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EFFECTIVENESS OF ANTIBIOTICS IN INCREASING THE FUNCTIONAL CAPACITY AND REDUCING THE ECONOMIC BURDEN IN FEMALE URINARY TRACT INFECTION PATIENTS

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ABSTRACT: Background: Urinary tract infection is a common medical problem for women throughout their lifetime. Recurrence after urinary tract infection (rUTI) is common in adult women. The majority of recurrences are believed to be reinfection from extra urinary sources such as rectum or vagina. The treatment of recurrent urinary tract infection also inflicts an economic burden on the patient's life. Hence, we must use an effective antibiotic that prevents the recurrence of UTI and improve the functional capacity and quality of life in women. This study aims to study the effectiveness of different antibiotics in increasing the functional capacity and reducing the economic burden in UTI women. **Methodology:** This is a prospective, observational study, conducted in a total of 50 patients at General Medicine Department of a tertiary care hospital in Coimbatore for a period of six months. The patient demographic details were collected from the medical records or direct patient interview. Urine analysis, urine culture and antibiotic sensitivity reports were also collected and entered in the data collection form. The functional capacity and quality of life scores before and after antibiotic administration were calculated using the Leicester Impact scale. **Results:** The study shows that the urinary tract infection mainly affects women between the ages 55 and 65 yrs. *Escherichia coli* is the principal microorganism that causes urinary tract infection the most and the major risk factor is menopause(24%) and the least risk factor is urosepsis (10%). Mostly prescribed antibiotic is combination of Cefoperazone and Sulbactam and its recurrence rate is 4%. **Conclusion:** From the study, it is concluded that amikacin is the most cost effective medication with no recurrence rate and with a mean number of days of hospital stay of four days.

INTRODUCTION: Urinary tract infection (UTI) is the presence of greater than 10^5 bacteria per milliliter of urine. The organisms have potential to invade tissues of urinary tract. Infection may be limited to growth of bacteria in urine, which frequently may not produce symptoms.

Urinary tract infections (UTIs) present as several syndromes associated with an inflammatory response to microbial invasion and it ranges from asymptomatic bacteriuria to pyelonephritis with bacteremia and sepsis. UTIs are designated as uncomplicated or complicated.

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Uncomplicated infections occur in individuals who lack structural or functional abnormalities of the urinary tract that interfere with the normal flow of urine or voiding mechanism. These infections occur in females of 15 to 45 yrs of age. Complicated UTIs are the result of a predisposing lesion of the urinary tract such as congenital

abnormality or distortion of the urinary tract, a stone, prostatic hypertrophy, obstruction that interferes with the normal flow of urine and urinary tract defenses¹. UTIs are the most common bacterial infection in any part of urinary system-kidneys, ureters, bladder and urethra and accounts for 8 million patient visits annually. Most infections involve the lower urinary tract-bladder and urethra². Women tend to get more bladder infections than men³. This is because women have shorter urethra, so it is easier for the germs to move into the bladder. Having sex can make easier for germs to get into urethra and women will get infection if they do not drink enough fluids³⁻⁴.

Approximately, one in three females will have urinary tract infection by age 24⁵. The prevalence varies with age and gender. In newborns and infants, up to six months of age, the prevalence of bacteriuria is approximately 1% and is more common in boys. Most of these infections are associated with structural or functional abnormalities of the urinary tract and have been correlated with lack of circumcision⁶. Between 1 and 6 years of age, urinary tract infection occurs mainly in females.

The prevalence of bacteriuria in females and males of this age group is 4.5% and 0.5%⁷. Before puberty, the prevalence is approximately 1% with 5% of females reported to have significant bacteriuria prior to leaving high school. This percentage increases to 1% to 4% after puberty in non-pregnant females as a result of sexual activity. Approximately 1 in 5 women will suffer a symptomatic urinary tract infection⁸. In elders, the ratio of bacteriuria in women and men is approximately equal. The rate of infection increases who are in nursing homes⁹.

The Quality of life (QOL) of patients is evaluated with Leicester impact scale. It measures the impact of urinary symptoms. It is used to determine the impact of urinary problems on daily activities and on mood and behavior. The scale consists of 21 questions with a minimum score of 0 and maximum score of 2. The Leicester impact scale is divided into four ranges: 0-14, 15-20, 21-30 and 31-42. A score of >14 indicates that the patient had some degree of functional or social handicap

(mild), a score of >21 indicates a major social or functional handicap (moderate) and a score of >31 indicates severe social and functional handicap (severe).

Escherichia coli (52%) is the particular microorganism which affects the urinary tract infection. Menopause (24%) is the major risk factor for urinary tract infection. Urgency (58%), burning micturition (50%), and suprapubic heaviness (34%) are the main symptoms of UTI. The first line treatment for UTI is combination of Cefoperazone and Sulbactam.

Management of women with frequent symptomatic recurrent UTI can be vexing for both patients and physicians. For the patients, each UTI recurrence is associated with days of urinary tract symptoms, general malaise, restrictions on everyday activities, therapy costs, and also a loss in the professional front too. The patients suffering from recurrent urinary tract infections can be treated safely and effectively with continuous antibiotic prophylaxis, post-coital therapy or self initiated therapy. Since recurrent urinary tract infection affects women in all fronts of their life, it is very essential to prevent the recurrence of UTI. The treatment of recurrent urinary tract infection also inflicts an economic burden on the patient's life. Hence, we must use an effective antibiotic that prevents the recurrence of UTI and improve the functional capacity and QOL of the women. This study aims at studying the prescribing pattern of UTI in a tertiary care hospital and also to assess the effectiveness of antibiotics in improving functional capacity and quality of life in women.

MATERIALS AND METHODS:

This study is done as a prospective, observational study. The study was conducted after obtaining ethical approval from the Institutional Ethical Board of the tertiary care hospital in which the study was conducted. The study was carried out in the General Medicine Department for a period of six months. The patients were included into the study if they satisfy the inclusion criteria – females greater than 15 years of age, diagnosed with UTI, have positive urine culture, and is prescribed at least one antibiotic. Informed consent was obtained directly from the included patients or from their

caretakers. The patient demographic details were collected from the medical records or from direct interview with the patient and was entered into the data collection form prepared exclusively for this study. Urine analysis, urine culture, and antibiotic sensitivity reports were collected. The functional capacity and QOL scores before and after antibiotic administration were calculated using the Leicester Impact scale.

RESULTS:

Of 50 patients included in the study, majority of the patients belong to the age group of 55-65 years with mean age being 55. The following Fig.1 shows age wise distribution of the study subjects

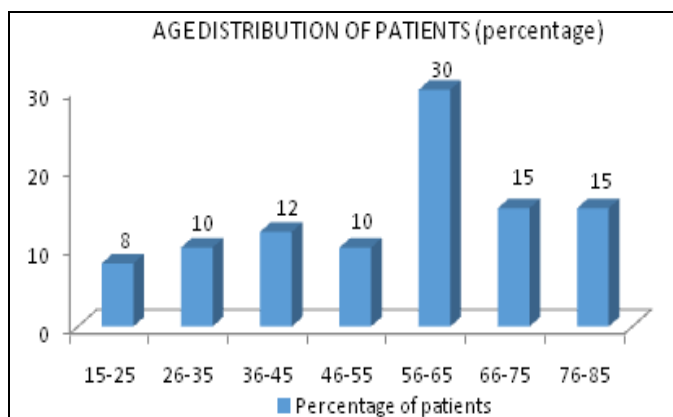


FIG.1: AGE DISTRIBUTION OF PATIENTS

The most predominantly isolated pathogen from urine culture is found to be E. coli (52%) followed by *Klebsiella pneumoniae* (24%), *Enterococcus species* (8%) and *Candida albicans species*(4%). The following Fig.2 shows distribution of patients based on microorganism isolated from urine culture.

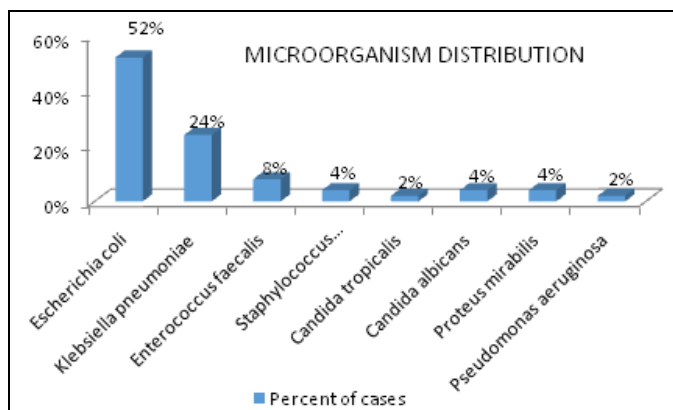


FIG. 2: PATIENT DISTRIBUTION BASED ON ISOLATED MICROORGANISM

Based on risk factors, it was found that menopause was the most common risk factor for UTI with 24% of the patients with menopause getting UTI followed by diabetes mellitus (22%), catheterization (17%) and renal impairment (15%). Fig.3 shows distribution of patients on the basis of risk factors for UTI.

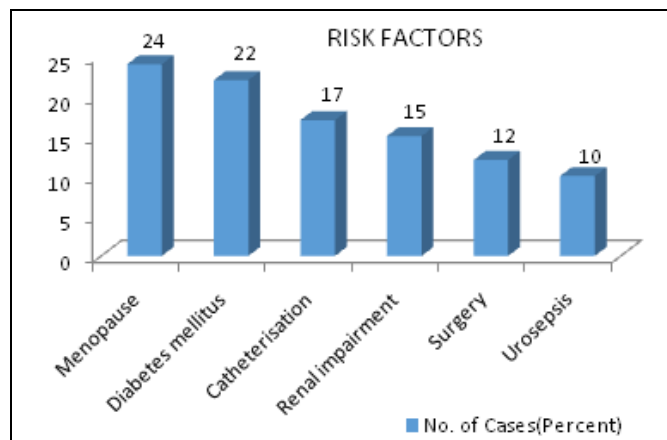


FIG. 3: PATIENT DISTRIBUTION BASED ON RISK FACTORS

The following Fig.4 shows the information on where the UTI patients get the infection from. It shows that 70% of the UTI cases are acquired from the hospital.

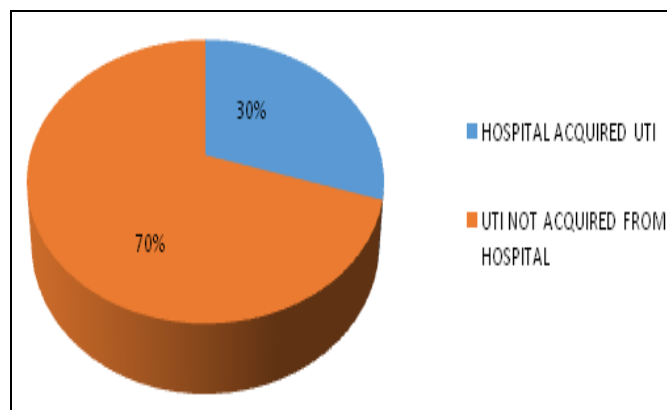


FIG.4: UTI PATIENTS GET THE INFECTION

Functional Capacity and QOL Assessment:

The functional capacity and Quality of life scores were assessed or evaluated using Leicester Impact scales. The scores were taken before and after antibiotic administration. The patient’s functional capacity and QOL improved significantly after antibiotic administration which is shown in Table 1.

TABLE 1: FUNCTIONAL CAPACITY AND QOL ASSESSMENT MEAN SCORE

FC & QOL Assessment Score Before Antibiotic Administration	MEAN	SD
	33.22 (Severe)	4.171
FC & QOL Assessment Score After Antibiotic Administration		
	20.44 (mild)	5.585

FC- Functional Capacity; SD-standard deviation

TABLE 2: FUNCTIONAL CAPACITY AND QOL ASSESSMENT P-VALUE

FC AND QOL Assessment Scores(Before &After Antibiotic Administration)	MD	SD	t-VALUE	DOF	P-VALUE
	12.780	6.510	13.882	49	0.00001

FC-Functional Capacity; MD-mean difference; SD-standard deviation; DOF-Degrees of Freedom; t-value – value from student's t-test; P-value – probability value.

TABLE 3: MEAN FUNCTIONAL CAPACITY & QOL SCORES BEFORE AND AFTER DIFFERENT ANTIBIOTIC ADMINISTRATION AND THE MEAN DIFFERENCES

S.No	Antibiotic Prescribed	MFC&QOL Scores(BAA)	MFC&QOL Scores(AAA)	MD
1.	Cefoperazone+Sulbactam	34.6	19.9	14.7
2.	Amoxicillin+Clavulanate	34.14	19.57	14.57
3.	Amikacin	31.8	17.6	14.2
4.	Tigecycline	33.3	21	12.3
5.	Ofloxacin	32	20	12
6.	Imipenem+Cilastatin	36	24	12
7.	Piperacillin+Tazobactam	35	23	12
8.	Ceftriaxone	32	21	11
9.	Cefepime+Tazobactam	24	13	11
10.	Ertapenem	30	19	11
11.	Ceftriaxone+Sulbactam	39	30	9
12.	Cefuroxime	26	17.5	8.5
13.	Faropenem	32	23.5	8.5
14.	Fluconazole	33.5	27	6.5
15.	Linezolid	32	29	3
16.	TMP/SMX	32	29	3

MFC-Mean Functional Capacity; BAA-Before antibiotic administration; AAA-After antibiotic administration; MD-mean difference.

TABLE 4: COST ANALYSIS OF THE ADMINISTERED ANTIBIOTICS

S. No	Antibiotics Prescribed	No. of patients	Recurrence Rate	Mean Cost in Rupees	No. of days of hospital stay (mean)	% increase in effectiveness
1	Cefoperazone+Sulbactam	18	2	400	8	35%
2	Amoxicillin+Clavulanate	7	10	201	9	35%
3	Amikacin	5	0	77	4	34%
4	Tigecycline	3	1	2758	14	29%
5	Ofloxacin	3	0	131	5	29%
6	Imipenem+Cilastatin	1	0	1777	8	29%
7	Piperacillin+Tazobactam	1	0	394	6	28%
8	Ceftriaxone	1	0	532	8	26%
9	Cefepime+Tazobactam	1	0	596	9	26%
10	Ertapenem	1	0	2616	7	25.8%

11	Ceftriaxone+ Sulbactam	1	0	139	3	22%
12	Cefuroxime	2	2	260	4	20%
13	Feropenem	2	2	427	5	16%
14	Fluconazole	2	2	220	5	15.8%
15	Linezolid	1	1	132	4	7%
16	Trimethoprim+ Sulfamethoxazole	1	1	14	9	7%

From the table above, it is noted that the mostly prescribed antibiotic is Cefoperazone +Sulbactam (36%) at a cost of Rs. 400 which increases the effectiveness by 35%. Rs. 2758 is the highest cost of medication which is tigecycline that increases the effectiveness by 29% and the lowest cost is Rs. 14 for Trimethoprim + Sulfamethoxazole which increases the effectiveness by 7%.

TABLE 5: NUMBER OF PRESCRIPTIONS AND THE RECURRENCE RATE OF THE ADMINISTERED ANTIBIOTICS

S.NO	Antibiotic Prescribed	Prescriptions given (%)	Recurrence Rate (%)
1.	Cefoperazone + Sulbactam	36%	4%
2.	Amoxicillin + Clavulanate	14%	2%-
3.	Amikacin	10%	-
4.	Tigecycline	6%	-
5.	Ofloxacin	6%	2%
6.	Cefuroxime	4%	2%
7.	Feropenem	4%	-
8.	Fluconazole	4%	2%
9.	Cefepime + Tazobactam	2%	-
10.	Ertapenem	2%	-
11.	Ceftriaxone + Sulbactam	2%	-
12.	Imipenem + Cilastatin	2%	-
13.	Piperacillin + Tazobactam	2%	-
14.	Ceftriaxone	2%	-
15.	Linezolid	2%	2%
16.	Trimethoprim + Sulfamethoxazole	2%	2%

DISCUSSION AND CONCLUSION:

In the present study, out of 50 patients, 15 patients (30%) have acquired urinary tract infection from the hospital setting. The findings of the study by Le Nicolle et al.¹⁰, shows that urinary tract infection is one of the most common hospital acquired infection and 80% of them is associated with indwelling urethral catheter.

The functional capacity and QOL assessment of the patients before and after antibiotic administration, shown in table 1, 2, 3. It was assessed based on the Leicester Impact Scale. The mean Leicester score before antibiotic administration is 33.22 (79%); (SD=4.171) and the Leicester score after antibiotic administration is 20.44 (49%); (SD=5.585). The mean Leicester score decreased from 79% before antibiotic administration to 49% after antibiotic administration showing a statistically significant decrease of 30% with $p < 0.00001$. These statistically significant reductions suggest a

lessening of social and functional handicap or improvement in the functional capacity and QOL after antibiotic administration. From our study, we found out that cefoperazone + sulbactam is the mostly prescribed drug (36%) for UTI, followed by amoxicillin + clavulanate (14%), amikacin (10%), tigecycline and ofloxacin (6%), cefuroxime(4%), feropenem (4%), cefepime + tazobactam (2%), ertapenem (2%), ceftriaxone + sulbactam (2%), imipenem + cilastatin (2%), linezolid (2%), piperacillin + tazobactam (2%), ceftriaxone (2%) and TMP/SMX (2%) which is shown in **Table 4**.

The prescription of antibiotics varies from hospital to hospital. The prescription of antibiotics is based on the particular hospital antibiotic guideline. In this study, the antibiotics were prescribed on the basis of antibiotic prescribing guidelines for urinary tract infection of this tertiary care hospital. According to the antibiotic guideline of this hospital, the first line treatment for ICU patients is

cefepime + tazobactam and the second line treatment antibiotic for UTI is amikacin. For patients admitted in the wards, the first line treatment is amikacin and the second line treatment for UTI is cefoperazone + sulbactam. For outpatients, the first line treatment for UTI is cotrimoxazole and the second line treatment is nitrofurantoin.

The antibiotics are selected based on the antibiotic sensitivity report. The recurrence rates are given in **Table 5**. The recurrence rates for the administered antibiotics are as follows: Cefoperazone + sulbactam (4%) which is followed by amoxicillin + clavulanate (2%), ofloxacin (2%), cefuroxime (2%), fluconazole (2%), linezolid (2%) and TMP/SFX (2%). The recurrence of UTI depends upon the uropathogen, its sensitivity to the administered antibiotic and also the resistance pattern and the risk factors of the patient. A study by Enrique Patricio Ubertazzi et al.,¹¹ cited that 50% of women experience at least one UTI in their lifetime; 25% and 44% of these patients will suffer recurrence of infection within 6 months and 1 year respectively. **Table 4** depicts the cost analysis of antibiotics used in the present study. Antibiotics of varying costs are administered.

The antibiotic of highest price is tigecycline (Rs. 2758) and the antibiotic of lowest price is TMP/SMX (Rs. 14). From the table, the cost effective antibiotic is found to be amikacin (Rs. 77) with no recurrence rate and with a mean number of days of hospital stay of four days. The costs of the

prescribed antibiotic is statistically significant with $p < 0.05$. There is no precise comparable studies for the cost analysis of only antibiotics used in urinary tract infection and their cost effectiveness. Further studies are needed to evaluate the cost effectiveness of antibiotics in treating urinary tract infection.

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