

Prescribing Pattern and Cost of Fluoroquinolones in Pyelonephritis Patients Hospitalized in Tertiary Care Hospital

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Abstract: Complicated urinary tract infections (cUTIs) impose a high burden on healthcare systems and are a frequent cause of hospitalization. Urinary tract infection (UTI) is a common illness affecting both males and females in almost all age groups. The objective was to determine the prescription pattern of antibiotics and cost of fluoroquinolones antibiotics in patients of UTI (pyelonephritis). We finalized the most significant 66 pyelonephritis patient's documents. All the information, related to the prescription cost of fluoroquinolones of antibiotics needed to treat the disease was arranged. Patient medication record was obtained from the patients' medical file, and added with the unit cost of services obtained from the hospital record mainly medication, to determine the prescription cost. Concomitant medication and medication of complications was not recorded. All costs were calculated in Pakistani rupees and in US dollar (average exchange rate in year 2018 was 1US\$=121.574 PKRs. The most commonly prescribed fluoroquinolone in our study for the treatment of pyelonephritis was ciprofloxacin. Average highest Cost of antibiotic combination of ciprofloxacin/levofloxacin was PKRs 8650 (\$71.150) and the average least antibiotic cost for treating pyelonephritis was PKRs1008 (\$8.291) with the combination of ceftriaxone 500gm/ciprofloxacin 400mg oral. The average fluoroquinolones prescription cost per hospitalized case of UTI (Pyelonephritis) varied from case to case, depending upon the type and combination of antibiotics used. A better knowledge of the reasons for variations in length of stays could facilitate a better standardised quality of care for patients with UTI (Pyelonephritis) and allow a more efficient allocation of healthcare resources.

Keywords: Antibiotics, Fluoroquinolones, Urinary Tract Infection (UTI), Prescription Cost

1. Introduction

Pyelonephritis is one of serious kidney infection caused by gram negative bacteria including *E. coli*, *Proteus*, *Klebsiella*, and *Enterobacter*; could be a life-threatening disorder. Globally, each year approximately 150 million people are affected by urinary tract infection (UTI) with profound health care expenditure. However, United States represents a societal cost of around US\$3.5 billion annually in treating those infections. [4]

According to a report, 40-50% of women are more prone

to suffer from UTI particularly once in their lifetime. [13]. In US, pregnant women (20-30%) are at high risk to have pyelonephritis usually during the second and third trimester compared to 17 and 4 cases per 10,000 of female and male every year. [2] A databased survey in USA estimated the incidence of pyelonephritis requiring hospitalization to be 11.7 cases/10,000 population among women [5]. It appears that women younger than 50 years of age with pyelonephritis are infrequently hospitalized. [12]

Pyelonephritis (upper UTIs) can be managed either as outpatients or inpatients. Young, geriatrics, immunocompromised, uncontrolled diabetic cases, impaired renal function and pregnant women are categorized as complicated pyelonephritis and treated as inpatients which may require short/long-term hospitalization followed by surgical procedures. Treating complicated UTIs is compulsory due to their potential mortality. The mainstay of treatment primarily based on fluoroquinolones which are extensively used antibiotics to treat UTIs because it accelerates the broad spectrum anti-bacterial activities. Oral cephalosporins or TMP-SMX are most likely to be prescribed for 14 days among outpatients' settings by considering a choice of drug to treat uncomplicated pyelonephritis. [1]. while complicated cases of acute pyelonephritis require intravenous antibiotic treatment until and unless the desired clinical output achieved. Ceftriaxone, ertapenem and levofloxacin are recommended in the treatment guidelines for complicated UTIs [6]. The finding of a registry-based study showed that the proportion of antibiotic prescription raised from 35.3 to 50.7% for pyelonephritis characterized by more use of broader-spectrum antibiotics. [7]

Based on classification of fluoroquinolones, both levofloxacin and ciprofloxacin are widely prescribed, have clinical significance and highly recommended in UTIs. In contrast to ciprofloxacin, levofloxacin has great benefit to deal regarding safety, effectiveness and chance of disease reoccurrence. Despite of having a clinical achievement and acceptable bacterial eradication, levofloxacin has no longer use where resistance level is supposed to be high (> 10%) or if pyelonephritis is hospital acquired [11]. It has been noticed that elderly patients are predominantly affected by the potential harm of fluoroquinolones for instance aortic aneurysm, hypoglycemia and a variety of neuropsychiatric symptoms, ranging from seizures to worsening of dementia. So, a substantial care must be taken to lessen the undesired effects.

2. Methodology

2.1. Study Design

It was a prospective and cost of prescription analysis study.

2.2. Length of Study

The study length was 4 months. Study conducted from in the year 2018. The study was finished in a 100 beds tertiary care center attached with a medical university found in Karachi. Examine consent was taken from the hospital administration.

2.3. Patients

Inpatients were incorporated with age more than 18 years old that were related, or determined to have pyelonephritis.

2.4. Sample Size

Over all we assessed 300 documents of Urinary tract infection patients from which we isolated the pyelonephritis patient's records. From isolated pyelonephritis patients records we finalized the most significant 66 pyelonephritis patient's documents.

2.5. Data Collection

Patients information gathered comprise of demographic characteristics including age, gender, co morbidity, fluoroquinolones antibiotics mainly and length of stay at hospital was taken from the patient record document. The patient records were checked on by principle investigator, who utilized an organized frame to record the required data, and the most important of these were assessed.

2.6. Cost Calculation

All the information, related to the prescription cost of fluoroquinolones of antibiotics needed to treat the disease was arranged. Patient medication record was obtained from the patients' medical file, and added with the unit cost of services obtained from the hospital record mainly medication, to determine the prescription cost. Concomitant medication and medication of complications was not recorded. All costs were calculated in Pakistani rupees and in US dollar (average exchange rate in year 2018 was 1US\$=121.574 PakRs. The medication costs were calculated as the average cost of the drugs for the hospital during year 2018 (data provided by the Pharmacy Service of the hospital).

2.7. Statistical Analysis

The medication expense results are accounted as average cost. In the first step the information was entered in the excel sheet and then investigated further on SPSS, mean, variance, valid frequency of answer, percentage and cumulative percentage was taken. All data were analyzed using SPSS 20 version.

2.8. Ethical Approval

Ethical approval permission was ensured from the Ethical review committee of the Ziauddin University Karachi. Permission was obtained before conducting the study from institution. Informed consent from the patients was taken before the study.

3. Results

Table 1. NO OF CASES OF UTI (Pyelonephritis).

| cases | Private hospital |
|----------------|------------------|
| Pyelonephritis | 66 |

We screened 300 files of urinary tract infection and selected 66 cases of pyelonephritis in which at least one fluoroquinolone was prescribed to analyze the prescribing trend and prescribing cost of fluoroquinolones for treating pyelonephritis admitted in a private hospital in Karachi, Pakistan.

Table 2. Ages of patients of pyelonephritis in private hospital.

| Patients ages | frequencies | percentages |
|---------------|-------------|-------------|
| 19- 40years | 11 | 16.67 |
| 41-60 | 26 | 39.39 |
| 61--71 | 18 | 27.27 |
| Above 72 | 11 | 16.66 |
| Total (n=66) | 66 | 100 |

Table 2 shows the ages of the patients diagnosed with pyelonephritis. patients with the age group between 41-60 were 39.39% followed by 61-71 years of age were 27.27%.

Table 3. Gender.

| Gender | Frequencies | percentages |
|--------|-------------|-------------|
| Female | 39 | 60 |
| Male | 27 | 40 |

Table 3 shows that the pyelonephritis was diagnosed more in female group than the male group of patients.

Table 4. Co morbidity of the diseases.

| Comorbidity | Frequencies | Percentages |
|-------------------------|-------------|-------------|
| diabetes | 22 | 33.33 |
| Cardiovascular diseases | 20 | 30 |
| Liver diseases | 5 | 7.57 |

Table 4 shows that the comorbidities found in patients diagnosed with pyelonephritis. Diabetes was more dominant as comorbidity in pyelonephritis cases followed by cardiovascular diseases.

Table 5. Causative organisms involved.

| Microorganisms | Frequencies | percentages |
|-------------------------|-------------|-------------|
| Escherichia coli | 49 | 74.24 |
| pseudomonas aeroginos | 7 | 10.60 |
| Acinetobacter baumannii | 2 | 3.03 |
| Klebsiella SPP | 7 | 10.60 |
| Staphylococcus aureus | 1 | 1.51 |

Above table shows the list of microorganisms identified as causative agent in pyelonephritis cases, in which Escherichia coli was more abundant as causative agent followed by pseudomonas aeruginosa.

Table 6. Duration of treatment of antibiotics.

| | Duration of treatment |
|---------------|-----------------------|
| Mean | 7.21 |
| Median | 7.00 |
| Std.deviation | 2.297 |
| Range | 8 |
| minimum | 4 |
| maximum | 12 |

Above table 6 shows that mean duration of treatment with antibiotic was 7.21 and median duration of treatment was 7 days and minimum duration of treatment was 4 days and the maximum duration of treatment was 12 days.

Table 7. Antibiotics prescribed.

| Antibiotics treatment option | No of patients n=66 | percentages |
|---|------------------------|-------------|
| ciprofloxacin 200mg IV+levofloxacin500mgIVstandard; | 4 | 6.06 |
| ciprofloxacin200mgIV+ ofloxacin200mgIV | 3 | 4.54 |
| ciprofloxacin200mgIV+ciprofloxacin400mgoral | 34 | 51.52 |
| Ceftriaxone1gmIV +ciprofloxacin200mgIV | 12 | 18.18 |
| Ceftriaxone500mgIV+ ciprofloxacin200mgIV | 4 | 6.06 |
| Ceftriaxone500mgIV+ciprofloxacin400mgoral | 5 | 7.57 |
| ciprofloxacin200mgIV +Ciprofloxacin400mgoral | 4 | 6.06 |

Note: IV =Intra venous, mg=milligram.

Above table shows that the most commonly prescribed fluoroquinolone in our study for the treatment of pyelonephritis was ciprofloxacin. Number of patients treated with ciprofloxacin were 34 and percentage of the patients were 51.52%, followed by ceftriaxone 1gm intravenous switch to ciprofloxacin 200mg intravenous infusion.

Table 8. Cost analysis of antibiotics.

| Antibiotics treatment option | Average Antibiotics cost per prescription In Pak rupies (US \$) |
|---|--|
| ciprofloxacin200mg IV + levofloxacin500mgIV | 8650Rs (\$71.150) |
| ciprofloxacin200mgIV+ ofloxacin200mgIV | 6854Rs (\$56.377) |
| ciprofloxacin200mgIV+ciprofloxacin400mgoral | 2621Rs (\$21.55) |
| Ceftriaxone1gmIV +ciprofloxacin200mgIV | 2690Rs (\$22.126) |
| Ceftriaxone500mgIV+ ciprofloxacin200mgIV | 2520Rs (\$20.728) |
| Ceftriaxone500mgIV + ciprofloxacin400mgoral | 1008Rs (\$8.291) |
| ciprofloxacin200mgIV + Ciprofloxacin400mgoral | 2218Rs (\$18.244) |

Above table shows the cost analysis of antibiotic prescribed for the treatment of pyelonephritis. Average highest Cost of antibiotic combination of ciprofloxacin/levofloxacin was PKRs 8650 (\$71.150) and the average least antibiotic cost for treating pyelonephritis was PKRs1008 (\$8.291) with the combination of ceftriaxone 500gm/ciprofloxacin400mg oral.

4. Discussion

Muraraiah and co-workers conducted a study regarding prescribing pattern in complicated urinary tract infections at a tertiary care hospital. The study comprised of total eighty-four patients. Forty-nine were males and thirty five were females. The individuals having age between 16 to 32 years were included. The average age was found to be 48.4 years. 38 individuals fell in age group of 16-40 years, 27 individuals in 41 to 60 years and 19 individuals were having age greater than 60 years [10]. We screened 400 files of urinary tract infection and selected 66 cases of pyelonephritis in which at least one fluoroquinolone was prescribed to analyze the prescribing trend and prescribing cost of fluoroquinolones for treating pyelonephritis admitted in a private hospital (Table 1). The patients having age range from 19 years to 70 years and above were included. Our analysis showed that the age group of 19-40 years having 16.67% of individuals diagnosed with pyelonephritis, age

group of 41-60 years contained 39.39% of patients diagnosed with pyelonephritis, age group of 61-71 years and above 72 years contained 27.27% and 16.66% of patients respectively. The age group of 41-60 years consisted highest number of patients in comparison to other age groups (Table 2). Our study observed that prevalence of pyelonephritis was higher in female group (60%) than the male group (40%) (Table 3) which was similar from the finding conducted by Dhodi and co-workers in which prevalence of Urinary tract infection was higher in females (60%) in comparison to males (41%) [3]. The study conducted by Sokhal and co-workers on Emphysematous pyelonephritis showed that there were 85% of patients having diabetes, 32% of patients having urolithiasis, 28% of patients having hypertension as comorbidities [14]. Our study also showed that diabetes mellitus (33.33%) was most dominant comorbidity. 30% of patients were diagnosed with cardiovascular diseases while 7.57% of patients were having liver diseases (Table 4). Mahesh et al conducted a study regarding complicated urinary tract infection in a tertiary care center in South India and found that *E. coli* (65.7%) was marked pathogen causing complicated UTI. They also stated that their finding was similar to worldly assessments. In many of the studies *E. coli* was reported to be most significant microbe causing complicated urinary tract infection. Some of the studies reported that *E. coli*, *Proteus mirabilis* and *Pseudomonas aeruginosa* are the most common micro-organisms causing urinary tract infections [8]. Our findings also reported *Escherichia coli* (74.24%) as dominant pathogen causing pyelonephritis followed by *pseudomonas aeruginos* (10.60%) and *Klebsiella SPP* (10.60%) (Table 5). We found that duration of treatment with antibiotic was 7.21 and median duration of treatment was 7 days and minimum duration of treatment was 4 days and the maximum duration of treatment was 12 days (Table 6). Dhodi et al evaluated prescribing pattern of antibiotics among patients of urinary tract infection with preexisting renal disorders in a tertiary care hospital and found that Quinolones like ciprofloxacin and levofloxacin were the most frequently administered first line medications followed by penicillin as well as cephalosporin. Ciprofloxacin was highly prescribed fluoroquinolones followed by norfloxacin and levofloxacin. Ofloxacin was least preferred. Second line antibiotic were administered to the patients who did not respond with first line antibiotic. Cefoperazone and linezolid combination was most frequently prescribed second line antibiotic [3]. Our findings revealed that most commonly prescribed fluoroquinolone in our study for the treatment of pyelonephritis was ciprofloxacin. Thirty four (34) patients (51.52%) initiated with ciprofloxacin 200 mg IV switched to ciprofloxacin 400 mg oral. Twelve (12) patients (18.18%) initiated with ceftiraxone 1gm IV switched to ciprofloxacin 200 mg IV, Five (5) patients (7.57%) initiated with ceftiraxone 500mg IV switched to ciprofloxacin 400 mg oral. Four (4) number of patients (6.06%) initiated with ceftiraxone 500 mg IV switched to ciprofloxacin 200mg IV, four (4) patients (6.06%) initiated with ciprofloxacin 200mg IV switched to ciprofloxacin 400mg oral. McKinnel

and co-workers studied regarding recommendation and cost analyzation of Nitrofurantoin in uncomplicated urinary tract infections. They found nitrofurantoin to be cost-minimizing when the prevalence of fluoroquinolone-resistant *E coli* in the community was 12%. When compared with Trimethoprim-sulfamethoxazole, nitrofurantoin was found to be cost-minimizing when *E coli* resistance to Trimethoprim-sulfamethoxazole was 17% [9]. In our study Table-8 showed cost analysis of antibiotic prescribed for the treatment of pyelonephritis. Our findings revealed that antibiotic ciprofloxacin 200mg IV in combination with levofloxacin 500 mg IV per prescription was having average highest cost (PKRs.8650) (\$71.150) followed by ciprofloxacin 200mg IV in combination with ofloxacin 200mg IV (PKRs.6854) (\$56.377). The average least antibiotic cost for treating pyelonephritis was PKRs.1008) (\$8.291). It was the cost of antibiotic combination of ceftiraxone 500gm and ciprofloxacin 400 mg oral.

5. Conclusion

This study highlights the prescribing pattern of fluoroquinolones antibiotics in urinary tract infection (pyelonephritis) patients and also calculates the medication prescription cost of fluoroquinolones antibiotics. It also gives us some idea about common organisms responsible for UTI, along with their drug sensitivity. Therapeutic option for UTI is at first empirical as there is delay in getting culture report. Third generation cephalosporin's are the most commonly used as it covers both Gram-positive and Gram-negative organisms. But as per observation, the most common causative organisms were *E. coli* and *Pseudomonas aeruginosa*. Most commonly prescribed fluoroquinolone was ciprofloxacin and the least commonly prescribed fluoroquinolone was ofloxacin. Therefore, due to the severity of the cases, most cases start with injections. It is also observed that most expensive combination of antibiotic was ciprofloxacin with levofloxacin and the least expensive combination of antibiotic was ceftiraxone with ciprofloxacin oral this is because of less severity of the diseases. The choice of antimicrobial drugs should be individualized based on patient compliance, adverse effects, availability and costing factors, along with sensitivity pattern in the locality. Whenever culture report is available, therapy should be according to the sensitivity report. Periodic review of antibiotic sensitivity should be done to modify the empirical treatment of UTI.

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