

## Drug utilization pattern of antihypertensive drugs in chronic kidney disease stage 5 patients in a tertiary care hospital of central India

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### ABSTRACT

**Background:** India is experiencing a rapid health transition and is projected to become a major reservoir of chronic diseases like Diabetes and Hypertension and 25 to 40% of these subjects may develop chronic kidney disease and end stage renal disease. Aim and objective of the study was to analyze utilization pattern of antihypertensive drugs in chronic kidney disease patients in a tertiary care hospital.

**Methods:** The present observational cross-sectional study was conducted in Sri Aurobindo Institute of Medical Sciences, Indore (M.P.) from 01.01.2018 to 31.03.2018 on patients with chronic kidney disease stage 5. The drug utilization pattern was studied with respect to age, sex, basic disease, duration of dialysis, type of antihypertensive used, etc. Comparison of mean between gender and dialysis / not on dialysis was done using unpaired 't' test. A p value of < 0.05 was taken as statistically significant.

**Results:** Of 198 patients, 63 (31.8%) were females and 135 (68.2%) were males, showing a male preponderance. Majority of the patients (54%) belonged to the age group 41-60 years. Majority of the patients were having diabetic nephropathy (40.9%), followed by CGN-CKD 5d (18.7%) and CIN-CKD 5d (17.2%). 11.6% patients were not on dialysis, while 88.4% were on dialysis with a mean duration of dialysis of 31.45±34.57 months. Calcium channel blockers were given in 87.4% patients, followed by centrally acting drugs in 56.1% patients, beta blockers in 51.0% and alpha blockers in 39.9%. 93.9% patients were on multidrug antihypertensive therapy. Mean number of antihypertensives required in patients on dialysis was lower than those not on dialysis (2.69±1.44 vs. 3.48±1.16, p <0.05), similarly mean number of antihypertensives use in males was higher than females (2.99±1.41 vs. 2.32±1.37, p <0.05).

**Conclusions:** In order to treat CKD, it is important to treat hypertension as hypertension and CKD are related to each other. Treatment of hypertension will help in controlling future development of comorbidities. Calcium channel blockers and centrally acting drugs are the treatment of choice in patients with CKD stage 5D with hypertension. Multi-drug antihypertensive therapy is a better choice than mono/single-drug antihypertensive therapy.

**Keywords:** Antihypertensive use, Chronic kidney disease, End stage renal disease, Hemodialysis, Hypertension

### INTRODUCTION

Hypertension is the most common modifiable risk factor for cardiovascular diseases (CVD), stroke and renal failure.<sup>1</sup> It is the second leading cause of chronic kidney

disease (CKD). It is estimated that more than one billion adults are hypertensive worldwide and this figure is projected to increase to 1.56 billion by the year 2025, which is an increase of 60% from 2000. Cardiovascular diseases and Hypertension are accounting for loss of 4%

gross domestic product for low and middle-income countries annually which is amounting 500 billion USD.<sup>2</sup> Clinical evidence suggests that lowering blood pressure (BP) with antihypertensive drugs reduces the risk of myocardial infarction, stroke, heart failure, revascularization procedures and end-stage renal diseases in hypertensive patients.<sup>3</sup>

The increasing prevalence of hypertension has been attributed to population growth, ageing and behavioral risk factors, such as unhealthy diet, excess use of alcohol, sedentary lifestyle, obesity, and exposure to persistent stress. A whopping 9.4 million deaths occur worldwide every year because of hypertension, with it being responsible for about 50% of mortality due to heart disease and stroke.<sup>4,5</sup> Epidemiological studies demonstrated that prevalence of hypertension is increasing rapidly in India, varying from 4 to 15% in urban and 2-8% in rural population.<sup>6,7</sup>

Several guidelines have been developed worldwide for the management of hypertension, and these serve as reference standards for clinical practitioners. However, many clinicians practice their own prescribing pattern in treating hypertensive patients according to their clinical experience. Primary care physicians need to be empowered in appropriate and evidence-based management of hypertension. A review of these prescribing patterns and guideline-based use of antihypertensive medications can give better insights into the concept of personalised, yet cost-effective pharmacological management of hypertension.

Aim of the study was to analyze utilization pattern of antihypertensive drugs in chronic kidney disease patients in a tertiary care hospital.

## METHODS

The present observational cross-sectional study was conducted in Sri Aurobindo Institute of Medical Sciences, Indore (M.P.) from 1<sup>st</sup> January 2018 to 31<sup>st</sup> March 2018 on patients with chronic kidney disease stage 5 presenting to institution during the study period.

A customized proforma was designed for collecting the information for the study. Before enrolling the patient into the study, a detailed information about the study, its procedures, risks/benefits, etc. were explained to them and after obtaining their voluntary written informed consent for participation, the data from the records of the patients were looked into and their demographic details and antihypertensives drugs prescribed were collected.

The data was then entered into the Microsoft Excel for analysis and online statistical software were used for calculating the p values.

A total of 198 patients were included in the study.

## Inclusion criteria

- All patients diagnosed to have chronic renal disease stage 5, undergoing treatment in Nephrology unit of this hospital ward
- Patients and/or his/her legally acceptable representatives willing to provide their voluntary written informed consent for participation in the study

## Exclusion criteria

- Children, pregnant and lactating women, surgical conditions like kidney stone, tumors and trauma
- Patients and/or his/her legally acceptable representatives not willing to provide their voluntary written informed consent for participation in the study.

A written permission has been obtained from the Institutional Ethics Committee for the conduct of the study in this institution. The present study is a non-interventional study and does not involve any procedures / tests. Only data from the records of the patients were collected and also written informed consent form was obtained from the patients for allowing the researchers to look into the medical records. All the personal data of the patients was kept confidential and only data was used for research purpose.

## RESULTS

In the present study there were 198 patients, of which 63 (31.8%) were females and 135 (68.2%) were males, showing a male preponderance of chronic kidney disease in this study in comparison to the women. Majority of the patients belonged to the age group 41-60 years – 107 (54.0%), followed by 48 (24.2%) patients of age group 61-80 years and 37 (18.7%) patients of age group 21-40 years.

There were 8.1% patients with ADPKD (Autosomal Dominant Polycystic Kidney Disease), 18.7% patients were having CGN-CKD 5d, 17.2% patients were having CIN-CKD 5d, 40.9% patients were having diabetic nephropathy, 9.1% patients were having hypertensive nephropathy, 2.5% patients were having obstructive uropathy and 3.5% patients were having SLE - lupus nephritis (Table 1).

Of the 198 patients, 23 (11.6%) patients were not on dialysis, while the rest were on hemodialysis. In 24.2% patients the duration of dialysis was 1-6 months, in 11.1% patients it was 6-12 months, in 15.2% patients it was 13-24 months, in 24.7% patients it was 25-60 months and in 13.1% patients it was > 60 months. Majority of them had 24.7% patients had duration between 25-60 months with a mean duration of dialysis of 31.45±34.57 months (Table 2).

**Table 1: Distribution of patients according to basic disease.**

Basic disease	Number	Percentage
ADPKD	16	8.1
CGN-CKD 5d	37	18.7
CIN-CKD 5d	34	17.2
Diabetic nephropathy	81	40.9
Hypertensive nephropathy	18	9.1
Obstructive uropathy	5	2.5
SLE – Lupus Nephritis	7	3.5
Total	198	100.0

**Table 2: Distribution of patients according to duration of dialysis.**

Duration of dialysis	Number	Percentage
1-6 months	48	24.2
6-12 months	22	11.1
13-24 months	30	15.2
25-60 months	49	24.7
>60 months	26	13.1
Not on dialysis	23	11.6
Total	198	100.0

**Table 3: Distribution according to various types of antihypertensives.**

	Number	Percentage
<b>Calcium channel blockers</b>		
Nifedipine	81	40.9
Amlodepin	66	33.3
Cilnidipin	26	13.1
<b>Beta blockers</b>		
Metoprolol	60	30.3
Atenolol	14	7.1
Carvedelol	27	13.6
Others	0	0.0
<b>ATRB</b>		
Losartan	5	2.5
Telmisartan	16	8.1
Olmesartan	3	1.5
Others	0	0.0
<b>ACE inhibitors</b>		
Ramipril	3	1.5
Enalapril	0	0.0
Others	0	0.0
<b>Centrally Acting Drugs</b>		
Clonidine	65	32.8
Maxonidine	36	18.2
Minoxidil	10	5.1
<b>Alpha Blockers</b>		
Prazocin	76	38.4
Doxazocin	3	1.5

The calcium channel blockers viz. Nifedipine was used in 40.9% patients, Amlodepin in 33.3% patients and Cilnidipin in 13.1% patients. Beta blockers viz.

Metoprolol was used in 30.3% patients, Atenolol in 7.1% patients and Carvedilol in 13.6%. ATRB viz. Losartan was used in 2.5% patients, Telmisartan in 8.1% patients and Olmesartan in 1.5% patients. ACE inhibitors viz. Ramipril was used in 1.5% patients. Centrally acting drugs viz. Clonidine was used in 32.8% patients, Maxonidine in 18.2% patients and Minoxidil in 5.1% patients. Alpha blockers viz. Prazocin was used in 38.4%, Doxazocin in 1.5% patients. Diuretics viz. Furasemide in 7.1% patients, Torsemide in 16.2% patients and Metalazone in 6.6% patients (Table 3).

In 6.1% patients no antihypertensives were used, in 66.2% patients 1-3 antihypertensives were used, in 24.2% patients 4-5 antihypertensives were used and in 3.5% patients more than 5 antihypertensives were used. Majority of the patients were on 1-3 antihypertensives.

The mean number of antihypertensives required in patients on dialysis was 2.69±1.44, while number of antihypertensives required in patients not on dialysis was 3.48±1.16. The difference was found to be statistically significant (P<0.05), showing that more number of antihypertensives are required for patients not on dialysis in comparison to the patients on dialysis (Table 4).

**Table 4: Comparison of mean number of antihypertensives between dialysis and non-dialysis patients.**

Dialysis	No.	Mean±SD	't' Value	P value
On dialysis	175	2.69±1.44	-2.535, df=196	0.012*
Not on dialysis	23	3.48±1.16		

Unpaired 't' test applied. P value = 0.012 Significant

The mean number of antihypertensives required in males was 2.99±1.41, while number of antihypertensives required in females was 2.32±1.37. The difference was found to be statistically significant (P<0.05), showing more number of antihypertensives requirement in males in comparison to the females (Table 5).

**Table 5: Comparison of mean number of antihypertensives in relation to gender.**

Gender	No.	Mean±SD	't' Value	P value
Male	135	2.99±1.41	3.167, df=196	0.002*
Female	63	2.32±1.37		

Unpaired 't' test applied. P value = 0.002 Significant

**DISCUSSION**

In the present study 198 patients were enrolled. There was a male preponderance in this study with corresponds to results published by Joseph et al, who also reported a higher incidence of hypertension in males in comparison to the females.<sup>8</sup>

Majority of the patients were having diabetic nephropathy, followed by CGN-CKD 5d and CIN-CKD 5d.

Higher number of the patients with hypertension belonged to the age group 41-60 years, which is similar to that reported by Saju et al, who reported an incidence of 33% in the age group 51-60 years.<sup>9</sup>

Only 23 (11.6%) patients were not on dialysis, while the rest majority of the patients 175 (88.4%) were on dialysis, with 24.7% patients having duration between 25-60 months with a mean duration of dialysis of 31.45±34.57 months.

In the present study, calcium channel blockers were given in majority of the patients (87.4%), followed by centrally acting drugs in 56.1% patients, beta blockers in 51.0%, alpha blockers in 39.9%, ARTB in 12.1% patients and ACE inhibitors in 1.5% patients. Study done by Bhanu et al, also reported calcium channel blockers to be the most commonly prescribed antihypertensives (39.5%), followed by diuretics (25.1%). Saju et al, also reported a 70% use of calcium channel blockers in their study.<sup>9,10</sup>

In the present study most of the patients (93.9%) were treated with multi-drug antihypertensive therapy, while no antihypertensive was given in 6.1% patients. Study done by Elhami et al, also reported similar trend - 50% on two drug therapy and 20% on three drug therapy.<sup>11</sup> Higher number of antihypertensives use was seen in patients not on dialysis in comparison to the lower number of antihypertensives use in patients on dialysis (p<0.05).

In this study we found that the mean number of antihypertensive requirement in the males was higher in comparison to the females (p<0.05).

## CONCLUSION

In order to treat CKD, it is important to treat hypertension as hypertension and CKD are related to each other. Treatment of hypertension will help in controlling future development of comorbidities. Calcium channel blockers and centrally acting drugs are the treatment of choice in patients with CKD stage 5D with hypertension. Multi-drug antihypertensive therapy is a better choice than mono/single-drug antihypertensive therapy. Patients who are on dialysis and females require lesser number of antihypertensives than those patients not on dialysis.

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