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MEDICATION PRESCRIBING PATTERN FOR CHRONIC KIDNEY DISEASE PATIENTS UNDERGOING MAINTENANCE HAEMODIALYSIS: A PROSPECTIVE OBSERVATIONAL STUDY.

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ABSTRACT

Background: Chronic kidney disease (CKD) results from various kidney disorders affecting structure and function due to diverse pathophysiological processes. It poses a global health threat, particularly in developing countries, with increasing incidence, poor outcomes, and high treatment costs. CKD is associated with comorbidities such as hypertension and diabetes, identified as major risk factors. This study aims to investigate medication prescribing patterns in hypertensive CKD patients undergoing maintenance haemodialysis.

Materials and methods: The study involved 100 participants, with an average age of 61.41 years (SD +/- 8.54), and a male preponderance of 5:1, comprising 80 male and 20 female participants. The majority of patients experienced conditions such as anaemia, atherosclerosis, infection, renal disease, hypertension, and diabetes mellitus. Among the 310 total prescriptions, antihypertensive medications were the most commonly prescribed, followed by antacids. Medications addressing comorbidities associated with chronic kidney disease were also prescribed, totalling 310 medications. For 59.05% of the drugs, dosage modification was unnecessary. Among the medications requiring dose adjustments, 72.66% were correctly adjusted, while 26 .66% were not.

Conclusion: According to the American Academy of Family Physicians, 73.87% of cases involving kidney cancer and hypertension included inappropriate drug prescriptions. This implies that, despite the fact that only 24% of medications were prescribed under their generic names, inappropriate prescribing remains a major concern at our hospital.

Keywords: Chronic kidney disease, hemodialysis, medication adherence, prescribing patterns.

INTRODUCTION

Chronic kidney disease (CKD) is marked by various disorders affecting kidney morphology and function through diverse pathophysiological mechanisms. It is typically diagnosed based on a sustained decline in nephron count, leading to reduced glomerular filtration rate (GFR) lasting over three months[1,2].

Globally, an estimated 200 million individuals suffer from CKD [2,3]. Population-based studies conducted in New Delhi and its vicinity reveal CKD prevalence rates of 4.2% in India, while Thailand and Congo report rates of 8.6% and 8%, respectively[3]. CKD poses a significant burden on public health in India, contributing to escalating morbidity rates, and is emerging as a noteworthy chronic ailment worldwide[3,4].

This condition poses a substantial threat to global health, particularly in developing nations, due to rising incidence rates, poor prognoses, and expensive treatment modalities. CKD's status as a widespread non-communicable disease exacerbates its impact, aggravated by comorbidities and polypharmacy[5,6].

Patients with CKD often present with comorbidities such as hypertension, diabetes mellitus, coronary artery disease, and infections, with hypertension and diabetes being the most prevalent risk factors. Managing renal failure involves treating these comorbidities while accounting for renal insufficiency, as they significantly contribute to CKD progression, ultimately leading to end-stage renal disease (ESRD)[7,8,9].

Evidence indicates that appropriately managing these comorbidities with judicious drug use delays CKD progression and reduces complications. Hence, meticulous drug selection and dosage adjustments are imperative to ensure safe and optimized therapy for each CKD patient[9,10].

Polypharmacy is common among CKD patients, particularly those undergoing haemodialysis, who often have complex drug regimens involving multiple doses daily.[11,12] The fluctuating nature of the disease, along with lifestyle restrictions, renders CKD patients vulnerable to drug-related problems (DRPs) and non-adherence to treatment [13]. Vigilance is crucial to identify and address potential drug interactions promptly to prevent serious adverse events.

This study aims to identify the types of drugs prescribed to renal failure patients, assess their appropriateness, and elucidate the consequences of irrational treatment. Such insights are expected to significantly enhance the safety of renal failure treatment and mitigate the progression of renal damage.

Materials and Method

A Prospective, observational, cross-sectional study is conducted in hemodialysis unit in government teaching hospital, Chamarajanagar Institute of Medical Sciences, Chamarajanagar and the study duration will be of 16 months i.e. from Jan 1stJan, 2018, to Dec 31st, 2018.

Study population here are adult patients aged 40-80years of either sex who have been diagnosed with Chronic Kidney Disease (CKD) and on maintenance on Hemodialysis at hemodialysis unit, Government teaching hospital, Chamarajanagar.

Inclusion criteria:

- ☼ Patients of either gender between 40 to 75 years of age.
- ☼ Patients with CKD stage 3, 4 and 5 with or without Albuminuria.
- ☼ Patients underwent Hemodialysis for more than once.
- ☼ Patients with any co morbid conditions other than renal tumors.
- ☼ Patients who have signed the informed consent.

Exclusion criteria:

- Patients who are HIV + Ve and HbsAg + Ve.
- Cancer patients who are terminally ill.
- Pregnant and lactating women.
- Patients with CKD stage 1 and 2.
- Patients with insufficient data.
- Patient with Psychiatric illnesses

The data collection process involved extracting information from files, which served as a comprehensive source of data on prescribed drugs, dose adjustments, demographics, comorbid conditions, and the stage of CKD. Additionally, a series of structured questionnaires were administered to ensure thorough data collection.

STATISTICAL ANALYSIS

The collected data will undergo statistical analysis utilizing descriptive statistics, specifically mean and standard deviation for age. In instances requiring it, the findings will be presented through percentages and graphical representations.

Recommendations are shaped by evidence-based clinical guidelines, ongoing research, and consensus within the medical community. It is strongly recommended that general practitioners (GPs) and other healthcare professionals consult these guidelines to uphold a high standard of care for patients, particularly concerning drug utilization in chronic kidney disease (CKD). Notably, the American College of Physicians (ACP) has crafted comprehensive guidelines addressing screening, monitoring, and treatment for adults with CKD stages 1 to 3. These guidelines are rooted in a systematic review of evidence, encompassing literature from 1985 to November 2011 and identified through sources such as MEDLINE and the Cochrane Database of Systematic Reviews. Key considerations include the effectiveness and potential drawbacks of systematic CKD screening, monitoring for deteriorating kidney function or damage, and the impact of treatment on clinical outcomes. The ACP offers specific recommendations, discouraging screening for CKD in asymptomatic adults lacking risk factors, advising against proteinuria testing in certain populations, and endorsing the use of angiotensin-converting enzyme inhibitors or angiotensin II–receptor blockers for managing hypertension in CKD patients. Additionally, the ACP provides guidelines for addressing comorbid conditions and risk factors associated with CKD, encompassing hypertension, diabetes, atherosclerosis, anaemia, renal vascular disease (RVD), and infections. These recommendations serve as valuable resources for clinicians, aiding in the optimization of care for individuals with CKD.[13]

Antihypertensives, including Angiotensin-Converting Enzyme Inhibitors, demonstrated a moderate strength of evidence compared to placebo, with no overall reduction in mortality. While there was a decreased risk of End-Stage Renal Disease (ESRD), this benefit was not observed in patients with only microalbuminuria or impaired Glomerular Filtration Rate (GFR). Angiotensin Receptor Blockers showed a high strength of evidence, indicating no overall reduction in mortality but a decreased risk of ESRD. Calcium-Channel Blockers, while demonstrating a high strength of evidence, did not exhibit a reduction in the risk of mortality. β-Blockers, compared to placebo, had a moderate strength of evidence, resulting in a reduced risk of mortality. Thiazides, among Diuretics, showed no reduced risk and mortality compared to placebo. Hypoglycaemic Agents include Metformin, Metformin + Sulfonylurea, Thiazolidinedione, SGLT-2 inhibitor, or DPP-4 inhibitor, and Insulin. Hypolipidemic Agents, specifically Statins with a preference for Atorvastatin, are recommended. Anaemia Treatment involves Recombinant Human Erythropoietin (RHE), with dose adjustments guided by The American College of Physicians (ACP).

Table1: Antihypertensive Agents: Dosing Requirements in patients with Chronic Kidney Disease[14]

Dose adjustment (% of usual dose) based on GFR ml/1.73m2				
Drugs	Usual Dose	>50	10 to 50	<10
ACE Inhibitors				
Captopril	25mg TID	100	75	50
Enalpril	5 to 10mg BD	100	75 to 100	50
Fosinopril	10mg daily	100	100	75 to 100
Lisinopril	5 to 10mg Daily	100	50 to 75	25 to 50
Ramipril	5 to 10mg Daily	100	50 to 75	25 to 50
β- Blockers				
Acebutalol	0.4 to 0.6g OD/BD	100	50	30 to 50
Atenolol	5 to 100mg Daily	100	50	25
Bisoprolol	10mg daily	100	75	50
Nadolol	40 to 80mg Daily	100	50	25
Diuretics				
Amiloride	5mg Daily	100	50	Avoid
Bumetanide	No adjustment needed	__	__	__
Furosemide	No adjustment needed	__	__	__
Metolazone	No adjustment needed	__	__	__
Spironolactone	50 to 100mg Daily	6 to 12hr	12 to 24hrs	Avoid
Thiazide	25 to 50mg Daily	100	100	Avoid

Table 2: Antimicrobial Agents: Dosing Requirements in Patients with Chronic Kidney Disease[14]

	Dose adjustment (% of usual dose) based on GFR ml/1.73m2			
Drugs	**Usual Dose**	**>50**	**10 to 50**	**<10**
Antifungal				
Fluconazole	200 to 400mg / 24hrs	100	50	50
Itraconazole	100 to 200 mg / 12 hrs.	100	100	50 (IV Is C/I
Ketoconazole	No adjustment needed	_	_	_
Miconazole	No adjustment needed	_	_	_
Carbapenems				
Imipenem	0.25 to 1 g every 6 hrs	100	50	25
Meropenem	1 to 2 g every 8 hrs	100	50 every 12hrs	50 every 24hr
Cephalosporins				
Cefadroxil	250 to 500 mg / 8 hrs	100	Every 12 to 24 hrs	Every 36 hrs
Cefepime	0.25 to 2 g / 8 to 12 hrs	100	50 to 100% / 24 hrs	25 to 50% / 24 hrs
Cefixime	200 mg / 12 hours	100	75	50
Cefoperazone	No adjustment needed	_	_	_
Cefotaxime	1 to 2 g / 6 to 12 hrs	Every 6 hours	Every 6 to 12 hrs	Every 24 hours
Cefpodoxime	100 to 400 mg / 12 hrs	Every 12 hours	Every 24 hours	Every 24 hours
Macrolides				

Azithromycin	No adjustment needed	_	_	_
Clarithromycin	250 to 500 mg /12 hrs	100	50 to 100	50
Quinolones				
Ciprofloxacin	400 mg IV or .5 to .75 g orally / 12 hours	100	50 to 75	50
Gatifloxacin	400 mg / 24 hours	100	400 mg initially, then 200 mg daily	400 mg initially, then 200 mg daily
Levofloxacin	250 to 750 mg /24 hrs	100	500 to 750 mg initial dose, then 250 to 750 mg every 24 to 48 hours	500 mg initial dose, then 250 to 500 mg every 48 hours
Moxifloxacin	No adjustment needed	_	_	_
Norfloxacin	400 mg / 12 hrs	Every 12 hours	Every 12 to 24 hrs	Avoid
Ofloxacin	200 to 400 mg 12 hrs	100	200 to 400 mg / 24hrs	200 mg /24 hrs

Table 3: Hypoglycaemic Agents: Dosing Requirements in Patients with Chronic Kidney Disease

Table 4: Statins: Dosing Requirements in Patients with Chronic Kidney Disease[14]

Drugs	Usual Dose	Special considerations
Atorvastatin	10 mg daily Maximal dosage: 80 mg daily	No adjustment needed
Fluvastatin	20 to 80 mg daily	50% dose reduction in patients with a GFR less than 30
Rosuvastatin	5 to 40 mg daily	Recommended starting dosage is 5 mg daily in patients with a GFR less than 30 mL (not more than 10mg)
Simvastatin	10 to 20 mg daily Maximal dosage: 80 mg daily	Recommended starting dosage is 5 mg daily in persons with a GFR less than 10

Upon scrutinizing the data and contrasting it with the benchmarks set by the American Academy of Family Physicians, an examination of age, gender distribution, co-morbidities, adherence, and treatment will be elucidated in terms of percentage.

RESULTS

Age distribution

A total of 100 patients participated in the study. Age range was 56 years and above with majority of patients belonging to the age group of 50 – 70 years. Age distribution is as depicted in Table-5

Table 5: Age and Gender distribution

Sl no.	Age Distribution	n	%
1	40-50	22	22.92
2	50-60	38	39.58
3	60-70	40	40.50

The study involved 100 participants, of which 80 (80.33%) were males. The subsequent figure illustrates the distribution of genders among the participants.

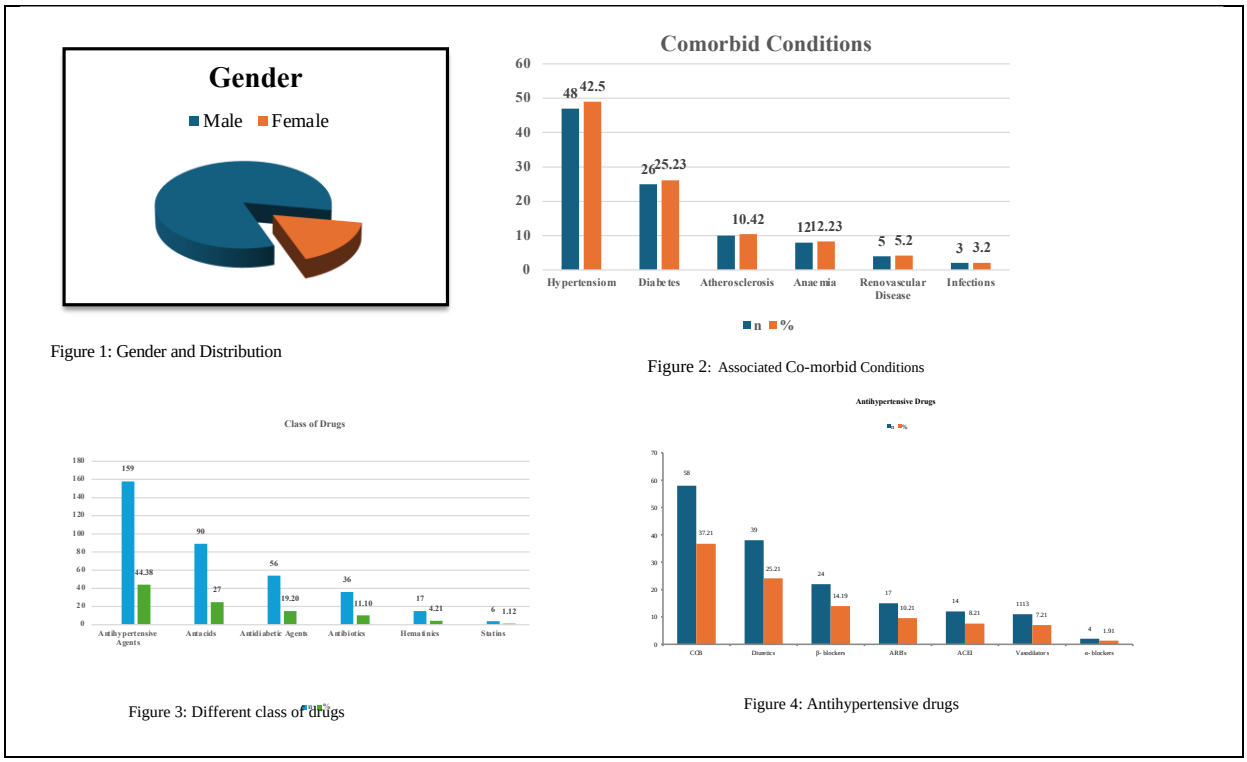


Figure 1: Gender and Distribution

Figure 2: Associated Co-morbid Conditions

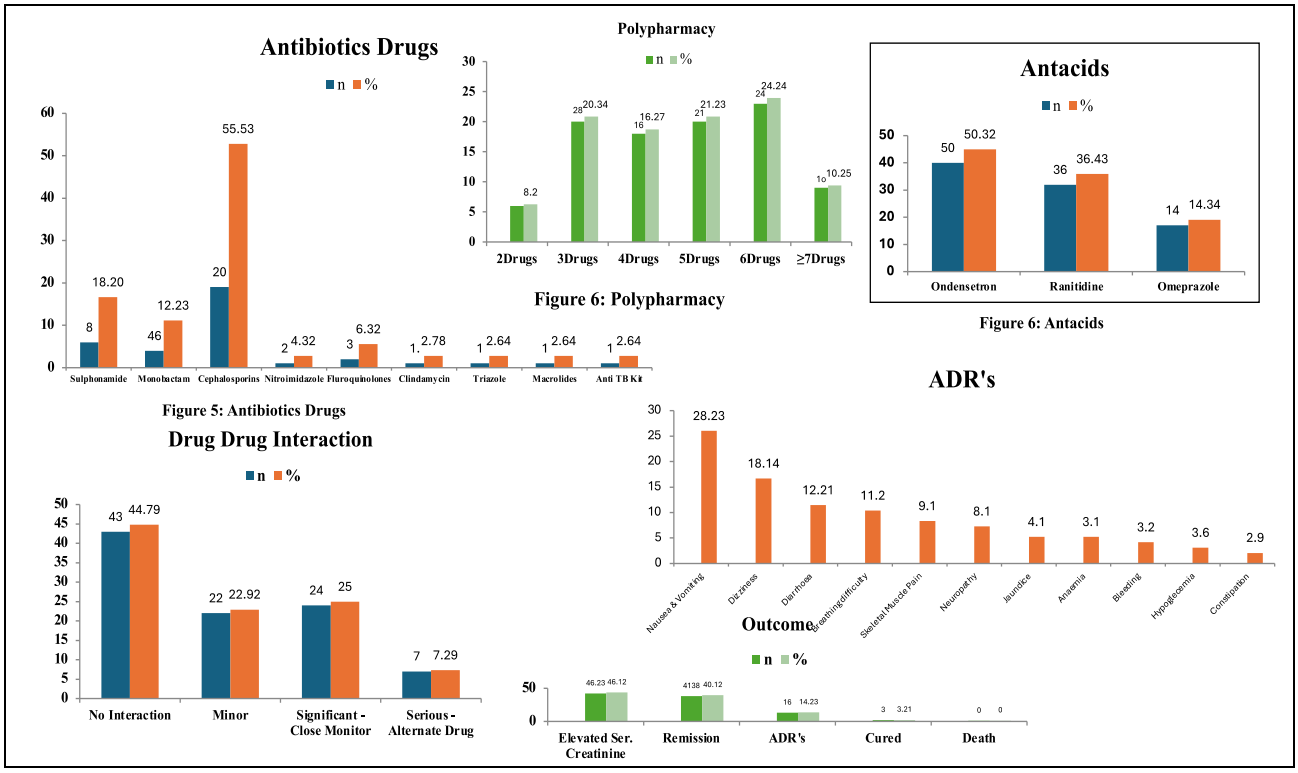
Figure 3: Different class of drugs

Figure 4: Antihypertensive drugs

Clinical data: The most common comorbidity was found to be hypertension, which was followed by infections, diabetes, atherosclerosis, anaemia, and kidney vascular disease (RVD). The prevalence of these comorbidities among the participants is shown graphically in Figure 2.

Drugs used: Many medications were prescribed to treat the comorbidities that come with chronic kidney disease (Figure 2). The medications that were prescribed are listed in Appendix 4, along with information on whether or not dose adjustments were necessary for those medications. This data is summarized in Table 3. The participants were prescribed 296 medications in total. The majority of drugs (64.09) did not require a change in dosage. While 81.44% of the medications requiring dose adjustments were correctly adjusted, 30.17% were not.
Various drug classes were prescribed based on the co-occurring conditions the participant was experiencing, as the information is summarized in the graph. Antacids (20%) and antihypertensives (80%) were the most frequently prescribed medications. (Table 4 & 6)

Antihypertensive Agents: The frequently prescribed antihypertensive medications include CCB (36.71%), followed by β-blockers (13.92%) and diuretics (24.05%), as depicted in the graph summarizing data on antihypertensive medications. Contrary to the American Academy of Family Physician guidelines for hypertensive CKD, only 28.13% of participants were treated with ACEIs and ARBs, the recommended first-line treatment. The majority, 71.88%, received alternative treatments (Figure 4).



Antimicrobials: As shown in the graph summarizing antibiotic data, cephalosporins (57.12%) are the most commonly used antibiotics, followed by sulphonamide (18.13%) and monobactam (12.01%) (Figure 5).

Almost all antimicrobial agents given orally or intravenously (IV) to CKD patients, regardless of underlying co-morbidities, were dosed based on GFR calculations. There was a significant correlation ($p<0.0001$) between the number of prescribed drugs and comorbidities.

Antacids: Among antacids, 5-HT antagonists like Ondansetron (47.12%) is most commonly used which is followed by H_2- blockers like Ranitidine (36.69%) and PPI like Omeprazole (20.09%) which is illustrated in the graph summarizes the information (Figure 6).

Polypharmacy: Polypharmacy was very common in CKD patients, regardless of any comorbid conditions. The majority of patients (88.16%) were treated with three or more medications. Only 4.08% of patients were treated with just two drug combinations. 8.12% were treated with seven or more medications. The above figure summarizes the details of polypharmacy (Figure 6).

Frequency and severity of drug interactions among the study participants

48 participants (48.18%) of the drug combinations did not have a potential drug to drug interaction. However, 06 participants 06.18% of the combinations had potential serious drug interaction that required the use of an alternative agent. 24% of participants had potential significant interaction which required close monitoring while 21.18% combinations had minor interactions.

Assessment of the outcome of the treatment: The renal function of 48 (48.61%) participants deteriorated following the prescription, as evidenced by an increase in serum creatinine. Following treatment, 11 (11.24%) of the participants developed ADRS. 36 (36.58%) of the participants had their comorbidity symptoms resolved. One participant was cured.

ADRS encountered: The most common adverse effect was nausea and vomiting, followed by dizziness, diarrhoea, difficulty breathing, musculoskeletal pain, and neuropathy, as illustrated in the above figure.

Adherence to the American Academy of Family Physicians. According to the American Academy of Family Physicians, 74.25% of drugs were prescribed inappropriately for hypertensive CKD patients. This indicates that there is a high incidence of inappropriate prescription in our hospital, but only 25% of the drugs were prescribed using their generic name.

DISCUSSION

the studies by Seck et al. 2015 observed a higher proportion of males compared to females, consistent with prior research findings. Notably, participants aged 53 to 70 years constituted over half of the study cohort, reflecting an age-related increase in Chronic Kidney Disease (CKD) prevalence, as documented in previous studies by Seck et al., 2015 [16].

Comprehensive comorbidity profiles were evident among participants, with no cases of isolated chronic renal failure. This aligns with existing literature indicating that CKD is commonly accompanied by other medical conditions, with isolated CKD representing a minority subset. Fraser et al. 2017 similarly noted this trend [17].

Hypertension and diabetes emerged as the predominant comorbidities in CKD, consistent with multiple studies. Additional comorbidities included anemia, atherosclerosis, and renal vascular disease [17,18]. The presence of comorbidities necessitates polypharmacy, heightening treatment costs, adherence challenges, and the risk of adverse drug reactions [19].

The mean number of medications per patient was 4.73±1.64, mirroring findings from Fraser et al., where the median number of drugs was 5, with over 63% of participants on four or more medications [17]. Only a small proportion of participants were prescribed seven or more drugs.

In managing hypertension, the most prevalent comorbidity, calcium channel blockers (CCB), diuretics, and β-blockers were commonly employed. Vasodilators, angiotensin-converting enzyme inhibitors (ACEIs), and angiotensin receptor blockers (ARBs) were utilized to a lesser extent, consistent with the findings of Dasari et al.[18]

CONCLUSION

In our research, we identified a diverse array of clinical diagnoses, including conditions like Hypertensive CKD and Diabetic CKD, showcasing the utilization of a wide range of medications. The prevalence of polypharmacy emerged as a common practice among patients with Chronic Kidney Disease (CKD). This not only results in increased treatment costs and a heightened risk of drug interactions but also contributes to the irrational prescription of medications.

Our study brought to light inappropriate drug prescriptions, with a significant percentage of 76.18% observed for Hypertensive CKD, based on the criteria set by the American Academy of Family Physicians. This high incidence highlights the issue of inappropriate prescription practices within our hospital. It is noteworthy that only 26% of the prescribed drugs were identified by their generic names.

Conflicts of Interest

There are no conflicts of interest.

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