



PRESCRIBING PATTERNS OF ANTI HYPERTENSIVE DRUGS IN CHRONIC KIDNEY DISEASE PATIENTS IN A TERTIARY CARE TEACHING HOSPITAL

Medicine

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ABSTRACT

Background: Chronic kidney disease most often results from a progressive loss of functioning nephrons caused by a primary kidney disease or as a secondary complication of certain systemic diseases, but it can also result from an acute event causing irreversible damage to the kidneys. Anti hypertensive treatment can slow the progression of CKD to renal failure; however, the treatment of hypertension can be challenging among CKD patients because of the bidirectional cause and effect relationship between hypertension and CKD. Additionally, hypertensive CKD patients often require treatment with multiple antihypertensive drugs. **Materials And Methods:** A Prospective, observational study was conducted in inpatient and outpatient Nephrology Department in association with Department of Pharmacology in Gandhi Medical College and Hospital, Secunderabad, over a period of 2 months. After obtaining the clearance and approval from the Institutional Ethics Committee, patients who gave informed consent were included in the study. **Results:** In this study, the prevalence of Chronic kidney disease was higher in males 32 (60%) than females 21(40%). Greater incidence of CKD was noted in the age group of 51-60 years with mean age of 52.13207547±21.213 ranging between 20 to 80 years. Among the chronic kidney disease patients on antihypertensive drugs 62.2% of patients were classified under stage 5 of CKD followed by 22.6% of patients belonged to stage 4 and 15% of patients belonged to stage 3 of CKD. Among Anti-hypertensives most commonly preferred were diuretics (83.3%), calcium channel blockers (77.3%), beta blockers (43.3%), alpha blockers (33.9%), centrally acting anti-hypertensives (15%), beta plus alpha blockers (11.3%) and Angiotensin receptor blockers (1.8%). **Conclusion:** Patients with chronic kidney disease on antihypertensive medication were assessed and analyzed for prescription trends. The preferential drugs employed among anti-hypertensives were diuretics, followed by calcium channel blockers, beta blockers, alpha blockers, beta plus alpha blockers, centrally acting anti-hypertensives and Angiotensin receptor blockers.

KEYWORDS

Anti-Hypertensives, CKD, Diuretics

INTRODUCTION :

Drug utilisation study is defined as “the marketing, distribution, prescription and utilization of drugs in the society with special emphasis on the resulting medical, social and economic consequences” and has the main aim of facilitating the rational use of drugs, which is very important in decision making for healthcare.¹

Chronic kidney disease most often results from a progressive loss of functioning nephrons caused by a primary kidney disease or as a secondary complication of certain systemic diseases, but it can also result from an acute event causing irreversible damage to the kidneys.²

The most common risk factors and other characteristics among the subjects diagnosed with CKD were hypertension (64.5%), anaemia (40.7%) and diabetes (31.6%)³. Furthermore, old age, hypertension (both SBP and DBP) and low haemoglobin level were correlated with decreased eGFR in the CKD subgroup⁴.

The Eight Report of the Joint National Committee (JNC 8) and National Kidney Foundation-Dialysis Outcomes Quality Initiative (NKF-DOQI) guidelines identify CKD as a higher-risk category requiring intensive blood pressure control to achieve a blood pressure goal of less than 130/80 mmHg⁵.

Antihypertensive treatment can slow the progression of CKD to renal failure^{6,7}; however, the treatment of hypertension can be challenging among CKD patients because of the bidirectional cause and effect relationship between hypertension and CKD.^{8,9} Additionally, hypertensive CKD patients often require treatment with multiple antihypertensive drugs.^{10,11}

Hypertension doubles the risk of cardiovascular diseases including coronary heart disease (CHD), congestive heart failure, ischaemic and haemorrhagic stroke, renal failure and peripheral arterial disease.¹²

So, proper control of BP in hypertensive patients is a must to prevent poor outcome in CKD patients.¹³

The numerous guidelines that have been developed worldwide for the management of hypertension are being used by clinical practitioners as a standard reference. However, many clinicians have their own prescribing pattern in treating hypertensive patients according to their

clinical experience. Clinical practitioners need to be empowered in appropriate and evidence-based management of hypertension. An analysis of these prescribing patterns and use of guidelines for antihypertensive medications can give better insights into concept of personalised and cost-effective pharmacological management of hypertension.

Hence this study was undertaken to analyse the utilization pattern of antihypertensive drugs in chronic kidney disease patients in a tertiary care hospital.

AIMS AND OBJECTIVES:

- To analyze the prescribing pattern of Antihypertensive drugs in chronic kidney disease in a Tertiary care teaching hospital.
- To find the preferable Antihypertensive drugs in chronic kidney disease patients in a Tertiary care teaching hospital.

MATERIALS AND METHODS:

A Prospective observational study was conducted in inpatient and outpatient Nephrology Department in association with Department of Pharmacology in Gandhi Medical College and Hospital, Secunderabad, over a period of 2 months. After obtaining the clearance and approval from the Institutional Ethics Committee, patients who gave informed consent were included in the study. The patients who were diagnosed of Chronic Kidney Disease by the consultant Nephrologist according to KDIGO (Kidney Disease Improving Global Outcomes) guidelines and who were on antihypertensive therapy were included in the study. Prescriptions of Chronic kidney disease patients diagnosed to have hypertension and on antihypertensive drugs were analyzed in terms of

- Names of the drugs
- Demographic details of the patients which include Age and Gender.
- Pattern of individual antihypertensive drugs prescribed in CKD patients.
- Preferable antihypertensive drug prescribed in CKD patients.
- Multiple anti hypertensives.

Inclusion Criteria:

- Patients above the age of 18 years of both genders were included.
- Patients who are diagnosed with Chronic Kidney disease along

with history of hypertension and on antihypertensive therapy were included in the study.

Exclusion Criteria:

- Patients with Kidney diseases other than Chronic Kidney disease, with surgical conditions like Kidney stones, tumors and trauma, were not included in the study.
- Pregnant and lactating woman were not included in the study.
- Patients who are co-infected with HIV or Hepatitis or with any Autoimmune disease or with any infective conditions.
- Patients with renal transplant, Congestive heart failure, patients on Dialysis were not included in the study.
- Patients who have psychiatric illness were not included in the study.
- Patients with history of Drug allergy.

Statistical Analysis:

The data collected from the case records was entered in to the MS Excel sheet and analyzed appropriately as percentages, mean $\pm$ SD was also calculated wherever it is necessary.

RESULTS:

Data of Fifty-three case records of in-patients and out-patients diagnosed of having chronic kidney disease and on antihypertensive medications were collected and analyzed over a period of two months in a tertiary care teaching hospital.

Table 1: Age Wise Distribution Of Patients

Age	No Of Patients	Percentage
20-30YEARS	4	7.5%
31-40YEARS	10	18.8%
41-50YEARS	11	20.7%
51-60YEARS	16	30.1%
61-70YEARS	7	13.2%
70-80YEARS	5	9.4%
MEAN $\pm$ SD	52.13207547 $\pm$ 21.21320344	

From the Table 1 it is clear that CKD is more common in patients with the age group of 51–60years (30.1%) followed by 31–40years (20.7%), 41-50 years (18.8%) >60years (22.6%) and 20 -30years (7.5%). The mean age of the patient in the study was 52.13 $\pm$ 21.21 years.

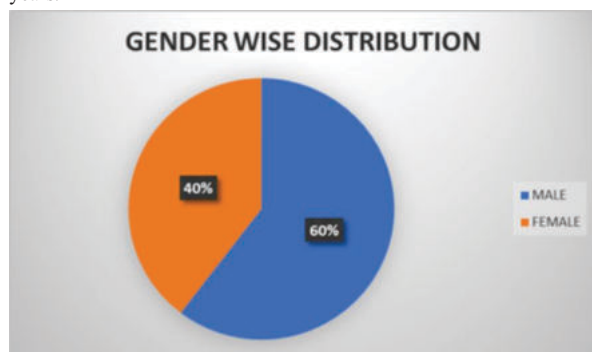


Figure 1: Gender Wise Distribution Of Patients Among Various Stages Of Hypertension

Out of 53 patients, 32 (60%) were males and 21(40%) were females, with male to female ratio of 3:2.

Table 2: Staging Of CKD

STAGING OF CKD	NO OF PATIENTS	PERCENTAGE
STAGE3	8	15%
STAGE4	12	22.6%
STAGE5	33	62.2%

Among chronic kidney disease patients 62.2% of patients belonged to stage 5 followed by 22.6% of patients belonged to stage 4 and 15% of patients belonged to stage 3 of CKD.

Table 3: Pattern Of Diuretics Prescribed In Ckd Patients

Diuretics	No Of Patients	Percentage
TORSEMIDE	27	50.9%
FUROSEMIDE	18	33.9%

METOLAZONE	4	7.5%
MEAN $\pm$ SD	16.33333333 $\pm$ 16.26345597	

Among the diuretics torsemide {27(50.9%)} is more frequently prescribed which is followed by furosemide {18(33.9%)} and metolazone {4(7.5%)}. The mean number of the patients prescribed with diuretics was 16.33 $\pm$ 16.26.

Table 4: Pattern Of Calcium Channel Blockers Prescribed In Ckd

Calciumchannel Blockers	No of Patients	Percentage
Cilnidipine	21	39.6%
Nifedipine	19	35.8%
Amlodipine	2	3.7%
Mean $\pm$ SD	14 $\pm$ 13.43502884	

Among calcium channel blockers cilnidipine{21(39.6%)} is more frequently prescribed which is followed by nifedipine {19(35.8%)} and amlodipine{2(3.7%)}. The mean number of the patients prescribed with calcium channel blockers were 14 $\pm$ 13.43.

Table 5: Pattern Of Alpha Blockers Prescribed In CKD Patients

Alphablockers	Noofpatients	Percentage
Prazosin	18	34%

Among the alpha blockers prazosin{18(34%)} was more frequently prescribed in chronic kidney disease patients.

Table 6: Pattern Of Beta Blockers Prescribed In Ckd Patients

Beta blockers	Noofpatients	Percentage
1.Nebivolol	15	28.3%
2.Metoprolol	8	15%
Mean $\pm$ SD	11.5 $\pm$ 4.949747468	

Among the beta blockers nebivolol{15(28.3%)} was more frequently prescribed which is followed by metoprolol {8(15%)}. The mean number of chronic kidney disease patients prescribed with beta blockers was 11.5 $\pm$ 4.94.

Table 7: Pattern Of Alpha Plus Beta Blockers Prescribed In Ckd Patients

Alphaplusbeta Blockers	Noofpatients	Percentage
Carvedilol	5	9.4%
Labetalol	1	1.8%
Mean $\pm$ SD	3 $\pm$ 2.828427125	

Among alpha plus beta blockers carvedilol{5(9.4%)} was frequently prescribed followed by labetalol {1(1.8%)} in chronic kidney disease patients. The mean number of chronic kidney disease patients prescribed with alpha plus beta blockers was 3 $\pm$ 2.8.

Table 8: Pattern Of Angiotensin Receptor Blockers Prescribed In Ckd Patients

Angiotensin receptor Blocker	No of patients	Percentage
TELMISARTAN	1	1.8%

Telmisartan {1(1.8%)} was prescribed among angiotensin receptor blockers in chronic kidney disease patients.

Table 9: Pattern Of Centrally Acting Sympatholytics Prescribed In Ckd Patients

Centrally acting Sympatholytics	No of patients	Percentage
Clonidine	8	15%

Among the chronic kidney disease patients the centrally acting drug was clonidine (8) with a percentage of 15%.

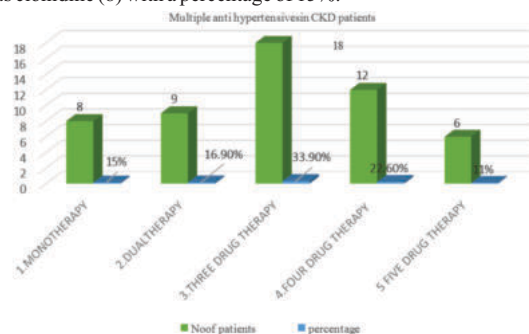


Figure 2: Pattern Of Multiple Anti - Hypertensive Therapies Prescribed In Ckd Patients

Among the Chronic kidney disease patients on antihypertensive medication 15% of patients were prescribed monotherapy, 16.9% of patients were given with dual drug anti-hypertensive therapy, 33.9% of patients received three drug anti-hypertensive therapy, 22.6% of patients were given four anti-hypertensive drugs and 11% of patients were prescribed with five drug anti hypertensive therapy. 45 patients constituting 90% were given multiple anti hypertensive drugs.

Table 10: Pattern Of Anti Hypertensive Drugs Prescribed In Ckd Patients

Antihypertensive Drugs	No of Patients	Percentage
1.Diuretics	44	83%
2.Calcium channel Blockers	41	77.3%
3.Betablockers	23	43.3%
4.Alpha blocker	18	33.9%
5.Alpha plus beta Blocker	6	11.3%
6.Angiotensin receptor Blockers	1	1.8%
7.Centrally Acting sympatholytics	8	15%
Mean±SD	20.14286±25.45584412	

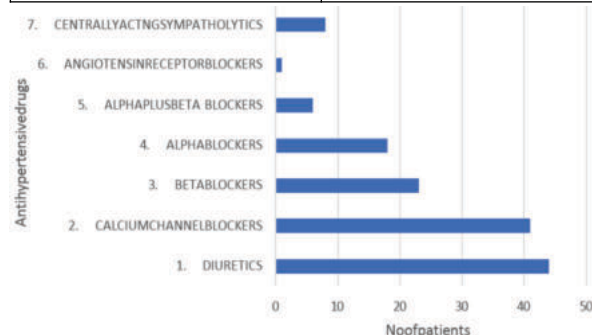


Figure 3: Pattern Of Anti Hypertensive Drugs Prescribed In Ckd Patients

Among the anti-hypertensives, most commonly prescribed were Diuretics which constitutes about 83%. Among them torsemide is prescribed in 28 patients followed by furosemide in 18 patients and metolazone was given only in 3 patients.

After diuretics, calcium channel blockers were frequently prescribed which constitutes about 77.3%. They include Cilnidipine prescribed for 21 patients, Nifedipine for 19 patients and Amlodipine only for 2 patients.

Third group of drugs in antihypertensives for CKD patients include β blockers which constitutes about 43.3%. They include Nebivolol given for 15 patients, followed by Metoprolol prescribed in 8 patients.

Fourth group of drugs include α blockers constituting about 33.9% which include prazosin given for 18 patients; centrally acting drugs were prescribed for 15% of patients like clonidine. Least commonly prescribed drugs were $\alpha+\beta$ blockers (11.3%) like Carvedilol (5) and Labetalol (1); and finally, Angiotensin receptor blockers (1.8%) like telmisartan which is administered only in one patient. Most frequently prescribed antihypertensive drug in this study was torsemide which is a diuretic and least prescribed was telmisartan which is an angiotensin receptor blocker. This might be because of their contraindication in chronic kidney disease patients.

DISCUSSION:

The attention paid globally to CKD is attributable to five factors: rapid increase in its prevalence, the enormous cost of treatment, recent data indicating that overt disease is the tip of an iceberg of covert disease, an appreciation of its major role in increasing the risk of cardiovascular disease, and the discovery of effective measures to prevent its progression.²⁶

In this study, the prescribing patterns of Anti hypertensive drugs used in the treatment of CKD have been studied. Also, an attempt has been made to find the preferable anti hypertensive drugs in chronic kidney disease patients.

A total of 53 patients who were diagnosed with chronic kidney disease and on antihypertensive than females medications were included in the study. Out of the 53 prescriptions evaluated, the prevalence of CKD

was more in males {32(60%)} {21(40%)} which is similar to a study done by P.Ansuman Abhisek et al.²¹

Patients aged between 51-60 years were the most affected which includes 30.1% followed by 41-50 years (20.7%), 31-40 years (18.8%), 61-70 years (13.2%), >70 years (9.4%), and <31 years (7.5%) respectively. The (mean±SD) age of the patients was 52.13±21. years with a range between 20 and 80 years.

Among chronic kidney disease patients {33(62.2%)} of patients belonged to stage 5 of CKD followed by {12(22.6%)} belonged to stage 4 and {8(15%)} belonged to stage 3 of CKD similar to study done by P. Ansuman Abhisek, et al.²¹

In this study the preferential classes of anti hypertensives prescribed for affording therapeutic benefit in chronic kidney disease patients were diuretics, calcium channel blocker, betablockers, alpha adrenergic blockers, centrally acting drugs, alpha plus beta blockers and ARBs. This study is similar to a study done by V.Jyothirmayee, et al.²⁴

Among the antihypertensives, diuretics 83.3% were the most frequently prescribed anti hypertensive drugs in our study which included torsemide, furosemide and metolazone followed by calcium channel blockers (77.3%) which included Cilnidipine, Nifedipine and Amlodipine. Cilnidipine has longer duration of action of 24 hours and also prevents reflex tachycardia as it selectively acts on both L and N type of calcium channels hence was most commonly prescribed among calcium channel blockers whereas torsemide is frequently used among diuretics because of its longer duration of action and increased potency.

The next group of drugs prescribed were Beta blockers (43.3%) which included nebivolol and metoprolol. Nebivolol being more frequently prescribed. Beta blocker is preferred in hemodialysis patients because of overactivity of Renin-Angiotensin-Aldosterone system and increased levels of sympathetic activity in hemodialysis patients. Hence Beta blockers might have been suggested to be more preferable in patients with chronic kidney disease undergoing hemodialysis. The fourth group of Antihypertensive drugs used were alpha blockers (34%) which included Prazosin.

The fifth group of drugs prescribed were centrally acting antihypertensives (15%) which consisted of Clonidine. Centrally acting Anti-Hypertensives act by lowering BP without compromising the renal blood flow or glomerular filtration rate.

The sixth group of drugs used were combined alpha plus beta blockers (11.3%) which included Carvedilol and Labetalol, carvedilol being more frequently prescribed.

The last group is Angiotensin Receptor Blockers (ARBs) like Telmisartan. Unlike CCBs, most of the Angiotensin Receptor Blockers (ARBs) need dose modification in renal failure. Effective results were found mainly in patients having proteinuria, whereas the benefit was less useful for those without proteinuria. One systemic review²⁷ showed that ARBs are very useful in CKD grade 1-3 patients, which reduces the End Stage Renal Disease risk. As most of the patients in this study are CKD stage 3 to 5, this might be contributed to under prescription of Angiotensin Receptor Blockers (ARBs).

In this study among the Chronic kidney disease patients on antihypertensive drugs majority of the patients were prescribed with multiple antihypertensive drugs, patients prescribed with dual drug therapy were 9 patients (16.9%), three anti hypertensives were preferred in 18 patients (33.9%), patients given with four anti hypertensive drugs were {12(22.6%)}, and patients receiving five anti hypertensives were {6(11%)} and lastly the remaining {8(15%)} received monotherapy which corroborates with the study of Ashika Ranjani. M et al.²²

CONCLUSION:

Patients with chronic kidney disease on antihypertensive medications were assessed and analyzed for prescription trends.

The preferential drugs employed among anti-hypertensives were diuretics, followed by calcium channel blockers, beta blockers, alpha blockers, beta plus alpha blockers, centrally acting anti-hypertensives and Angiotensin receptor blockers.

Among the antihypertensives prescribed Diuretics were more frequently prescribed and Angiotensin receptor blockers were least prescribed.

It provides a framework for continuous prescription audit in a hospital-based setting and suggests possible improvement and provide better insights into the prescription practices for practitioners in prescribing anti hypertensives to the patients suffering from chronic kidney disease.

Abbreviations:

1. CKD: Chronic Kidney Disease.
2. eGFR: Estimated glomerular filtration rate.
3. GFR: Glomerular filtration rate
4. AER: Albumin excretion rate.
5. ACR: Albumin to creatinine ratio.
6. RAAS: Renin angiotensin aldosterone system.
7. FSGS: Focal segmental glomerulo sclerosis.
8. CCBS: Calcium channel blockers.
9. EHR: Electronic health record data.
10. RHTN: Resistant hypertension.
11. ACE: Angiotensin converting enzyme.
12. ARB: Angiotensin receptor blocker.

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