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Original Article

CLINICAL ASSESSMENT OF ANTIBIOTICS USED IN CHRONIC KIDNEY DISEASE: A LONGITUDINAL OBSERVATIONAL STUDY

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ABSTRACT

Objective: The study was conducted to clinically evaluate the safety and efficacy of antibiotic drug consumption based on laboratory data, specifically White Blood Cells(WBC) and Glomerular Filtration Rate (GFR) before and after antibiotic use in patients with chronic kidney disease.

Methods: This retro-prospective longitudinal study was conducted on 115 patients with Chronic Kidney Disease (CKD) based on 6 mo of data at a tertiary care teaching institute, Geetanjali Medical College and Hospital, in Udaipur, Rajasthan. Inclusion criteria were all the patients who were admitted in the nephrology department and were above 18 y, who were receiving antibiotics, and Creatine Clearance (CrCl) was ≤ 60 ml/min were included into this study. Exclusion criteria patients with renal replacement and lacking information of laboratory data (WBC, CrCl) and those who were below the age of 18 were excluded from the study. The data were analysed using descriptive analysis.

Results: The mean age of the CKD patients was 50.10 (standard deviation=17.47) y. Males were found in greater numbers than that of females with 66 (58%) and 49(42%) respectively. Patients admitted with stage 5 CKD (66%) were greater than the patients with stage 4 CKD. 10 different types of antibiotics were provided to CKD patients, of which seven had irrational doses. Piptaz, Meropenem, and Teicoplanin have the highest irrational doses incidence.

Conclusion: Patients with CKD Stages 4 and 5 were given systemic antibiotics at unreasonable dosages, most frequently in the forms of piptaz, aztreonam, and meropenem injections. The incidence of irrational antibiotic dosages provided to the CKD patients was still high.

Keywords: Chronic kidney disease, Creatine clearance, Antibiotics, Clinical assessment

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INTRODUCTION

The existence of anomalies in the structure or function of the kidneys or a decline in the Glomerular Filtration Rate (GFR) for three months or more is referred to as Chronic Kidney Disease (CKD) [1].

Patients with severe CKD are more prone to experience problems and have a higher chance of progressing to end-stage renal disease that requires renal replacement therapy. Furthermore, early intervention will typically decrease the progression of CKD and reduce its catastrophic consequences. The National Kidney Foundation created criteria as part of its Kidney Disease Outcomes Quality Initiative (NKF KDOQITM) to help with the assessment of CKD severity and to help patients with the process of being stratified [2]. Phase 1: normal eGFR ≥ 90 ml/min per 1.73 m2 plus ongoing albuminuria; Phase 2: eGFR ranging from 60 to 89 ml/min per 1.73 m2; Phase 3: eGFR ranging from 30 to 59 ml/min per 1.73 m2; Phase 4: eGFR ranging from 15 to 29 ml/min per 1.73 m2; Phase 5: eGFR of less than 15 ml/min per 1.73 m2 or end-stage renal disease Due to the high prevalence of glomerulonephritis and interstitial nephritis in developing countries, people with chronic kidney disease still have a high infection rate.

[3]. The US (13.1%), Japan (12.9–15.1%), Australia (11.2%), Norway (10%), Taiwan (9.8–11.9%), China (3.2–11.3%), Korea (7.2–13.7%), Thailand (8.45–16.3%) are the countries where the prevalence of CKD has increased most dramatically. West Malaysia has a 9.07% CKD prevalence [4, 5]. Additionally, a study found that the death rate of patients receiving haemodialysis was roughly 100–300 times higher than that of individuals not receiving the treatment [6]. The existence of CKD and associated complications during treatment are still unsettled issues. Patients with CKD typically have co-morbidities that have contributed to an illness that causes an infection that lowers renal function. Compared to non-CKD patients, hospitalized CKD patients had greater rates of pneumonia and sepsis [7]. Thus, strategies to foresee and address these issues, such as the use of antibiotics, must always be pursued in order to prevent more unfavorable clinical outcomes [8].

One important family of medications that physicians give to treat a variety of bacterial illnesses is called antimicrobials [9].

The kidneys remove the bulk of antibiotics. It is not recommended to use certain of the following with people with CKD and require dose modifications [10]. Antibiotics for infection in CKD patients, however, should not be prescribed without first adjusting the dosage. This could lead to the buildup of the parent chemicals and their metabolites in the body and harmful effects on the kidneys and other organs [11-13]. Patients with renal problems frequently receive inappropriate doses, which can result in negative medication reactions and inadequate therapeutic improvement [14, 15]. The ultimate negative outcome is death. Patients with CKD have their doses adjusted according to their GFR and creatinine clearance [1]. Therefore, clinical pharmacists should constantly do medication reviews as a crucial step in the management of chronic kidney disease (CKD) [16].

There are now a lot of papers on drugs provided to individuals with chronic kidney disease. But in the study on evaluating antibiotics used in clinical settings, there is still little association with renal function. Consequently, the current study was conducted to clinically evaluate the safety and efficacy of antibiotic drug consumption based on laboratory data, specifically WBC and GFR, before and after antibiotic use in patients with chronic kidney disease [7].

MATERIALS AND METHODS

The subject enrolled in the study was patients who were admitted to the nephrology department at a teaching institute, Geetanjali Medical College and Hospital (GMCH), Udaipur, with CKD. We

assessed the data by clinical pharmacist workup of therapy monitoring and daily follow-up of patients.

Study design

This retro-prospective longitudinal study was conducted on 200 patients with CKD based on 6-month data at a tertiary care teaching institute Geetanjali Medical College and Hospital in Udaipur, Rajasthan. The study was conducted to study the clinical assessment of antibiotics in CKD patients by evaluating serum creatine followed by CrCl and WBC, of every patient before and after administration of antibiotics.

All patients admitted to the nephrology department who were above 18 y old were receiving antibiotics and CrCl was ≤ 60 ml/min were included in this study. Patients with renal replacement and lacking information on laboratory data (WBC, CrCl) and those who were below the age of 18 were excluded from the study.

Data collection

The GMCH, dean permitted us to collect the data from medical records. Data was collected using a predesigned patient data collection form from the medical record room of the hospital and during ward rounds. Data gathered were demographic data (age, gender, length of stay, date of admission), body weight, past medical history, presenting complaints, antibiotics used during hospitalization, laboratory data (WBC, CrCl) before and after administration of antibiotics, and outcome. CrCl was calculated using the Cockcroft-Gault equation by the National Kidney Foundation.

C_{cr}:

C_{cr}:

$$(140 - \text{age} * \text{weight}) \div (72 * \text{Scr}) * 0.85 \text{ (if female)}$$

Whereas,

C_{cr}: Creatine Clearance (ml/min)

Scr: Serum creatine (mg/dl)

Analysis of Data: to determine the antibiotic utilized for the management of infections, all antibiotics and their doses administered were entered into Microsoft Excel, and mean age, gender of the patients, and correlation of laboratory data were analyze dusing the descriptive analysis

RESULTS

The total number of admissions of CKD patients during the study period was 200 out of which 115 were included who fulfilled the inclusion criteria. The mean age of the CKD patients was found to be 50.10, with a standard deviation of 17.47. In our study, males were found in greater numbers than females, with 66 (58%) and 49(42%), respectively.

The number of patients admitted with stage 5 CKD was greater than the patients with stage 4 CKD, i. e., 76 (66%) patients with stage 5 and 39 (34%) patients with stage 4.

The mean length of stay was 8.68 days, with the mean LOS for stage 5 CKD patients being 8.71 and stage 4 being 9.11 days. Patients with stage 4 CKD show a higher length of stay in the nephrology ward.

In this study, we found various chief diagnoses of which four occurred most commonly; they were CAP (community-acquired pneumonia) which was seen in 35 patients (30 %), followed by Urosepsis in28 patients (24 %), Diabetic ketoacidosis in 10 patients (8.6 %) and 5 patients (4. 3%) with Anemia. Comorbidity was present in most CKD patients.

In this investigation, Co-morbidities were identified as follows, Diabetes mellitus, Hypertension, CAP, urosepsis, renal stone disease, chronic cardiac failure, obstructive uropathy, and dementia shown in fig. 1.

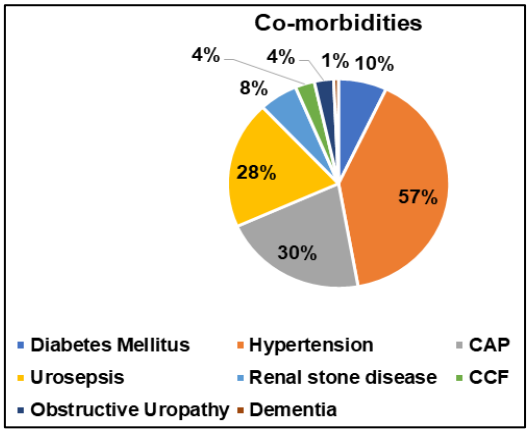

Fig. 1: Distribution of comorbidities in CKD patients

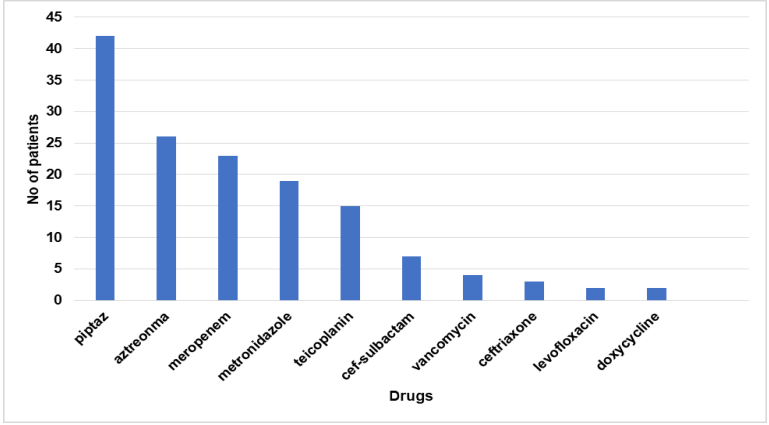

Fig. 2: Total number of antibiotics used for the 115 patients with CKD

Fig. 2 shows the total number of antibiotics used for the 115 patients with CKD. This study shows that there were 10 different types of antibiotics with different doses and different dosing units were administered to the patients. The top medications used in decreasing order to treat infections in individuals with CKD were Piperacillin Tazobactam, Aztreonam, Meropenem, Metronidazole, Teicoplanin, Cefo-Sulbactam, Vancomycin, Ceftriaxone, Levofloxacin and Doxycycline.

Irrational dosing of antibiotics prescribed to CKD patients is listed in table 1. Based on the frequency analysis it was found that 60 opportunities of irrational dosing occurred in the study period amongst 115 patients.

Clinical Assessment of Antibiotics used in CKD patients was performed by analysis of CrCl and WBC by comparing before and after administration of antibiotics. Table 2 shows the result of the clinical assessment of antibiotics used in CKD patients.

Table 1: Overall irrational dosing of administered antibiotics

Antibiotics	Occurrence of irrational dose	Dose administered	Recommended dose according to CrCl
Piperacillin Tazobactam	24	4.5 gm IV QID	CrCl 30-59 ml/min: 3.375 gm IV TDS CrCl<20 ml/min: 2.25 gm IV TDS
Meropenem	17	1 gm IV TDS	CrCl 15-29 ml/min: 5200 mg IV BD CrCl<10 ml/min: 500 mg IV OD
Teicoplanin	12	200 mg IV BD	CrCl 15-29 ml/min: 50% usual dose
Aztreonam	4	2 gm IV TDS	CrCl 15-29 ml/min: 50% usual dose CrCl<10 ml/min: 25% usual dose
Vancomycin	1	1 gm IV BD	CrCl 15-29 ml/min: 1.9 mg/kg/24 h
Ceftriaxone	1	2 gm IV BD	CrCl 15-29 ml/min: 2 gm per day
Levofloxacin	1	750 mg IV OD	CrCl 15-29 ml/min: 250 mg IV OD

Table 2: Clinical assessment of antibiotics used in CKD patients

Stage of CKD	CrCl pre	CrCl post	Outcome	WBC pre	WBC post	Outcome
Stage 4	19.904±3.3	21.2±3.8	Improved	12.91±10.3	13.03±14.8	Worse
Stage 5	8.77±2.94	16.48±11.42	improved	10.24±6.05	8.83±3.92	Improved

Data is expressed in mean±SD.

DISCUSSION

Rational antibiotics provision is important to optimize the treatment outcomes. Assessment of antibiotics provided to CKD patients and analysis of their rationality are the key points that should always be performed by clinical pharmacists to improve the treatment and to achieve optimal outcomes.

According to this study, the top ten antibiotics used to treat individuals with CKD were piptaz, aztreonam, meropenem, metronidazole, teicoplanin, cefo-sulbactam, vancomycin, ceftriaxone, levofloxacin, doxycycline. These variations may have been caused by a variety of factors, such as the patients' diverse range of comorbidities, the suitability of their treatments, and the CKD patients' varying degrees of infection severity [17, 18]. Patients with increased co-morbidity had longer lengths of stay in the hospital (LOS). Another study found that 23% of patients with CKD also had diabetes [19], and over 805 of these patients also had hypertension [20]. As with the other studies, the most common comorbidity among CKD patients in this was also diabetes mellitus, followed by hypertension. Polypharmacy continues to be the standard procedure in the clinical setting since CKD patients have concomitant illnesses [21].

Injection metronidazole did not require dose adjustment in CKD patients because it is not considered necessary as the elimination half-life is not significantly altered. Further doxycycline is 23% renal excreted. Hence prescription of this drug does not require dose adjustment in mild to moderate renal impairment.

There are currently a few obstacles to the successful care of CKD at GMCH, such as the empirical approach used in the selection of antibiotics to treat infections in CKD patients. First of all, despite the fact that culture and sensitivity tests are conducted on the patient's samples, doctors are unable to quickly test for the timely selection of antibiotics because of the extended time required for these tests to complete (about one week). Second, haemodialysis and rapid treatment are necessary for infected patients in order to ensure their safety [22]. Finally, the optimal selection of antibiotics is nearly impossible, even if GMCH reviews the inhibitory power of the supplied antibiotics every six months based on culture and sensitivity test results. Data show that, over time, bacterial resistance to antimicrobial treatments spreads quickly [23].

In an effort to maximize results, the Pharmacy and Therapeutic Committee (PTC) of GMCH periodically reviews and updates the formulary pertaining to the use of medications, including antibiotics, based on scientific clinical evidence. The WHO states that the action programs' subjects of antibiotic use and infection control might serve as the main focal points for PTC efforts [24].

LIMITATIONS

There are some limitations of the study as the weight of the patient is essential for the eGFR, but in critical ill patients, it is quite difficult to carry out the weight. Antibiotics used in community pharmacies have no track; there should be a proper channel with more focused and elaborative studies to assess the utilization of antibiotics and assess irrational uses of antibiotics.

CONCLUSION

Patients with Stages 4 and 5 of CKD were treated with different types of antibiotics. The three most frequently given were meropenem injection, aztreonam, and piptaz. At Geetanjali Medical College and Hospital, patients with CKD Stages 4 and 5 were given systemic antibiotics at unreasonable dosages most frequently in the forms of piptaz, aztreonam, and meropenem injections. In GMCH, the incidence of unreasonable antibiotics doses remained elevated. Despite its limitations, the study's findings should be carefully considered by healthcare practitioners when deciding whether to provide patients with CKD antibiotics in an effort to improve outcomes. To prevent drug toxicity in individuals with CKD, it is crucial to comprehend and apply dose adjustments.

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AUTHORS CONTRIBUTIONS

Together, DS, RC, and HS worked to ensure the depth and coherence of the manuscript. All authors reviewed and approved the

manuscript. DS and RC played a crucial role, and HS helped as a guide in developing and implementing the study, conducting an exhaustive literature review, and shaping the methodological framework. SR served as a guide and supervisor, providing invaluable insights, guidance, and oversight throughout the entire process.

CONFLICT OF INTERESTS

Declared none

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