism	Number of isolates	Percentage of isolates
Gram Negative bacteria (66%)	*E coli*	24	48
	Klebisiella pneumonia	5	10
	Pseudomonas aeruginosa	2	4
	Serratiasps	1	2
	Citrobacterkoseri	1	2
Gram Possitive bacteria (28%)	*Enterococcus sps*	8	16
	MRSA	3	6
	Staphylococcus aureus	2	4
	MSSA	1	2
Fungus (6%)	*Candida sps*	3	6
	Total	**50**	**100**

Table 3: Sensitivity pattern of the antibiotics used in UTI patients

Antibiotic	Sensitive	(%)	Resistance	(%)
Netilmicin	24	100	0	0
Amikacin	24	100	0	0
Imipenem	22	100	0	0
Cefoperazone-Sulbactam	21	95.5	1	4.5
Piperacillin-Tazobactam	17	77.2	5	22.8
Gentamicin	14	58.3	10	41.7
Cotrimoxazole	6	25	18	75
Norfloxacin	3	15	17	85
Amoxicillin-Clavulanic acid	2	8.3	22	91.7
Ampicillin/Amoxicillin	2	8.3	22	91.7
Cefotaxime/Ceftriaxone	2	8.3	22	91.7
Cefuroxime	2	8.3	22	91.7
Cefpirome, Cefepime	1	4.5	21	95.5
Aztreonam	0	0	22	100
Ticarcillin-Clavulanic acid	0	0	14	100
Cefazolin/Cefodroxil	0	0	4	100
Ciprofloxacin/Levofloxacin	0	0	4	100

Out of 106 UTI cases admitted to the general medicine unit, 105 (99%) are prescribed with antibiotics. Amongst these antibiotic prescriptions, 55 (52.4%) prescriptions had a single antibiotic followed by 2, 3 and 4 antibiotic containing [i.e., 30 (28.6%), 19 (18.1%) and 1 (1%)] prescriptions, but they were not necessarily administered simultaneously. Most of the patients received antibiotics parenterally (41.5%), followed by both parenteral and oral route (40.6%) and oral route alone (17%). The total number of antibiotics prescribed among the 106 patients was 176. The average number of antibiotics per prescription was 1.68 ± 0.8 (mean ± SD). The mean, median and interquartile range (IQR) of antibiotic cost per the management UTIs was 2249.14 ± 2181.94, $ 26.38 (Rs. 1729) &: $ 40.10 (Rs. 2628) (Table 3, 4, 5).

Cephalosporin combination with β-lactamase inhibitors was the most prescribed class of antibiotic 38 (36%) followed by penicillin in combination with β-lactamase inhibitors, because of good spectrum of activity and suggestive culture sensitivity. The resistant organism was treated with drugs like Linezolid and Piperacillin/Tazobactam. Even we can observe

Table 4: Antibiotics usage pattern in UTI treatment

Number of antibiotics	Frequency of use	%
0	1	100
1	55	52.4
2	30	28.6
3	19	18.1
4	1	1.0
Total	**105**	**100.0**

Table 5: Mode of administration of antibiotics in UTI treatment

Mode of antibiotic administration	Frequency of use	%
None	1	.9
Injection	44	41.5
Oral	18	17.0
Injection+ Oral	43	40.6
Total	**106**	**100.0**

Table 6: Class of antibiotics used in treatment of Urinary tract infection

Antibiotics usage pattern	Number of prescriptions (%)
Cefaperazone+Sulbactum	38(35.84)
Amoxycillin+Clavalunic acid	17(16.03)
Nitrofurantoin	11 (10.3)
Linezolid	8 (7.54)
Cotrimoxazole	7 (6.6)
Ciprofloxacin	6 (5.6)
Piperacillin+Tazobactum	5 (4.7)
Amikacin	3 (2.83)
Others	11 (10.3)
Total	106

Table 7: Classification of Drug interactions based on severity

DDI Severity	Yes(%)	No(%)
Mild	8(12.63)	55(87.4)
Moderate	38(60.31)	25(39.68)
severe	17(26.98)	46(73.1)
Total	63(100)	

commonly used drugs like Co-trimoxazole, Nitrofurantoin and Ciprofloxacin because of economic consideration and severity of the disease (Table 6).

Of all the UTI cases, 63 (60%) patient treatment charts showed drug-drug interactions. Of these, 38 are moderate, followed by 17 severe and 8 mild (Iron with Ciprofloxacin, Omeprazole and Vitamin with Omeprazole, Nitrofurantoin). The entire drug-drug interactions are informed to respective physicians with evidence/literature. Among these severe drug-drug interactions were considered significant and an alternative therapy was prescribed (eg: Alprazolam with codeine sulphate) and sometime close monitoring were observed (e.g. aspirin/naproxen with duloxetine) If not possible, then the dosing interval was changed (e.g. amitriptyline with duloxetine and linezolid combination)(Table 7, 8, 9).

The outcome of the most (68; 64.1%) of the patients showed were improved, followed by stable (26; 24.5%), died (5; 4.7%) and worsened (1; 0.95%) during hospitalization. A minor fraction (8.5%) of patients was discharged against medical advice and discharge on request due to Financial constrains (Figure 1).

The mean age, average days of hospitalization and the mean number of drugs per prescription of the study population was 67.8 ± 6.64, 11.65 ± 8.94 and 7.41 ± 2.31, respectively.

DISCUSSION

Urinary tract infections are one of the most common infections in geriatrics due to physiological variations. If chronic diseases like diabetes, HTN are concomitantly present, the chances of an UTI are higher and can even sometimes lead to mortality.[6] The research on treatment pattern/drugs used by the pharmacist becomes complimentary for physicians to achieve rational drug usage and provide a better outcome.

Our study showed that the UTI was more prevalent among males (53%) than females (47%) which is similar to the study conducted by Faryabi *et al.* (males vs. females: 54.2% vs. 45.8%),[14] Mahesh *et al.* (males vs. females: 62.4% vs. 37.6%)[15] and Arul Prakasam *et al.*[16] where UTI was predominantly observed in male (85.7%). In contrast, the study conducted by Prakash and Saxena (males v.s females: 35.14% vs. 73.57%) showed the opposite.[17] UTI was most commonly witnessed in both the genders in the age group of 60-65 years, whereas in the study carried out by Dinesh and his team,[13] UTI was more common in females of age group 31-45 years.[17,18] This difference might be because our study was conducted in geriatric populations whose comorbidities such as diabetes mellitus and increasing risk of age related prostate disorders increased its incidence.

In our study population, out of all UTI cases, 64.1% of cases have a history of diabetes mellitus whereas the study conducted by Pargavi *et al.* in diabetic patients showed an incidence of 37% of UTI,[18] Marques *et al.* study[19] showed 23.52% had DM-UTI and in Mahesh *et al.* study,[15] 42.6% of the study population has a history of diabetes mellitus. This shows that diabetes mellitus is one of the major risk factors for the incidence of UTI. Fu *et al.* study also showed 20.2% elderly DM patients had UTI in their DM management follow ups.[20]

The average length of hospitalization was11.65 ± 8.94 days, which is closer to Faryabi *et al.* (10.72 ± 5.2 days) study.[14] Most of the patients (52.4%) was prescribed with single antibiotic, whereas in a study conducted by Faryabi *et al.* dual drug (antimicrobial agent) regimens were high (38%) but more or less same for a single drug regimen (31.3%).[14]

The most commonly prescribed antibiotics were Cephalosporin (36%) which is similar to studies conducted by Faryabi *et al.* and Ramanath and Shafiya.[21] Next, extended spectrum penicillin in combination with β-lactamase inhibitors was routinely prescribed identical to Faryabi *et al.* study.[14] Aminoglycosides were the least prescribed antibiotics, even though highly sensitive to commonly isolate organisms in UTI patients. This is due to the renal toxicity of drugs and age related renal impairment among the patients which is considered to be significant.

Gram negative organisms such as *E. coli* (24; 48%) were the frequent cause of UTI which was in lines with the data available worldwide and confirmed by Faryabi *et al.*,[14] Arslan *et al.*,[22] Peterson *et al.*[23] and Marques *et al.*[19] studies (75.6% E. coli). Among gram positive organisms which accounts for 28% of isolates, it chiefly constituted Enterococcus sps (8) and Staphylococcus sps (MRSA; 3, *Staphylococcus aureus*; 2 and MSSA; 1).

In our study, *E. coli* was completely sensitive to amikacin, netilmicin, imipenam followed by cefoperazone sulbactam (95.5%) which is similar to the study conducted by Faryabi *et al.*[14] *E. coli* is highly resistant to fluoroquinolones (levofloxacin/ciprofloxacin; 100% and norfloxacin; 85%) which area contrast to study conducted by Shalini *et al.* which showed, levofloxacin (75%), ciprofloxacin (73.9%) and norfloxacin

Table 8: List of moderate Interactions

Drug+Drug	Effect
Insulin Regular+Linizolid	↑ the Hypoglycemia condition
Insulin+Norfloxacin	↑ risk of hypoglycemia or hyperglycemia
Asprin+Furosemide	↓ diuretic and anti-hypertension
Nefidipine+Metorprolol	↑ Hypotension, Bradycardia
Atorvastatin+Niacin	↑ the Risk of myopathy
Glipizide+Metformin+Ciproflaxacin	↑ Hypo or hyperglycemia
Glimiperide+Propronalol	↑ Hypo/hyper or HTN
Pantorpazole+Propranalol	↑ Prorporonalol toxicity
Metaprolol+Tamsulosin	Exaggerate Hypotensive alpha blocker.
Metprolol+Metformin	↑ Hypo or Hyperglycemia or HTN
Amlodipine+Clopidegraol	↓ antiplatelet effect
Asprin+Clopidegrol	↑ the risk of Bleed
Ramipril+Amiloride/Spironolactone	Hyperkalemia
Asprin+Amiloride/Amlodipine/Diclofenac	GI haemorrahge,Antagonist effect of Hypotensive effect
Clopidegrol+Omepragole	↓ clopidegrol effect
Ferrous Feumarate+Pantoprazole	↓ Iron Bioavailability
Asprin+Calcium carbonate /Vitamin D.-	↓ Salicylate effectiveness
Asprin+Insulin lispro/Glimepiride	↑ Risk of hypoglycemia
Ferrous fumarate/Folic acid+Pantoprazole-	↓ Iron bioavailability
Carvidalol+Isophane Insulin/Metformin	Hypoglycemic or Hyperglycemia
Carvedilol+Tamsulosin	Exaggerate hypotensive
Metformin/Glimiperide+Levothyroxine-	↓ antidiabetic effect
Levothyroxine+Pantoprazole-	↓ TSH level
Amlodipine+Asprin	Hypotensive effect, GI hemorrhage
Asprin+Furosemide	↓ Diuretic effect and antihypertensive effect
Glimiiperide+TriMethorpim+SulphaMethaxazole	Excessive hypoglycemia
Calcium carbonate+Hydro.chlorthiazide/Telmisartan	↑ risk of hypercalcemia
Prednisalone+HydroChloroThiazide/Telmisartan	Hypokalemia
Clonidine+Insulin Glargine	Hypoglycemia or Hyperglycemia
Atorvastatin +Clopidegrol	high on-treatment platelet reactivity
Atorvastain+Digoxin	↑ plasma concs of digoxin
Digoxin+Omeprazole,furosemide	digoxin toxicity
Levothyroxine+MetforminHcl	↓ effectiveness of the antidiabetic agent
Ciprofloxacin+ferrous fumarate-	↓ ciprofloxacin effectiveness,
Cefaperazone/warfarin+pantaprazole	increased risk of bleeding
diclofenac+ramipril	↓ Ramipril effectiveness
diclofenac+Ramipril+glimiperide	↑ hypoglycemia
Furosemide+ramipril-	Postural hypotension (first dose).
Omeprazole+Propranalol	↑ propranolol exposure
Calcium carbonate/vit D-propranalol HCL	↓ propranolol bioavailability
Calcitrol+Magnisum HCL	Hypomagnesemia.
Clonazepam+theophylline	↓ benzodiazepine effectiveness
Iron+zinc	↓ gastrointestinal absorption of iron and/ or zinc
Asprin+Metaprolol/telmisartan	↓ the antihypertensive effect
Asprin+Prednisalone	↑ the risk of GI bleed

Table 9: List of severe Interactions

Drug+drug	Effect
Atorva statin+Fenofibrate	↑ Myopathy/Rhabdomyolysis
Clonidine+Diltizeam	↑ Sinus Bradycardia
furosemide+Metalazone	↑ electrolyte & fluid imbalances
Azithromycin+Salmetraol	↑ QT prolongation
Aspirin--Prednisolone	↑ risk of gastrointestinal ulceration and Sub therapeutic aspirin serum concentrations
Amitryptlin/TCA+Levothyroxine-	↑ therapeutic and toxic effects of both levothyroxine and tricyclic antidepressant
Amitryptilin/Duoloxetine/Linezolid+acitamenophenon/ Tramadaol-	↑ of seizures, serotonin syndrome & ↑ Tramdolconc
Insulin human (R)+HCT/losartan	↑ hypoglycemia
Alprazolam+Codeine sulfate	↑ respiratory depression
Aspirin +Hydrochlorothiazide/Losartan	↓ antihypertensive effects and ↑ renal impairment
Digoxin+Spiranolactone	↑ digoxin exposure
Asprin+Duoloxetin	Increased risk of bleeding
Duoloxetin+Napraxean	↑ risk of bleeding
Ciprofloxacin+Hydralazine HCl	↑ risk for Bleeding

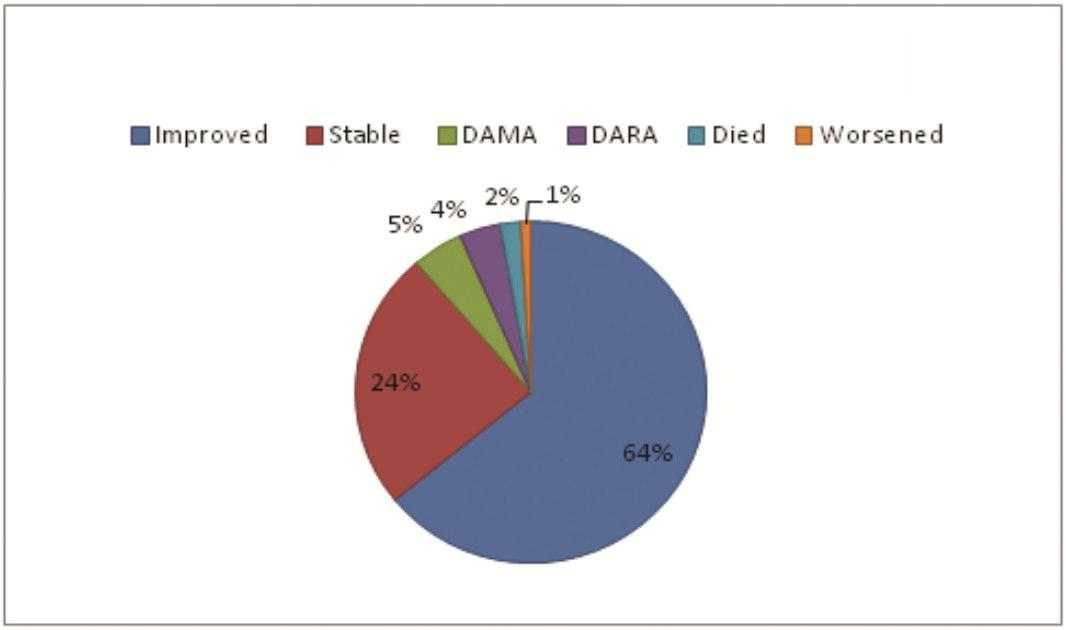

Figure 1: Clinical outcomes of UTI treatment patients

(69.6%) as sensitive.[24] Antibiotic susceptibility pattern of other organisms isolated was not considered as significant in view of less numbers of isolation.

CONCLUSION

This study clearly suggests that pharmaceutical care services are vibrant in elderly for the prevention and/or minimization of drug interactions, proper usage and rational promotion of drugs even though it was conducted only in selected medicine departments of the hospital. This study also suggests that educational interventions regarding strict control and monitoring of the chronic disease condition help in avoiding recurrence of UTIs. In addition, home medication review research studies can prove to be vital to elderly patients having financial constraints.

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CONFLICT OF INTEREST

The author declare no conflict of interest.

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