Prospective Study on Prevalence of Comorbidities and Drug Utilization in Chronic Kidney Disease Patients in Tertiary Care Hospitals of Khammam Region

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Abstract- The aim of the study was to describe treatment options for CKD patients to slow the progression of renal failure and potentially reduce morbidity and mortality. Highlight common comorbid conditions, such as cardiovascular disease and diabetes, and stress the importance of managing these conditions to potentially reduce morbidity and mortality among CKD patients. The study was a prospective observational study conducted over a 1-year period from January 2020 to December 2020. The prevalence of different comorbidities and drugs prescribed under the system was investigated. Among the 301 patients, the most prevalent comorbidities were cardiovascular disease (146) and diabetes mellitus (100). Drugs prescribed for various comorbidities and chronic kidney disease have been reported and classified according to the ATC system. Calcium channel blockers (79), alpha and beta blockers (62), diuretics (109), antihistamines (68), HMG-CoA reductase inhibitors (77), protons (190), antibiotics (116), have been widely used in our studio. This study demonstrates the variability of drug use in CKD patients. Studies on drug use on a regular basis provide a framework for healthcare professionals and help develop management strategies. However, the correct choice of drugs and the appropriate doses will reduce the incidence of nephrotoxicity and produce better clinical results. Infection management and antibiotic prescribing in CKD are critical to improving the quality of life of CKD patients.

Keywords: Co morbidities, chronic kidney disease, Drug utilization, Hypertension, Diabetes,

I. INTRODUCTION

Globally, CKD is a major threat due to an increasing incidence, a long hospital stay, a high cost of treatment, and a poor prognosis. CKD is a series of heterogeneous disorders that also affect renal structure and function [1]. The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) defines CKD as kidney damage and / or a reduced glomerular filtration rate of less than 60 mL / min / 1.73 m2 for three months or more [2]. Hypertension (HTN) has been reported in the majority of CKD patients (stages III-V) [3,4]. Impaired kidney function causes a number of complications including metabolic abnormalities, endocrine complications, and an increased risk of cardiovascular disease. These complications, if not treated properly, can lead to an increase in the mortality rate [5].

Due to the various comorbid conditions and complications, doctors have to use multiple drugs in the management of CKD, which, conversely, results in a drug interaction and suboptimal action. Patients with CKD are more susceptible to infections and are likely to be prescribed with antimicrobial agents. Dosage of all drugs, including antibiotics, should be optimized and controlled to prevent adverse drug reactions, avoid further kidney damage and facilitate treatment outcomes [6-9].

Furthermore, CKD was associated with altered pharmacokinetics of a variety of drugs, particularly drugs for renal excretion. Pharmacokinetic alterations may include changes in drug bioavailability, level of protein binding, drug distribution and elimination. Unfortunately, this condition will make patients vulnerable to drug-related problems (DRP). DRP is defined as "an event that occurs as a result of drug therapy that actually or potentially interferes with desired health outcomes" [10]. It has been evident that the occurrence of DRP can cause significant morbidity and decrease the health-related quality of life of patients in various clinical settings. In relation to CKD, numerous studies have reported that DRP cases are remarkably prevalent and are attributed to significant implications [11-14]. The main objective of the study was to evaluate the prevalence of Comorbidities and drug utilization in chronic kidney disease patients.

II. METHODOLOGY

This study was a prospective observational study conducted over a 1-year period from January 2020 to December 2020 in tertiary care hospitals of Khammam region with a sample of 301 cases. Inclusion criteria include patients over 20 years of age, patients with elevated serum creatinine levels, GFR levels, ESR levels, and patients with acute renal failure. The exclusion criteria include patients who had kidney transplant, patients whose data are not relevant to the study, and patients who are unwilling to participate in the study. Patients were prospectively selected for study by simple random sampling. Patient data was collected after having signing the written consent from them. The work was done after obtaining the institutional ethical committee approval. Statistical analysis will be carried out by Microsoft Office (MS-Word, MS-Excel).

III. RESULTS

Among them 301 cases who met out inclusion criteria were included in our study. Prevalence of Comorbidities and drug utilization was listed out in every system.

A. Co morbidities in chronic kidney patient

Total Comorbidities in Cardiovascular system were 146 (48.50%), the highest reported comorbidity was Hypertension 113 (37.54%), it is one of the leading cause of CKD due to the deleterious effects that increased BP has on kidney vasculature. Long-term, uncontrolled, high BP leads to high intra glomerular pressure, impairing glomerular filtration (Table 1).

Comorbidities in Hormonal system were 129 (42.85%), the highest reported comorbidity was Diabetes mellitus 100 (33.22%), with diabetes, and the small blood vessels in the body are injured. When the blood vessels in the kidneys are injured, kidneys cannot clean blood properly; it will cause salt and water retention, which can result in weight gain and ankle swelling (Table 2).

In blood system Comorbidities were 32 (10.63%), the highest reported comorbidity was Anemia 8 (2.65%), it is the main cause of higher risk of developing severe renal impairment due to lack of oxygen supply (hypoxia) it may cause inflammation and fibrosis and loss of capillaries which contributes to the decline in GFR (Table 3).

In renal system Comorbidities were 33 (10.96%), the highest reported comorbidity was Fluid overload 10 (3.32%), it may associated with other risk factors (like cardiovascular risk factors) for CKD and it worsen the condition of patients having renal impairment (Table 4).

In respiratory system Comorbidities were 10 (3.32%), the highest reported comorbidity were Tuberculosis (0.99%)&Chronic obstructive pulmonary disease (0.99%), both of the condition influences the other risk factors associated with CKD by doing some infection in respiratory system and it may effects the kidney function (Table 5).

In rest of the system Comorbidities were 48 (15.94%) given in table 6 it also may effects the kidney function & may worsen the CKD condition.

Table 1: Comorbidities in Cardiovascular System

System	Comorbidities	Number	Percentage
Cardiovascular system	Hypertension	113	37.54
	Heart diseases	19	6.31
	Coronary artery disease	8	2.65
	Congestive heart failure	3	0.99
	Hypotension	3	0.99

Table 2: Comorbidities in Hormonal system

System	Comorbidities	Number	Percentage
Hormonal system	Diabetes mellitus	100	33.22
	Hypothyroidism	21	6.97
	Steroid induced hyperglycemia	2	0.66
	Hypoparathyroidism	1	0.33
	Glucose intolerance	1	0.33
	Diabetic cystopathy	1	0.33
	Peripheral neuropathy	1	0.33
	Hyperthyroidism	1	0.33
	Hemithyroidectomy	1	0.33

Table 3: Comorbidities in Blood System

System	Comorbidities	Number	Percentage
Blood system	Anemia	8	2.65
	Hyperlipidemia	6	1.99
	Thrombocytopenia	5	1.66
	Septic shock	4	1.32
	Malaria	2	0.66
	Cholesterol	2	0.66
	Chronic Lymphocytic leukaemia	1	0.33
	Dyslipidaemia	1	0.33
	Hyponatremia	1	0.33
	Uraemia	1	0.33
	Severe metabolic acidosis	1	0.33

Table 4: Comorbidities in Renal System

System	Comorbidities	Number	Percentage
Renal system	Fluid overload	10	3.32
	Renal calculi	7	2.32
	Urosepsis	4	1.32
	Anuria	3	0.99
	Urinary tract infections	3	0.99
	Proteinuria	2	0.66
	Obstructive nephropathy	2	0.66
	Jaundice	1	0.33
	Nephrotic syndrome	1	0.33

Table 5: Comorbidities in Respiratory System

System	Comorbidities	Number	Percentage
Respiratory system	Tuberculosis	3	0.99
	Chronic obstructive pulmonary disease	3	0.99
	Interstitial lung disease	2	0.66
	Asthma	1	0.33
	Right lung small cell carcinoma	1	0.33

Table 6: Comorbidities in other system

Systems	Comorbidities	Number	Percentage
Hepatic system	Alcoholic hepatitis	3	0.99
	Cholecystectomy	1	0.33
Central nervous system	Dementia	1	0.33
	Depression	1	0.33
	Parkinson's disease	1	0.33
Ophthalmic system	Glaucoma	2	0.66
	Retinopathy	1	0.33
	Cataract	2	0.66
Immune system	Human immunodeficiency virus	1	0.33
	Systemic lupus erythematosus	1	0.33
Gastro-intestinal system	Ulcerative colitis	1	0.33
	Acute Gastroenteritis	1	0.33
	Uremic gastritis	1	0.33
Digestive system and endocrine system	Chronic pancreatitis	1	0.33
Integumentary system	Right leg cellulitis	1	0.33
	Psoriasis	1	0.33
Articulatory System	Septic arthritis	1	0.33
	Osteoarthritis	2	0.66

	Gout	5	1.66
Miscellaneous	Right breast mastectomy	1	0.33
	Chicken pox	1	0.33
	Severe dehydration	1	0.33
	Retropharyngeal Absces	1	0.33
	Hypokalaemia periodic paralysis	2	0.66
	Febrile illness	4	1.32
	Deaf & dumb	1	0.33
	Obesity	7	2.32
	Small vessel disease	2	0.66

B. Prescription pattern in cardiovascular system

There were different types of drugs prescribed, and they were included according to system in which they belong. In Cardiovascular system 287 (20.01%) drugs were prescribed, 79 (5.50%) different types of Calcium channel blockers were prescribed, Calcium channel blockers have been demonstrated to exert beneficial effects on the reduction of proteinuria, reducing mortality, or effective blood pressure control in end stage renal disease (Table 7).

ACE inhibitors can cause acute increase in SCr and/or potassium; continue medication if increase is < 30%; monitor renal function and potassium levels with initiation and with each dosage change, every 1-2 weeks until values return to baseline (usually within 4-6 weeks)

In renal system 232 (16.17%) drugs were prescribed, 109 (7.60%) different types of Diuretics were prescribed, Diuretics are useful in the management of most patients with CKD. They reduce Extracellular fluid volume; lower blood pressure; potentiate the effects of ACE inhibitors, ARBs, and other antihypertensive agents; and reduce the risk of cardiovascular disease in CKD (Table 8).

In autocoids 136 (9.48%) drugs were prescribed, 68(4.74%) different types of Antihistamines were prescribed; these are helpful to decrease the condition of allergic reactions which may give some sorts of effects to worsen the CKD condition (Table 9).

In hormonal system 251 (17.50%) drugs were prescribed, 77(5.36%) different types of HMG-CoA reductase inhibitors were prescribed, these are mainly helpful to decrease the bad cholesterol level in our body, if it is untreated for long it may cause some serious cardiovascular disease (like stroke, atherosclerosis) which is associated with kidney disease and it will reduce kidney function (Table 10).

In blood system 61 (4.25%) drugs were prescribed, 25(1.74%) different types of Iron supplement were prescribed, iron supplement are useful to reduce the condition of Anemia. Approximately 150 mg of iron is necessary for an increase of 1 g/dl in hemoglobin level (Table 11).

In gastro intestinal system 238 (16.5%) drugs were prescribed, 187(13.04%) different types of Proton-pump inhibitors were prescribed, CKD patients may loss the normal appetite or may develop new disease like gastro esophageal reflux disease (GERD) and in this condition Proton-pump inhibitors are useful (Table 12).

In central nervous system 30 (2.09%) drugs were prescribed, 11(0.76%) different types of Benzodiazepines were prescribed, Benzodiazepines are given to decrease some symptoms like anxiety and spasm which may associated with pain medications (Table 13).

Antibacterial drugs 120 (8.36%) were prescribed. Antibiotic therapy is frequently required in patients with renal failure, particularly in those on regular dialysis treatment who are constantly at risk of infections (Table 14).

Table 7: Prescription pattern in Cardiovascular System

System	Class	Drug	Number	Percentage
Cardiovascular system	Calcium channel blockers	Nifedipine, Verapamil, Amlodipine, Diltiazem, Cilnidipine	79	5.50
	Alpha and beta blockers	Carvedilol	62	4.32
	Nitrates	Glyceryl trinitrate	43	2.99
	Angiotensin II receptor antagonists	Valsartan, Losartan, Telmisartan	21	1.46
	Beta blockers	Metoprolol, Atenolol, Propranolol	18	1.25
	Alpha-agonist hypotensive agents	Clonidine	14	0.97
	Calcium channel blocker+ Angiotensin receptor blocker	Cilnidipine & Telmisartan	12	0.83
	Alpha-blockers	Prazosin	11	0.76
	Angiotensin-converting enzyme (ACE) inhibitors	Lisinopril	9	0.62
	Electrolytes	Potassium Chloride	5	0.34
	Calcium channel blocker+ Beta blocker	Cilnidipine & Metoprolol	4	0.27
	Vasodilators	Nitroglycein, Hydralazine	3	0.20
	Antiarrhythmic drugs	Amiodarone	2	0.13
	Potassium channel activators	Nicorandil	1	0.06
	Antihypertensives	Sodium Nitropruside	1	0.069
	Vasopressors	Norepinephrine	1	0.06
	Digitalis glycosides	Digoxin	1	0.06

Table 8: Prescription pattern in Renal System

System	Class	Drug	Number	Percentage
Renal system	Diuretics	Furosemide, Torsemide, Hydrochlorthiazide, Metolazone	109	7.60
	Alkalinizing agents	Sodium bicarbonate	32	2.23
	Nutritional supplements	Alphaketo analogue	27	1.88
	Xanthine oxidase inhibitors	Allopurinol, Febuxostat	26	1.81
	Phosphate binder	Sevelamer	13	0.90
	Uremic detoxification	Lobun	9	0.62
	Anti-inflammatory	Phenazopyridine HCL	8	0.55
	Crystalloid substance	Sodium chloride	4	0.27
	Antioxidants	Acetyl cysteine	2	0.13
	Aldosterone receptor antagonists	Spironolactone	1	0.06
	Potassium removing agents	Patiromer	1	0.069

Table 9: Prescription pattern of Autocoids

System	Class	Drug	Number	Percentage
Autacoids	Antihistamines	Cyproheptadine, Cetirizine, Diphenhydramine HCL, Meclizine, Hydroxyzine pamoate, Fexofenadine	68	4.74
	Analgesics	Paracetamol, Acetaminophen, Tramadol	32	2.23
	Non-selective cyclooxygenase(COX) inhibitor	Acetyl salicylic acid	21	1.46
	H_2 blockers	Ranitidine	7	0.48
	Non-steroidal anti-inflammatory drugs	Diclofenac, Naproxen, Celecoxiv	5	0.34
	Histamine analogue	Betahistine	3	0.20

Table 10: Prescription pattern in Hormonal System

System	Class	Drug	Number	Percentage
Hormonal system	HMG-CoA reductase inhibitors	Atorvastatin, Rosuvastatin, Simvastatin, Pitavastatin, Lovastatin	77	5.36
	Anti-thyroid drugs	Thyronorm, Neo-Mercazole	41	2.85
	Fast-acting insulin	Insulin lispro	36	2.51
	Steroids	Protein powder	30	2.09
	Sodium-glucose co-transporter 2 (SGLT2) inhibitors.	Canagliflozin	12	0.83
	Corticosteroid	Dexamethasone, Deflazacort, Alclometasone dipropionate, Omnacortil,	12	0.83
	Hypoglycemia Antidotes	Dextrose	11	0.76
	Anti-diabetic medicines	Teneligliptin	10	0.69
	Sulfonylureas	Glimipride, Glipizide, Glibenclamide, Glimepiride	8	0.55
	Dipeptidyl peptidase-4 (DPP-4) inhibitors	Linagliptin, Sitagliptin	4	0.27
	Biguanides	Metformin	3	0.20
	Amino acid	S-Adenosyl methionine	2	0.13
	Glucocorticoids	Methylprednisolone	2	0.13
	Ovulatory stimulants	Clomiphene citrate	1	0.06
	Imidazoles	Carbimazole	1	0.06
	Biguanides +Dipeptidylpeptidase-4 inhibitors	Metformin and Linagliptin	1	0.06

Table 11: Prescription pattern in Blood System

System	Class	Drug	Number	Percentage
Blood	Iron supplement	Ferrous Fumarate, Ferrous sulphate, Iron sucrose	25	1.74
	Antiplatelet medications	Clopidogrel	13	0.90
	Antithrombotic drug	Tinzaparin	8	0.55
	Colony-stimulating factors	Erythropoietin	7	0.48
	Erythropoiesis-stimulating agents	Epoetin Alfa	5	0.34
	Anticoagulant	Acenocoumarol	2	0.13
	Fibrates	Gemfibrozil	1	0.06

Table 12: Prescription pattern in Gastro Intestinal System

System	Class	Drug	Number	Percentage
Gastro -intestinal system	Proton-pump inhibitors	Pantoprazole, Domperidone +Rabeprazole, Rabeprazole, Esomeprazole	187	13.04
	5-HT3 antagonist	Ondansetron, Granisetron	29	2.02
	Antacids	Calcium carbonate	9	0.62
	Laxative	Sorbitol, Lactulose	8	0.55
	Fungal *Diastase*	Diastase & pepsin	1	0.06
	Fungal *Diastase*	Diastase & pepsin	1	0.06

Table 13: Prescription pattern in Central Nervous System

System	Class	Drug	Number	Percentage
Central Nervous system	Benzodiazepines	Diazepam, Lorazepam, Clonazepam, Chlordiazepoxide HCl	11	0.76
	Anticonvulsants	Primidone, Ethosuximide, Levetiracetam, Clobazam, Valproate, Pregabalin	8	0.55
	Antidepressants	Amitriptyline hydrochloride, Nortriptyline, Pregabalin+Nortriptyline	3	0.20
	Wakefulness promoting agents	Modafinil	3	0.20
	Selective serotonin receptor agonists	Sumatriptan	2	0.13
	Phenothiazines	Prochlorperazine maleate	2	0.13
	Decarboxylase inhibitors	Levodopa	1	0.06

Table 14: Prescription pattern in various other systems

System	Class	Drug	Number	Percentage
Antibacterial	Antibiotics	Levofloxacin, Piperacillin sodium & Tazobactam sodium, Artesunate, Cefuroxime, Ciprofloxacin, Faropenem, Meropenem, Ceftriaxone, Cefoperazone + Sulbactum, Nitrofurantoin, Ethambutol, Aztreonam, Metronidazole, Cefoperazone sodium, Cefotaxime, Cefixime, Cefpodoxmine Proxetil, Doxycycline	116	8.08
	Beta-lactamase inhibitor	Tazobactum, Amoxicillin	4	0.27
Antiprotozoal	HIV integrase inhibitors	Dolutegravir	1	0.06
	Nucleotide reverse transcriptase inhibitors (NRTIs)	Emtricitabine-tenofovir	1	0.06
Anti-parasitic	Antimalarials	Quinine sulfate	1	0.06
	Anthelmintic drug	Diethyl carbamazine	2	0.13
Autonomic Nervous system	Muscarinic antagonist	Ipratropium Bromide	1	0.06
	Anticholinergics	Aclidinium Bromide	3	0.20
Respiratory system	Bronchodilators	Deriphyllin, Acebrophylline	2	0.13
	Antitussive	Levocloperastine	6	0.41
Anti-viral	Nucleoside analogues	Entecavir	1	0.06
Ophthalmic system	Prostaglandin analogs	Travoprost	2	0.13
Hepatic system	Gallstone dissolution agents	Ursodeoxycholic Acid	8	0.55
Miscellaneous	Vitamins	Cyanocobalamine, Phytonadione, Folic acid, Calciferol, Paricalcitol, B vitamins complex	51	3.55

C. Prescribing indicators

Total number of prescriptions were analyzed were 301 and and total number of drugs prescribed in our study were 1434. The average number of drugs per prescription was 4.76.

Table 15: Prescribing indicators

Prescribing indicators	Frequency
Prescription analysed	301
Total number of drugs prescribed	1434
Average number of drugs per prescription	4.76

D. ATC Classification

Drugs prescribed in our study were classified according to ATC classification and were given in table 16.

Table 16: ATC classification of Drugs

Drug classes (based on ATC classification)	Number	Percentage
A - Drugs for gastrointestinal tract and metabolism	238	79.06
B – Drugs for treatment of disorders of blood and blood forming organs	61	20.26
C – Drugs for cardiovascular system	287	95.34
D – Dermatological drugs	0	0
G – Drugs for genitourinary system and sex hormones	232	77.07
H – Hormones for systemic use except sex hormones	251	83.38
J – Anti infectious drugs for systemic use	122	40.53
L – Antineoplastic and immunomodulating agents	0	0
M – Drugs for musculoskeletal systems	0	0
N – Drugs acting on nervous system	34	11.2
P – Drugs against parasites and insecticides	5	1.66
R – Drugs for respiratory system	8	2.65
S– Drugs for eye and ear	2	0.66
V - Various others (antihistamines, analgesics, vitmains)	195	64.7

IV. DISCUSSION

Chronic kidney disease (CKD) is a highly prevalent noncommunicable disease responsible for the increase in morbidity in India. It is a global threat to health in general and to developing countries in particular, due to the increased incidence of lifestyle-related diseases such as diabetes and cardiovascular disease. Due to these comorbid conditions in combination with CKD, patients invariably end up with complex multi-drug drug therapy for CKD [15].

In our study, comorbid conditions such as hypertension, diabetes, hypothyroidism, anemia, hyperlipidemia and fluid overload were more common among these patients and were found relevant in concurrent studies [16]. The average number of drugs per prescription used was 4.76. According to the ATC classification system, the drugs most commonly used were Drugs for the cardiovascular system [17], Hormones for systemic use [18], Drugs for the genitourinary system, Drugs for the gastrointestinal tract, Anti-infectious drugs for use systemic in our study.

Hematinics and multivitamins [19] are commonly prescribed medications, as CKD patients are more likely to develop anemia and weakness from the disease. They are also more susceptible to stress, ulcers and dyspepsia, which is why antacids are also commonly prescribed for CKD patients. Keto analogs have mainly been prescribed for CKD stages II to IV as recommended to reduce kidney damage. Phosphate binder was also used significantly in this study population. Patients with CKD are at high risk for infections and end up in recurrent hospital admissions. Reduced or absent excretion by the kidneys in renal insufficiency causes an increase in the volume of distribution (Vd) and ultimately increases the half-life (T½) of the drug, leading to accumulation of drug metabolites resulting in toxicity. Respiratory tract infections remain the most common infection. Therefore, protocols are being developed to vaccinate these high-risk patients with pneumococcal and influenza vaccines. Depending on the severity of the infection, the virulence and the susceptibility pattern of the bacteria, various antibiotic dosage forms have been used. Most patients were treated with oral antibiotics in our study.

Evaluating the use of drugs in CKD patients from time to time will help ensure that the rationale for prescribing is maintained and that the information obtained from the study can be used to prevent drug-related problems, evaluate the efficacy of therapy with drugs and make the changes in the treatment regimen for patients, as needed.

For the general management of CKD, patients should also undergo frequent clinical and laboratory evaluations. Preventing progression and treating the ongoing disease process is the main goal of pharmacotherapy for CKD. Treatment of CKD is not only disease-directed but also includes the management of comorbid conditions associated with CKD.

V. CONCLUSION

Cardiovascular disease and diabetes were the most reported comorbidities in our study. In our study we identified a wide variety of drug classes that were prescribed in a cohort of CKD patients with morbidity. Diuretics, antihypertensives, antidiabetics, gastrointestinal tract drugs and anti-infective drugs have been used more frequently in patients with chronic renal failure due to the high prevalence of comorbidities. Incorporating standard assessment and treatment can reduce the complications and adverse reactions seen in these patients. This in turn would improve their quality of life and reduce the risk of mortality in this population.

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