ORIGINAL ARTICLE

DRUG UTILIZATION STUDY OF URINARY TRACT INFECTIONS IN MEDICINE DEPARTMENT IN A TERTIARY CARE HOSPITAL

Rajat Mishra[1], Pradeep J[2], Prashant Dass[3], Shivraj Patil[4], Gayathri A[5], Waseem[6]

ABSTRACT: BACKGROUND: The WHO in 1977 provided the proper definition of Drug Utilization. It has been defined as the marketing, distribution, prescription and use of drugs in society with special emphasis on the resulting medical and social consequences. Urinary tract infection (UTI) is caused by pathogenic invasion of the urinary tract which leads to an inflammatory response of the urothelium. Urinary tract infections are common burden in patients with diabetes mellitus. Cystitis, ascending infection leading to pyelonephritis, impaired leucocyte function, recurrent vaginitis, emphysematous complications and renal/perinephric abscesses are well recognized in this group of patients if glycemic control is poor. The present study was undertaken to identify the common pathogens and drug sensitivity pattern of the isolate among patients who attended the medicine outpatients department so as to guide empirical treatment. **OBJECTIVES:** To evaluate prescription pattern of antibiotics in UTI in medicine department in a tertiary care hospital. Study of type of patients along with type of UTI major symptoms, precipitating factors, evaluation of uropathogens. To analyze rationality among the prescriptions. **METHODS AND MATERIALS:** This prospective, observational and analytical study was done to assess the antibiotics prescribed in UTI in medicine department in a tertiary care hospital. Gender distribution, age wise distribution, type of patients (outpatients, inpatients), type of UTI (complicated, uncomplicated), presenting symptoms, lab investigations related to UTI, microorganisms isolated from urine culture, antibiotics prescribed for UTI, precipitating factors for UTI, route of drug administration, adjuvant drugs along with antibiotics for UTI and outcome of the treatment were evaluated. Patients receiving antibiotic therapy in UTI of either gender of age >18 years, visiting medicine department were included. Approval from the institutional ethics committee was obtained before starting the study. The study was carried out between March, 2014 and July, 2014 (5months). 120 consecutive patients receiving antibiotics for UTI were included in the study. **RESULTS AND CONCLUSION:** The incidence of urinary tract infections was more in females compared to males (1.18:1). It was more common in the age group between 31-50 years. Majority of the cases were outpatients and majority of them were uncomplicated UTI. The most common presenting symptom was dysuria. The most common organisms isolated from the urine culture and sensitivity test was E. coli. The most commonly prescribed antibiotic was amikacin. Majority of the patients recovered.
KEYWORDS: Urinary tract infections, Drug utilization studies, Antibiotic use.

INTRODUCTION: The WHO in 1977 provided the proper definition of Drug Utilization. It has been defined as the marketing, distribution, prescription and use of drugs in society with special emphasis on the resulting medical and social consequences. [1] Drug utilization research is an essential part of pharmacoepidemiology as it describes the extent, nature of drug exposure. [2] Pharmacoepidemiology is defined as the study of the uses of and effects of drugs in large number of people.

ORIGINAL ARTICLE

Pharmacoepidemiology is a discipline that provides us with valuable information regarding clinical and economic outcomes of drugs, devices, and biologics, particularly after their approval for clinical use. [3]

Urinary tract infection (UTI) is caused by pathogenic invasion of the urinary tract which leads to an inflammatory response of the urothelium. The clinical manifestation of UTI depend upon the portion of the urinary tract involved, the etiologic organism, the severity of the infection and patients ability to mount an immune responds to it.[4] Signs and symptoms include fever, chills and rigor, dysuria, lower abdominal pain, urinary urgency, incontinence cloudy or malodorous urine.

With increasing age the prevalence of urinary tract infection (UTI) increases in both women and men. [5, 6] More than half of all women have at least one UTI in their lifetime and the risk of contracting a UTI increases in postmenopausal women. [7-9] The prevalence and incidence of UTI is higher in women than in men due to several clinical factors including anatomical differences, hormonal effects and behavioral pattern. Malnutrition, poor hygiene, low socioeconomic status are associated with UTI. [10]

The term uncomplicated urinary tract infection refers to the invasion of a structurally and functionally normal urinary tract by a nonresident infectious organism. Complicated UTI refers to the occurrence of infection in patients with an abnormal structural or functional urinary tract, or both. For symptomatic UTI, $\geq 10^5$ colony-forming units (CFU)/ml is one of the most common diagnostic standards. [11]

Urinary tract infections are common burden in patients with diabetes mellitus. Cystitis, ascending infection leading to pyelonephritis, impaired leucocyte function, recurrent vaginitis, emphysematous complications and renal/perinephric abscesses are well recognized in this group of patients if glycemic control is poor.[12] Infections particularly in pregnancies and in the elderly can be asymptomatic, but asymptomatic bacteruria is associated with an increased risk of intrauterine growth retardation and low birth weight babies. Furthermore, untreated asymptomatic bacteruria leads to development of cystitis in approximately 30% of cases, and can lead to the development of pyelonephritis in about 50% of cases. Thus it is important to identify and treat UTI to avoid such complication. [13]

A large prospective study of sexually active young women showed that recent sexual intercourse, use of diaphragm with spermicide and alteration of vaginal flora by OCP use was strong risk factors for UTI development. Bacteruria develops in at least 10-15% of hospitalized patients with indwelling urethral catheters. UTI is mostly caused by gram negative aerobic bacilli found in GI tract. Included in this family are the E. coli, Klebsiella, Enterobactor, Citrobacter, Proteus and serratia species. Other common pathogens include Staphylococcus epidermidis, Staphylococcus saprophyticus and Enterococcus species which presumably result in UTI following colonization of the vagina or perianal skin. Less common organism such as Gardenella vaginalis, Mycoplasma species and Ureaplasma urealyticum may infect patients with intermittent or indwelling catheters. [14]

Therapeutic decision should be based on accurate and up-to-date antimicrobial susceptibility.

The antibiotic drugs which have been used for the treatment of the UTI include penicillins, cotrimoxazole, older quinolones such as nalidixic acid and cephalosporins. Newer fluorinated quinolone (ofloxacin, ciprofloxacin), gentamicin, amikacin and imipenim demonstrated excellent effectiveness against the organisms, but are best reserved for treatment failures and more complicated infections since overuse of these agents can lead to resistance.

ORIGINAL ARTICLE

The present study was undertaken to identify the common pathogens and drug sensitivity pattern of the isolate among patients who attended the medicine outpatients department so as to guide empirical treatment.

OBJECTIVES:
1. To evaluate prescription pattern of antibiotics in UTI in medicine department in a tertiary care hospital.
2. Study of type of patients along with type of UTI major symptoms, precipitating factors, evaluation of uropathogens.
3. To analyze rationality among the prescriptions.

MATERIALS AND METHODS: This prospective, observational and analytical study was done to assess the antibiotics prescribed in UTI in medicine department in a tertiary care hospital. Gender distribution, age wise distribution, type of patients (outpatients, inpatients), type of UTI (complicated, Uncomplicated), presenting symptoms, lab investigations related to UTI, microorganisms isolated from culture urine, antibiotics prescribed for UTI, precipitating factors for UTI, route of drug administration, adjuvant drugs prescribed along with antibiotics for UTI and outcome of the treatment were evaluated.

Patients receiving antibiotic therapy in UTI of either gender of age >18 years, visiting medicine department were included in this study. Patients of <18 years of either gender and asymptomatic UTI were excluded from the study. Approval and clearance from the institutional ethics committee was obtained before starting the study. The study was carried out between March, 2014 and July, 2014 (5months).

120 consecutive patients receiving antibiotics for UTI were included in the study.

Data Analysis: Data was analyzed on MS Excel and descriptive statistics was used for analyzing the result of study.

RESULTS:

Gender	No. of cases	Percentage
Male	55	46 %
Female	65	54 %
Total	120	100
Table 1: Shows total no of cases with gender distribution		
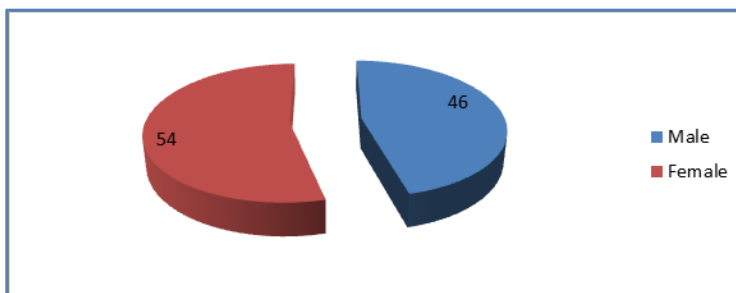
Figure 1: Percentage

ORIGINAL ARTICLE

Age in years	Male n	Male %	Female n	Female %	Total n	Total %
18-30	7	13	16	25	23	19
31-50	8	15	36	55	44	37
51-70	20	36	8	12	28	23
71-85	12	21	5	8	17	14
>85	8	15	0	0	8	7
Total	55	100	65	100	120	100
Table 2: Shows distribution of the patients according to age groups						
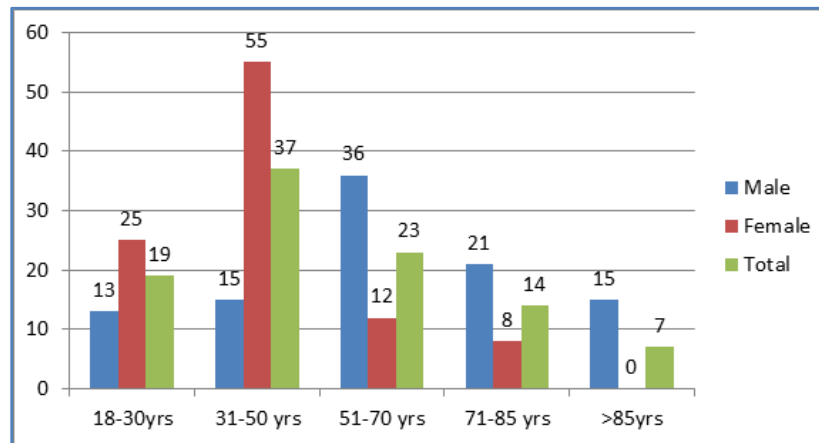
Figure 2: Percentage

Type of patients	Male n	Male %	Female n	Female %	Total n	Total %
Outpatients	20	36	47	72	67	56
Inpatients	35	64	18	28	53	44
Total	55	100	65	100	120	100
Table 3: Depicts type of patients with UTI						
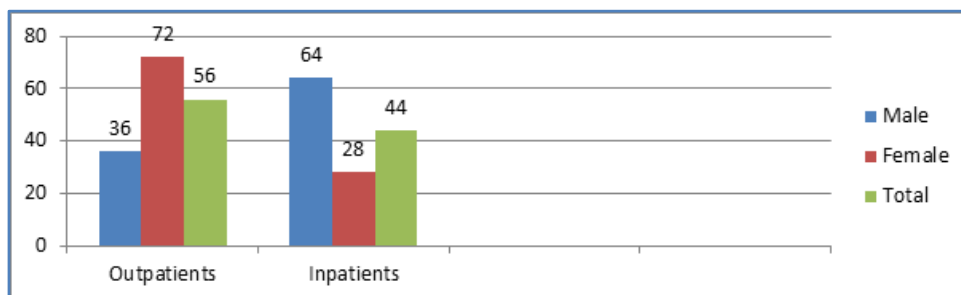
Figure 3: Percentage

ORIGINAL ARTICLE

Type of UTI	Male n	Male %	Female n	Female %	Total n	Total %
Uncomplicated	22	40	46	71	68	57
Complicated	33	60	19	29	52	43
Total	**55**	**100**	**65**	**100**	**120**	**100**
Table 4: Shows type of UTI						
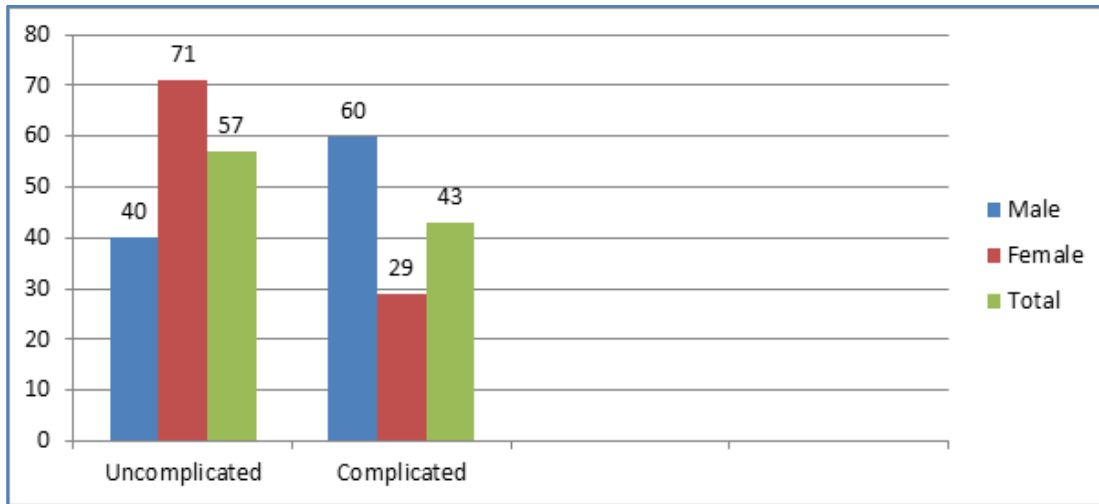
Figure 4: Percentage

Presenting symptoms	Total no. of complains (n)	Percentage (%)
Fever	40	25
Dysuria / burning micturition	56	35
Chills and rigor	18	12
Pain in loin	12	8
Suprapubic pain	10	6
Incontinence	8	5
Urgency	7	4
Others	8	5
Total	**159**	**100**
Table 5: Shows most common presenting symptoms for UTI		

The symptoms here are overlapping with each other that is why value of n is > than total no of cases.
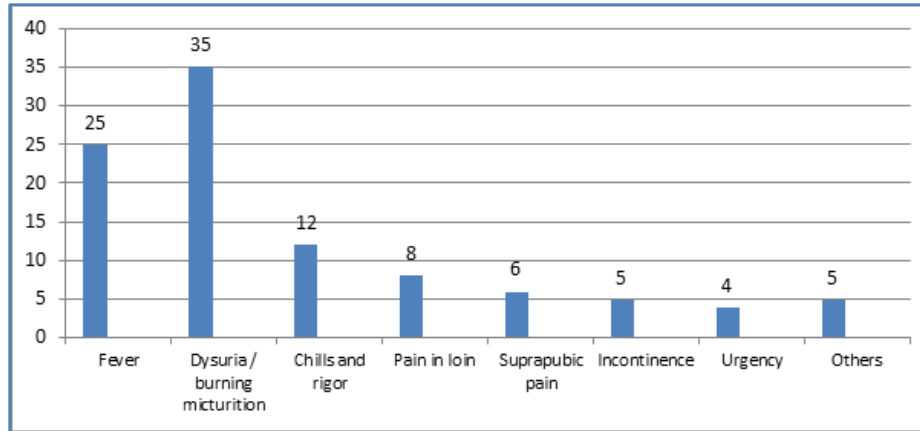
ORIGINAL ARTICLE

Figure 5: Percentage

Investigations	Total no (n)	Percentage (%)
Blood (TLC, DLC)	50	25
Routine urine	62	31
Urine culture	60	30
Ultrasound abdomen	22	11
Others	6	3
Total	**200**	**100**
Table 6: Depicts various investigations related to UTI		

The investigations are overlapping with each other that is why value of n is > than total no of cases.
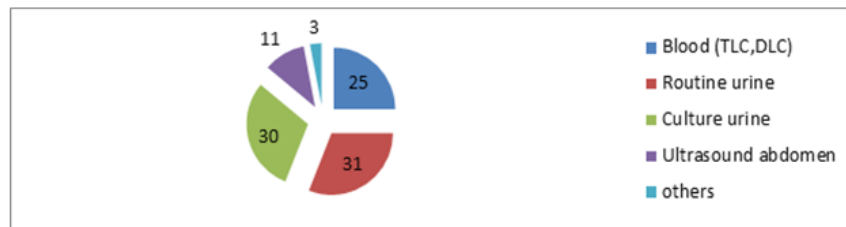

Figure 6: Percentage

Type of organisms	n	%
E.coli	39	65
Proteus	11	18
Klebsiella	7	12
Staphylococcus	1	2
Enterococcus fecalis	2	3
Total	**60**	**100**
Table 7: Shows organisms obtained from urine culture		

ORIGINAL ARTICLE
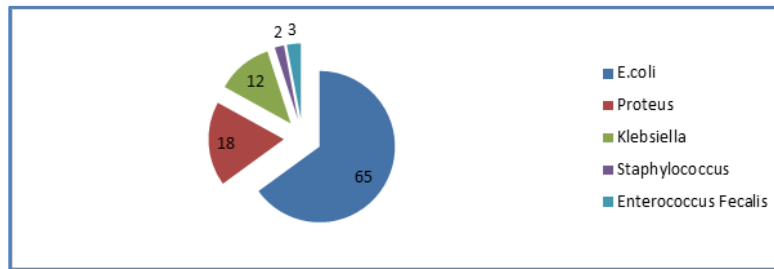
Figure 7: Percentage

Antibiotic	Total no. prescribed (n)	Percentage (%)
Amikacin	35	29
Levofloxacin	27	22
Ofloxacin	23	19
Norfloxacin	9	7
Ciprofloxacin	4	3
Nitrofuratoin	3	3
Amoxicillin + Clavulanic acid	2	2
Amoxicillin	2	2
Ampicillin	1	1
Cefepime	1	1
Ceftriaxone	13	11
TOTAL	**120**	**100**
Table 8: Shows distribution of patients according to antibiotic prescribed for UTI		
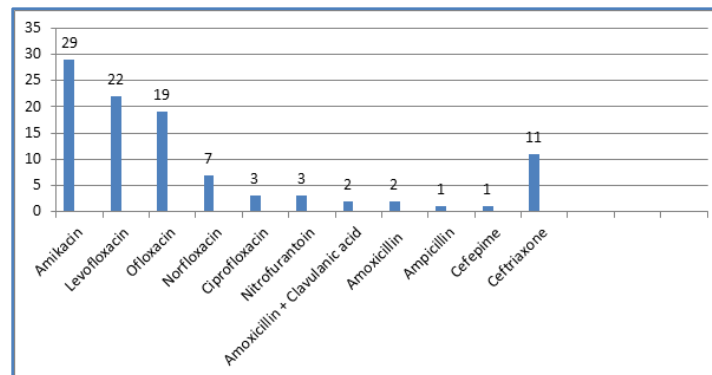
Figure 8: Percentage

Route of administration	Total no. of cases	Percentage (%)
Oral	58	48
Intravenous (IV)	53	44
Intramuscular (IM)	9	8
Total	**120**	**100**
Table 9: Shows the various route of administration		

ORIGINAL ARTICLE
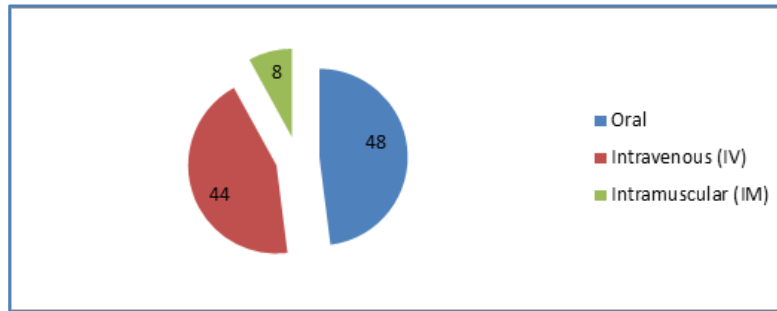
Figure 9: Percentage

Precipitating factors	Total no. (n)	Percentage (%)
Diabetes mellitus	42	24
Benign prostate hyperplasia (BPH)	26	15
Recurrent UTI	6	3
Renal stones	4	2
Smoking and drinking	52	29
Pregnancy	3	2
Post-menopausal	18	10
Oral contraceptive pills / Intrauterine contraceptive device users	26	15
Total	**177**	**100**
Table 10: Shows precipitating factors of UTI		

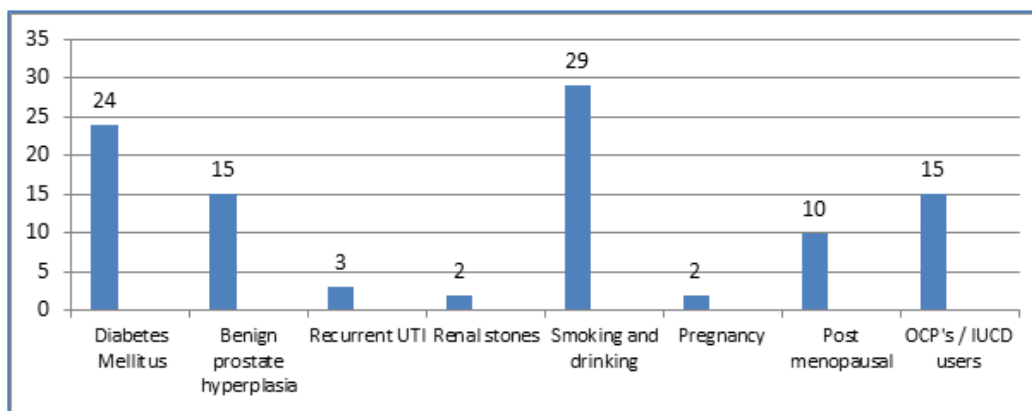These factors are overlapping with each other that is why value of n is > than total no of cases.

Figure 10: Percentage

ORIGINAL ARTICLE

Adjuvant drugs	Total no. (n)	Percentage (%)
Paracetamol	26	12
Diclofenac	14	6
Domperidone	3	1
Ondansetron	5	2
Dicycloverine	22	10
Pantoprazole	24	11
Terazosin	12	5
Doxazosin	8	4
Finasteride	6	3
Estrogen and Progesterone (Hormonal Replacement Therapy)	12	5
Insulins	6	3
Metformin	5	2
Metformin + Glimepiride	20	9
Glimepiride	8	4
Sitagliptin + Glibenclamide	3	1
Disodium hydrogen citrate (urine alkaliser)	15	7
Phenazopyridine Hydrochloride	31	14
Total	**220**	**100**
Table 11: Depicts the distribution of patients according to adjuvant drugs prescribed along with antibiotics for UTI		

Here the value of n is > than total no of cases as the adjuvant drugs prescribed are overlapping with each other.
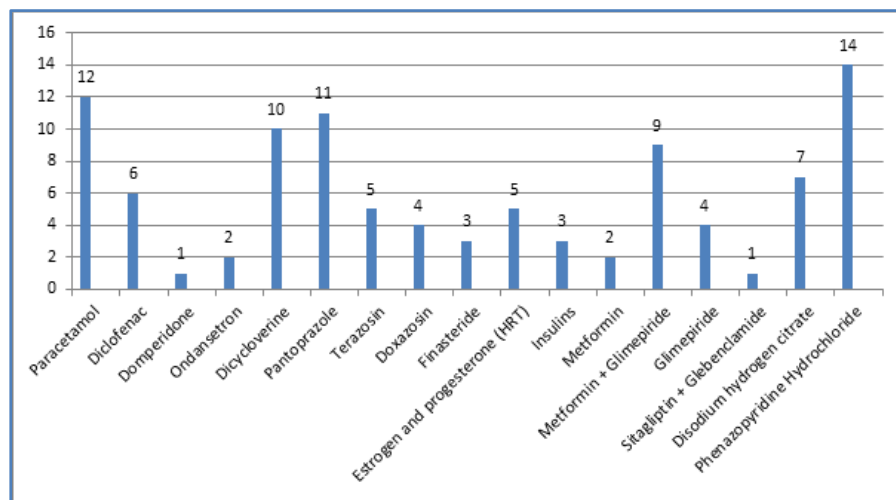

Figure 11: Percentage

ORIGINAL ARTICLE

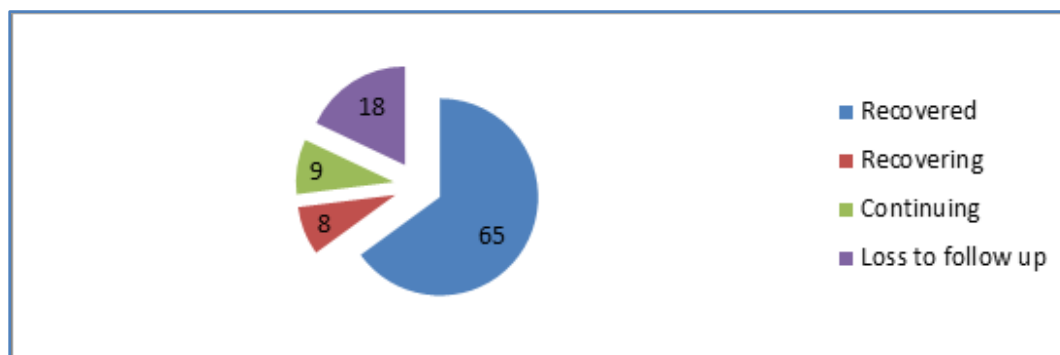| Outcome of treatment	Total no. of cases (n)	Percentage (%)
Recovered	78	65
Recovering	9	8
Continuing	11	9
Loss to follow up	22	18
Total	120	100
Table 12: Shows various outcomes of treatment		

Figure 12: Percentage

DISCUSSION: Drug utilization studies are important for obtaining data about the patterns and quality of use, the determinants of drug use and the outcomes of use. The main aim is to facilitate the rational use of medicines in populations. [15]

The present study is a prospective, observational and analytical study done on 120 consecutive patients to assess the antibiotics prescribed in UTI in medicine department in a tertiary care hospital.

Table-1 shows total number of cases along with gender distribution. Out of 120 cases female patients were 65 (54%) and male patients were 55 (46%). Figure-1

Table-2 shows distribution of patients according to age group. The majority of the patients out of 120 were in the age group 31-50 (n=44, 37%) followed by 51-70 (n=28, 23%) than 18-30 (n=23, 19%) followed by 71-85 (n=17, 14%) and last is in >85 years age group (n=8, 7%). Figure-2

Table-3 shows type of patients suffered from UTI. Out of 120 patients 67 (56%) were outpatients and 53 (44%) were inpatients.Figure-3

Table-4 shows types of UTI. 68 patients (57%) suffered from uncomplicated UTI and remaining 52 patients (43%) suffered from complicated UTI. Figure-4

Table-5 shows common presenting symptoms for UTI. Majority of the patients complained of dysuria (n=56, 35%) followed by fever (n=40, 25%) chills and rigor (n=18, 12%) than pain in the loin (n=12, 8%), suprapubic pain (n=10, 6%), incontinence (n=8, 5%), urgency
(n=7, 4%) followed by others (n=8, 5%) which includes nausea, vomiting and hematuria. Figure-5

Table-6 shows investigations associated with UTI which was done. Routine urine was done in 31% of patients followed by culture urine in 30% of cases than blood investigations in 25% of the cases and remaining 3% of the cases were subjected to IV cystography and X ray KUB (Kidney, ureter and bladder).Figure-6

ORIGINAL ARTICLE

Table-7 shows type of organisms which were isolated from culture urine. Out of 120 patients culture urine was done for 60 patients. Of which 35 of them (65%) showed isolation of E.coli followed by isolation of proteus in 11 cases (18%) than klebsiella in 7 cases (12%), enterococus fecalis in 2 cases (3%) and last is staphylococcus in 1 case (2%). Figure-7

Table-8 deals with most common antibiotics prescribed for UTI. Amikacin in 35 cases (29%) followed by Levofloxacin in 27 cases (22%) than Ofloxacin in 23 cases (19%), Ceftriaxone in 13 cases (11%) followed by Norfloxacin in 9 cases (7%) and rest were prescribed as 4 cases of Ciprofloxacin, 3 cases of Nitrofurantoin and 2 cases each of Amoxicillin and Amoxicillin + Clavulanic acid and 1 case each of Ampicillin and Cefepime.Figure-8

Table-9 shows route of administration of antibiotics for UTI. Out of 120 cases 58 of them (48%) took the drug by oral route followed by 53 cases (44%) who took the drug by intravenous route (IV) and remaining 9 cases (8%) took the drug by intramuscular route (IM). Figure-9

Table-10 shows precipitating factor associated with UTI. These precipitating factors were overlapping with each other so the numerical value (177) were more than total no of cases (120). 52 patients (29%) were smokers followed by 42 patients (24%) who suffered from diabetes mellitus, 26 patients (15%) each were having BPH and were using OCP's / IUCD followed by 18 cases (10%) in post-menopausal age, recurrent UTI in 3 cases (6%), 4 cases of renal stones(3%) and 3 cases of pregnancy.Figure-10

Table-11 shows adjuvant drugs prescribed along with the antibiotics for UTI. Here the adjuvant drugs prescribed were overlapping with each other. Majority of them were prescribed Phenazopyridine Hydrochloride (14%) for burning micturition / dysuria followed by Paracetamol (12%) than Pantoprazole (11%), Dicycloverine (10%) cases, Disodium hydrogen citrate (7%) urine alkaliser, Diclofenac (6%), Terazosin (5%), Doxazosin (4%) Finasteride (3%), Estrogen and progesterone (5%) as HRT. Rest were on Insulins and Oral hypoglycaemic agents and antiemetics like Domperidone and Ondansetron. Figure-11.

Table-12 shows outcome of treatment. This was assessed at the end of 5 months of study. Out of 120 cases 78 of them (65%) recovered while 9 cases were recovering (8%) followed by 11 cases (9%) who were continuing to have UTI while remaining 22 cases (18%) there was loss to follow up. Figure-12.

CONCLUSION: To conclude the incident of UTI is more common in females than in males. Uncomplicated UTI in general practice is high among young females in reproductive age groups. Complicated UTI is more common in old age especially in males.

Predominant risk factors to complicated UTI include diabetes mellitus, BPH, and recurrent UTI. OCP/IUCD use, pregnancy and sexual activity are the risk factors in young females. E. coli is found to be the most common cause of UTI in all age groups. This isolates shows resistance to commonly used antibiotics and susceptible only to injectable antibiotics like Amikacin. Amikacin, Levofloxacin, Ofloxacin and Ceftriaxone are the major antibiotics prescribed in UTI. In our study high percentage of cases recovered fully but few percentage also showed loss to follow up.

LIMITATIONS: Urine culture was done only for half (60) out of the total no of cases (120) for which empirical treatment had to be applied rather than specific antibiotic treatment and also due to time and financial constraints probable side effects and ADRs might have been overlooked.

ORIGINAL ARTICLE

REFERENCES:

1. World Health Organization. The selection of essential drugs. WHO Technical report 1977; 615: 36.
2. Sjoqvist F, Birkett D. Drug Utilization. In: Bramley DW editor. Introduction to Drug Utilization Research. (WHO booklet) New York: WHO office of publications; 2003:76-84.
3. Strom BL, ed. Pharmacoepidemiology. New York, Wiley; 1994.1977.
4. G Sibi, Aheibam Premita Devi, K Fouzia, Bhimanagouda R Patil. Prevalence, microbiologic profile of urinary tract infection and its treatment with Trimethoprim in diabetic patients. Research Journal of Microbiology; 2011; 6(6): 543-551.
5. Griebling TL. Urologic diseases in America project: trends in resource use for urinary tract infections in men. J Urol.2005; 173: 1288-1294.
6. Griebling TL. Urologic diseases in America project: trends in resource use for urinary tract infections in women. J Urol. 2005; 173: 1281-1287.
7. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Am J Med. 2002; 113: S5-S13.
8. Harrington RD, Hooton TM. Urinary tract infection risk factors and gender. J Gend Specif Med. 2000; 3: 27-34.
9. Shortliffe LM, McCue JD. Urinary tract infection at the age extremes: pediatrics and geriatrics. Am J Med. 2002; 113: S55-S66.
10. Bankole Henry Oladeinde, Richard Omoregie, Mitsan Olley, Joshua A Anunibe. Urinary tract infection in a rural community of Nigeria. North American Journal of Medical Sciences. 2011; 3 (2): 75-77.
11. Nicolle L. Best pharmacological practice: urinary tract infections. Expert Opin Pharmacother. 2003; 4: 693-704.
12. Mahesh E, Medha Y, Indumathi V A, Prithvi S Kumar, Mohammed Wasim Khan, Punith K. Community acquired urinary tract infection in the elderly. British Journal of Medical Practitioners; 2011; 4 (1): 406.
13. M Al Haddad. Urinary tract infection among pregnant women in Al-Mukalla district, Yemen. Eastern Mediterranean Health Journal, 2005; 11(3): 505-510.
14. Chedi B A Z, Wannang N N, Halliru M A, Bichi L A. A seven months retrospective study of urinary tract infection among patients at Aminu kano teaching hospital, Kano-Nigeria. Bayero Journal of Pure and Applied Sciences 2009; 2 (2): 95-98
15. World Health Organization. Introduction to drug utilization research; Oslo: 2003.

ORIGINAL ARTICLE

AUTHORS:
1. Rajat Mishra
2. Pradeep J.
3. Prashant Dass
4. Shivraj Patil
5. Gayathri A.
6. Waseem

PARTICULARS OF CONTRIBUTORS:
1. Post Graduate Resident, Department of Pharmacology, Mahadevappa Rampure Medical College, Gulbarga.
2. Post Graduate Resident, Department of Pharmacology, Mahadevappa Rampure Medical College, Gulbarga.
3. Post Graduate Resident, Department of Pharmacology, Mahadevappa Rampure Medical College, Gulbarga.
4. Post Graduate Resident, Department of Pharmacology, Mahadevappa Rampure Medical College, Gulbarga.
5. Post Graduate Resident, Department of Pharmacology, Mahadevappa Rampure Medical College, Gulbarga.
6. Post Graduate Resident, Department of Pharmacology, Mahadevappa Rampure Medical College, Gulbarga.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Rajat Mishra,
Post Graduate Resident,
Department of Pharmacology,
Mahadevappa Rampure Medical College,
Gulbarga-585105, Karnataka.
Email: mishra.rajat13@gmail.com