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EVALUATION OF ANTIBIOTIC PRESCRIPTION PATTERN USING WHO AWaRe CLASSIFICATION AND ANTIBIOTICS DOSAGE ADJUSTMENT IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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ABSTRACT

Irrational antibiotic therapy cause bacterial resistance, increase side effects of drugs, increase morbidity, increase total hospital costs. The Access, Watch, Reserve (AWaRe) classification of antibiotics formulated by World Health Organisation with the goals of better accessibility and clinical outcomes, a decreased probability of antimicrobial resistance, safeguarding the effectiveness of last-resort antibiotics and to evaluate the rational use of antibiotics. In this study a retrospective observational analysis was conducted over a period of six months in a tertiary care hospital. The objectives of the study was to evaluate the dosage adjustments of antibiotics in chronic kidney disease using Cockcroft – Gault formula and to examine prescription pattern of antibiotics using AWaRe classification of WHO. A total of 100 patient case records satisfying the inclusion criteria were analysed. High consumption of watch-group antibiotics was observed in the study. Ceftriaxone+ sulbactam was the most commonly prescribed antibiotic followed by cefixime. There were 13 irrational antibiotics prescribed in the study population, which are Inj. Piperacillin + Tazobactam , Tab. Cefixime, Inj. Imipenem, Inj. Ceftriaxone etc. Incidence of irrational dosage promotes the need for individualized dosage regimen to patients with Chronic Kidney Disease. Understanding and implementation of dosage adjustment is important to avoid drug toxicity.

KEY WORDS: Chronic Kidney Disease, AWaRe classification, Dosage adjustment, Antibiotics, World Health Organisation

INTRODUCTION

Chronic Kidney Disease (CKD) is defined by a reduction in the glomerular filtration rate (GFR) and/or urinary abnormalities or structural abnormalities of the renal tract. [1]

CKD affects renal drug elimination and other pharmacokinetic processes like absorption, drug distribution, metabolism. Incidence of infection among patients with chronic kidney disease (CKD) remains high in developing countries as a consequence of the high incidence of glomerulonephritis and interstitial nephritis.

However, provision of antibiotics to treat infection in patients with CKD without proper dose adjustment could result in accumulation of the parent compounds and their metabolites in the body and toxic effects on organs, including kidneys. Furthermore, progression of kidney damage could also be induced by the nephrotoxicity of few antibiotics. The ultimate negative outcome is death. Therefore, appropriate dosing of antibiotics therapy for patients with CKD is crucial to avoid adverse drug reaction, to prevent additional renal injury, and to optimize clinical outcomes. Dose rationality analysis of the systemic antibiotics provided to the CKD patients was undertaken based on the magnitude of creatinine clearance (ClCr) or glomerular filtration rate and should be calculated using online or electronic calculators.

$$\text{ClCr (ml/minutes)} = ([140-\text{age}]\ \text{body weight})/72 \times \text{SCr (In male)}$$

$$\text{ClCr (ml/minutes)} = ([140-\text{age}]\ \text{body weight})/72 \times \text{SCr} \times 0.85 \text{ (if female)}$$

In which, SCr: serum creatinine concentration of the patient with CKD

In 2017, World Health Organisation (WHO) commissioned comprehensive reviews on antibiotic use for specific infection in order to update the Essential Medicine List. The expert committee then formulated the Access, Watch, Reserve (AWaRe) classification of antibiotics with the goals of better accessibility and clinical outcomes, a decreased probability of antimicrobial resistance, and safeguarding the effectiveness of last-resort antibiotics. The WHO AWaRe classification (2019) was used to evaluate the rational use of antibiotics.

ACCESS: This group includes antibiotics that have activity against a wide range of commonly encountered susceptible pathogens while also showing lower resistance potential than antibiotics in the other groups.

WATCH: This group includes antibiotic classes that have higher resistance potential and includes most of the highest priority agents among the Critically Important Antimicrobials for Human Medicine These medicines should be prioritized as key targets of stewardship programs and monitoring.

RESERVE: This group includes antibiotics and antibiotic classes that should be reserved for treatment of confirmed or suspected infections due to multi-drug-resistant organisms.

MATERIALS AND METHOD

A retrospective observational study was conducted over a period of six months in a tertiary care hospital. A total of 100 patient case records satisfying the inclusion criteria were identified from medical record department.All the inpatients above 18 years in both the gender diagnosed with chronic kidney disease stage 3 to 5 were included and excluded pregnant and lactating women from the study.Case records were retrospectively reviewed for the demographic data, clinical presentation, investigational management and outcomes. Data analysis were conducted using Microsoft Excel 2010, SPSS.

RESULTS AND DISCUSSION

Distribution Of Antibiotics In The Study Population

Sl. No	Antibiotics	Antibiotics Prescribed (n=134)	Relative Frequency(%)
1	Cephalosporin	29	21.64
2	Cephalosporin + Beta lactamase inhibitors	32	23.88
3	Penicillin + Beta lactamase inhibitors	24	17.91
4	Carbapenem	20	14.92
5	Macrolide antibiotics	12	8.95
6	Fluroquinolones	8	5.97
7	Glycopeptide antibiotics	1	0.74
8	Oxazolidinones	5	3.73
9	Lincosamide antibiotics	2	1.49
10	Nitrofuran derivatives	1	0.74
11	Rifaximin	2	1.49
12	Nitroimidazole	4	2.98

Table no:1

Distribution of Antibiotics In The Study Population

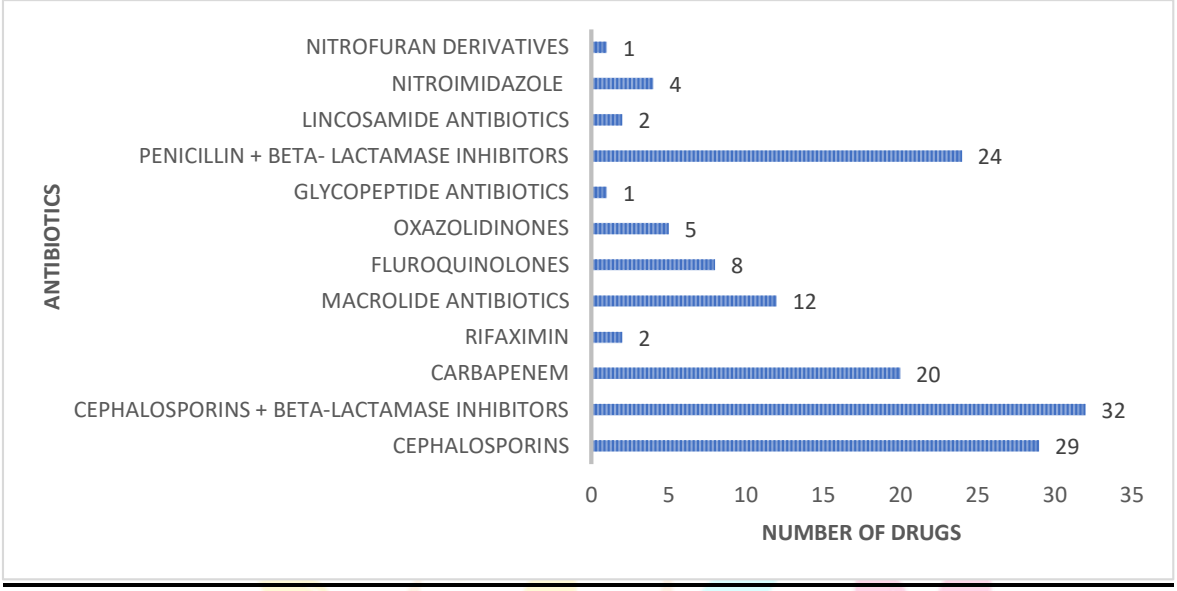

Figure no: 1

The above table revealed that majority of the patients n=32 (23.88%) were treated with cephalosporins + beta lactam antibiotics, followed by cephalosporins n=29 (21.64%). This is because cephalosporins are beta lactam antimicrobials used to manage a wide range of infections from gram positive and gram negative bacteria. This is similar to the study conducted by *Azizah,et al*, in which the most utilized antibiotics were cephalosporins (690) followed by ciprofloxacin (255).[6]

AWaRe CLASSIFICATION OF PRESCRIBED ANTIBIOTICS (n=26)

ACCESS	WATCH	RESERVE
Amoxicillin/ Clavulanic acid n=8 (5.97%)	Azithromycin n=9 (6.71%)	Linezolid n=5 (3.735%)
Clindamycin n=2 (1.49%)	Cefixime n=15 (11.19%)	Faropenem n=10 (.46%)
Nitrofurantoin n=1 (0.74%)	Cefepime n= 2 (1.49%)	Ceftazidime n=2 (1.49%)
Metronidazole n=4 (2.98%)	Cefopodoxime Proxetil n=1, (0.74%)	Imipenem + cilastatin n=4 (2.98%)
	Cefotaxime n=3 (2.23%)	
	Ceftriaxone n=12 (8.95%)	
	Cefuroxime n=1 (0.74%)	

		Clarithromycin n=1 (0.74%)	
		Norfloxacin n=1 (0.74%)	
		Ofloxacin n=2 (1.49%)	
		Piperacillin + Tazobactam n=16 (11.94%)	
		Rifaximin n=2 (1.49%)	
		Cefoperazone + Sulbactam n=15 (11.19%)	
		Levofloxacin n=3 (2.23%)	
		Vancomycin n= 1 (0.74%)	
		Ciprofloxacin n=3 (2.23%)	
		Cefuroxime axetil n=1 (0.74%)	
		Meropenem n=10 (7.46%)	
TOTAL	4	18	4

Table no: 2

The table indicated that majority of the antibiotics prescribed were in the Watch class followed by Access and Reserve class. Of 26 antibiotics prescribed, 4 were Access, 18 were Watch, and 4 were Reserve. High consumption of watch-group antibiotics was observed in the study, which is similar to the study conducted by *Vinodkumar Mugada et al*, where 4 antibiotics was prescribed from the Access category and 5 antibiotics from the Watch category. [7]

IRRATIONAL DOSING OF THE ADMINISTERED ANTIBIOTICS IN THE STUDY POPULATION

Sl No	Drugs	OID	Patient' s Creatinine Clearance (ml/min) Range	Dose Administered	Recommended Dose
1	Inj. Piperacillin+Tazobactum	1	12	4.5gm IV 1-1-1	Crcl- <20 ml/min - Max- 4.5g Every 12 Hours Or 2.25g Every 6 Hours & Max 0.5g Of Sulbactam
2	Tab. Cefixime	6	38 17 18.54 33 14.7 10.78	200mg P/O 1-0-1	Crcl >20 To <60 ml/min – 300mg OD. Crcl ≤ 20 ml/min - 200mg OD.
3	Inj. Imipenem	2	21 11.75	500mg IV 1-1-1 2g IV 1-1-1	Crcl ≥ 15 To < 30 ml/min -250mg Every 8 Hours / 500mg Every 12 Hours. Crcl ≤ 15 ml/min - Don't Administer Imipenem/ Cilastatin Until Haemodialysis Instituted Within 48 Hours.
4	Inj. Ceftriaxone	2	8.62 14.37	1g IV 1-0-1	Adult – 1g IV Q24h. Patient >80 Kg – 2g Q24h

5	Cap. Amoxicillin +Clavulanic Acid	1	9.36	625mg P/O 1-0-1	Crcl <10 ml/min: 500/125mg P/O Q24hr.
6	Inj. Meropenem	4	14 16 9.09 24.90	1g IV 1-0-1 500mg IV 1-0-1 500mg IV 1-1-1	Crcl-10 to 25 ml/min : 500mg Every 12 Hrs. Crcl<10 ml/min – 500mg Every 24 Hrs.
7.	Tab. Ciprofloxacin	2	11 12	500mg P/O 1-0-1	Crcl <30 ml/min - 500mg Every 24hrs.
8.	Tab. Ofloxacin	1	22.50	200mg P/O 1-0-1	Crcl- 20 :50 ml/min - Administer Half The Usual Recommended Dose Every 24hrs (200mg Every 12 Hours For 3 Days)
9.	Tab. Nitrofurantoin	1	24	100mg P/O 0-0-1	Crcl <30 ml/min –Avoid Use.
10.	Tab. Norfloxacin	1	9	400mg P/O 1-0-1	Crcl≤30ml/min- 400mg Once Daily.
11.	Inj. Cefepime	2	41 54	1g IV 1-0-1	Crcl-30 – 60 ml/min : 1g Every 24hrs.
12.	Inj. Ceftazidime	1	10	1g IV 1-0-0	Crcl ≤ 15 ml/min – 500mg Every 24 Hrs.
13.	Tab. Cefpodoxime Proxetil	1	14.06	200mg 1-0-1	Crcl <30 ml/min Administer Usual Recommended Dose Every 24 Hours.

Table no: 3

*OID- occurrence of irrational drug

There are 13 irrational drugs that were prescribed in the study population, which are Inj. Piperacillin + Tazobactam, Tab. Cefixime, Inj. Imipenem, Inj. Ceftriaxone, Cap. Amoxicillin + Clavulanic acid, Inj.Meropenem, Tab.Ciprofloxacin, Tab.Ofloxacin, Tab.Nitrofurantoin, Tab.Norfloxacin, Inj. Cefepime, Inj. Ceftazidime, Tab. Cefpodoxime proxetil which is similar to the study conducted by *Azizah, Syeid Sulaiman, Shafie asrul Akmal* (2015) , where Inj.Ceftriaxone, Tab. Ciprofloxacin, Inj. Ceftazidime, Cap. Cefadroxil , Cap. Amoxicillin are the antibiotics prescribed irrationally .[6]

CONCLUSION

In our study we evaluated 100 patients with CKD. Around 134 antibiotics are prescribed in this study population, among them there were 13 antibiotics prescribed irrationally. Out of which the most irrationally prescribed antibiotics are Tab. Cefixime (OID-6) followed by Inj. Meropenem (OID-4). High consumption of Watch-group antibiotics followed by Access and Reserve class was observed in the study.Appropriate dosing of antibiotics therapy for patients with CKD is crucial to avoid adverse drug reaction, to prevent additional renal injury, and to optimize clinical outcomes. Hence, medication reviews in the management of CKD is the key point that should always be performed by clinical pharmacists through a structured examination of patient's medications including evaluation and analysis of antibiotic dosing to avoid adverse drug reaction, to prevent additional renal injury, to improve CKD management and to achieve optimal outcomes. Antibiotic resistance possesses a significant threat to global public health, economic growth and global economic stability. The major contributing factor to this resistance is inappropriate or irrational use of antibiotics. Our results shows that an active intervention by a clinical pharmacist in process of antibiotic prescription among patients with CKD will improve the rational use of antibiotics in patients.

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COMPETING INTEREST

We declare that there was no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

ETHICAL APPROVAL

Approval from the Ethical Committee of SH Medical Centre Hospital, Kottayam was obtained.

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