

AN OBSERVATIONAL STUDY ON DRUG UTILIZATION PATTERN IN CHRONIC KIDNEY DISEASE PATIENT USING ANTIHYPERTENSIVE DRUGS IN A TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Background: Chronic renal disease and hypertension have a substantial correlation.

CKD patients have a high prevalence of HTN, which raises their risk of cardiovascular disease.

CKD drug usage trend for antihypertensive medications is the study's main goal. The study's goals were to ascertain the frequency of CKD stages in patients with chronic renal disease, the incidence of co-morbidities, and the development of an anti-hypertensive treatment strategy.

Methodology: This research was conducted over a six-month period at Dhiraj General Hospital in Vadodara using an observational/cross-sectional design. According to the study's criteria, CKD patients who were administered antihypertensive medications were included. By completing the patient medical record form, data was gathered.

Results: Based on inclusion and exclusion criteria, 60 CKD patients with HTN were included in the research. Among the sixty patients, we found that only thirty-three were OPD patients, compared to the sixty-seven inpatients. When it comes to gender proportionality, between the ages of 18 and 65, men make up 63% and women make up 37%. The research population as a whole had recorded systolic blood pressure in moderate cases of 140-159 mmHg and diastolic blood pressure of 90-99 mmHg. The mild instance had a diastolic blood pressure of 100–109 mmHg and a systolic blood pressure of 160–179 mmHg. Serum blood pressure in severe instances was measured to be

≥180 mmHg and ≥110 mmHg at the diastolic level. Antihypertensive calcium channel blockers were administered to 34.18% of patients, whereas furosemide was the most often suggested medication for patients with chronic hypertension in renal disease (19.34%). Multi-drug treatment was used to treat the majority of subjects.

Conclusion: In keeping with the National Kidney Foundation Kidney Disease Outcome Quality Initiative recommendations, calcium channel blockers and furosemide were strongly advised for patients with hypertensive CKD.

Keywords: drug use pattern; antihypertensive; chronic renal disease.

I. INTRODUCTION

Chronic Kidney Disease encompasses high degree kidney loss functionally. The kidney mainly functions to filter waste products and fluids from the blood and consequently release them into the urine. The underlying causes or risk factors of CKD are Hypertension, Diabetes, Obesity, elderly, family history of kidney diseases, low birth weight, smoking, alcohol consumption, cardiovascular diseases, hyperlipidemia, metabolic syndrome, etc [1]. Regardless of the underlying cause, once the reduction of renal function and loss of nephrons reaches a certain level, begins irreversible process resulting into the progressive decline of Glomerular filtration rate [2]. According to the National Health and Nutrition Examination Survey (NHANES) study, the prevalence of CKD in stage 3 was rise to 24.5% from 18.8%

during the year 2003-2006 from the year 1988-1994 respectively. Moreover, the overall prevalence of CKD in the SEEK (Screening and Early Evaluation of Kidney Diseases) study in India, the prevalence of the CKD stages 1,2,3,4, and 5 was 7%, 4.3%, 4.3%, 0.8%, and 0.8% respectively. On the other hand, the general population worldwide found a consistent estimated global CKD prevalence of 11-13% [3]. HTN is most often associated with co-morbid conditions with CKD. Moreover, it is considered the most modifiable risk factor of CKD and has been reported to occur in 85% to 95% of patients with CKD. It also considers as one of the leading causes of CKD due to the deleterious effects that increased BP has on kidney vasculature. Longterm, uncontrolled high BP patients are more vulnerable to CKD. Elevated BP results in increasing intraglomerular pressure and impairing the glomerular filtration, which ultimately leads to the damage of glomeruli and abnormally increased amounts of protein in the urine [4]. The National Kidney Foundation clinical practice guidelines recommended a blood pressure goal of ≤ 130 mmHg systolic and ≤ 80 mmHg diastolic for all CKD patients [5]. Moreover, International guidelines recommend lowering BP to 140/90 mmHg or less in patients with uncomplicated hypertension, and 130/80 mmHg or less in patients with diabetic or chronic renal diseases [6]. Several classes of antihypertensive agents play a significant role as nephroprotective in the treatment of CKD with HTN. Anti-hypertensive provides renal protection via two mechanisms: a reduction of BP and effects on intrarenal mechanisms of damage, such as glomerular pressure and proteinuria [7]. The present study was taken for assessing the prescription pattern of anti-hypertensive and also to assess the medication adherence in CKD patients. This helps in better controlling and hence improves the quality of life of CKD patients.

II. METHODOLOGY

It was a prospective cross-sectional study conducted for 6 months at the Department of General Medicine and Nephrology of the Dhiraj General Hospital, Vadodara. The study obtained ethical approval from the Sumandeep Vidyapeeth Institutional Ethics Committee (Ref no: (SVIEC/ON/Phar/BNPG18/D19006). All adult patients from Department of General Medicine and Nephrology between 18-65 years old having CKD with HTN were included in a study after explaining to the patients, the details of the study, the Informed consent form was taken. Patient's medical records were checked and following information were noted in Patient Medical Record sheet: Patient's demographic details, Patient Medical History, Diagnosis of the patient – CKD stages, age of onset of hypertension and chronic kidney disease and its duration, time since last hypertension and chronic kidney disease occur, family history of hypertension and chronic kidney disease and presence of other co-morbidities, Prescribed drugs including Anti- hypertensive (Frequency, Dose and Duration) was also collected, number of anti-hypertensive, doses was collected along with details of hypertension control on hypertensive, Lab investigations reports (which are already mentioned in patient medical records) All the relevant data was obtained from the patients' medical records and through counselling the patients who visited the OutPatient Department (OPD) or In-Patient Department (IPD). All the relevant data collected and recorded electronically. Descriptive statistics used for the analysis of the data. After the data collection, all the data were exported to statistical software for statistical analysis. All the quantitative data were represented in mean \pm standard deviation. Comparative statistical differences were calculated using appropriate parametric tests.

III. RESULTS

A total of 60 patients were included in the study. we noticed that the number of inpatients was 67% (n=40) while the number of OPD patients was just 33% (n=20). Comparing the gender proportionality, male represents 63% (n=38) and female represents 37% (n=22) of the total population. In our study, the age of patients varies from 18 to 65 years with a mean age of 53 ± 12.4 years. The maximum number of patients were from the age group of 45-65 years [71.67% (n=43)] followed by the age group 31-45 years [25.00% (n=15)], and lastly, the least number of patients were found in the age group of 18-30 years 3.33% (n=2)]. The average number of comorbidities of the overall study population was found to be 2.6 (± 1.15). The maximum number of co-morbidities was found to be 5. Out of 60 patients, 42% (n=25) had 2 number of comorbidities, 18% (n=11) had 3 number of comorbidities, 18% (n=11) had 4 number of comorbidities, 15% (n=9) had 1 number of comorbidities, 7% (n=4) had 5 number of comorbidities. The analysed data of 60 patients were then categorized based on the severity of CKD. There is a total of 5 CKD stages. The maximum number of patients having stage 5 CKD. Out of 60 patients, 58% (n=35) had stage 5 CKD, 27% (n=16) had stage 4 CKD, 7% (n=4) had stage 3B CKD, 7% (n=4) had stage 3A CKD, 1% (n=1) had stage 2 CKD, 0% (n=0) had stage 0 CKD.

Table 1. Patient's demographic data

Gender	No. of patients	Percentage
Male	38	63.33
Female	22	36.67
Age		
18-30	2	3.33
31-45	15	25.00
46-65	43	71.67
Co-morbidity		
1	9	15.00
2	25	41.67
3	11	18.33
4	11	18.33
5	4	6.67
CKD stages		
Stage 1	0	0
Stage 2	1	1.67
Stage 3A	4	6.67
Stage 3B	4	6.67
Stage 4	16	26.67
Stage 5	35	58.33

Hypertension is defined by the presence of an elevation of systemic arterial pressure above a certain threshold value. There are three types of classification of hypertension that is grade 1

(mild), grade 2 (moderate), and grade 3 (severe). [8] The recorded systolic BP in mild case in the overall study population was found to be 140-159 mmHg and diastolic BP was found to be 90-99 mmHg. In moderate case systolic BP was 160-179 mmHg and diastolic BP was found to be 100-109 mmHg. In severe cases systolic BP was ≥ 180 mmHg and diastolic BP was found to be ≥ 110 mmHg. Most of the CKD patients with HTN were treated with polypharmacy. 66.67% (n=40) of patients were taking multi-drug therapy (polypharmacy), 28.33% (n=17) of patients were taking double therapy and 5% (n=3) of patients were taking single therapy. Antihypertensive drugs used in the study population were identified and categorized based on their classification of drugs. Maximum antihypertensive class prescribed was calcium channel blocker [34.18% (n=63)] and minimum anti-hypertensive class prescribed was beta blocker non-selective [1.66% (n=3)]. Total no. of anti-hypertensive classes that were prescribed to 60 patients was 10. It was found that calcium channel blockers 34.18 (n=63) having frequency of 34.35% (n=113), diuretics-aldosterone antagonist 2.21% (n=4) having frequency of 2.43% (n=8), diuretic-loops 23.20% (n=42) having frequency of 24.92% (n=82), beta blockers-cardio selective 8.29% (n=15) having frequency of 6.69% (n=22), beta blockers-non selective 1.66% (n=3) having frequency of 1.52% (n=5), mixed alpha beta blockers 6.08% (n=11) having frequency of 4.56% (n=15), alpha-1 blocker 3.31% (n=6) having frequency of 3.34% (n=11), angiotensin receptor blockers 3.87% (n=7) having frequency of 2.74% (n=9), ACEinhibitors 2.21% (n=4) having frequency of 1.52% (n=5), central alpha 2 agonist 14.36% (n=26) having frequency of 17.93% (n=59) were the various antihypertensive classes prescribed to the study population. A total of 60 case records of patients having chronic kidney disease and on antihypertensive medications were collected and analysed. Maximum anti-

hypertensive drug prescribed was furosemide [19.34% (n=35)] and minimum antihypertensive drug prescribed was Azilsartan, Benidipine, Bisoprolol, Moxonidine [0.55% (n=1)]. Total no. of anti-hypertensive drugs that were prescribed to 60 patients was 181 and its

Table 2. Total number of patients having systolic BP

Grade	Systolic	No of patients	Percentage
Mild	140-159	20	51.28
Moderate	160-179	9	23.08
Severe	≥180	10	25.64

Table 3. Total number of patients having diastolic BP

Grade	Diastolic	No of patients	Percentage
Mild	90-99	27	61.36
Moderate	100-109	10	22.73
Severe	≥110	7	15.91

Table 4. Clinical parameters

Urea (mg/dL)	Creatinine (mg/dL)	Hemoglobin (g/dL)	Total Count	Differential count	
				Neutrophils	Lymphocytes
128.58	7.55	9.44	10150.65	74.30	17.91

Table 5. Treatment pattern in patients

Therapy	No. of patients	Percentage
Multi drug therapy (polypharmacy)	45	65.67
Double therapy	17	28.33
Single therapy	3	5

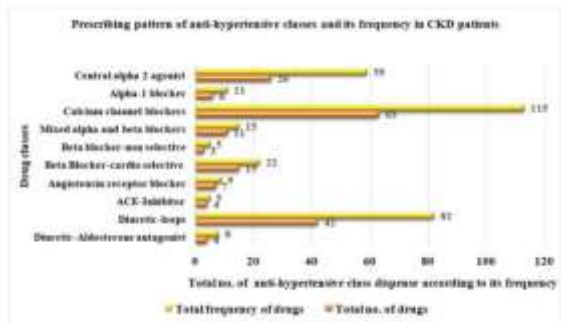


Fig. 1. Prescribing pattern of anti-hypertensive classes and its frequency in CKD patients

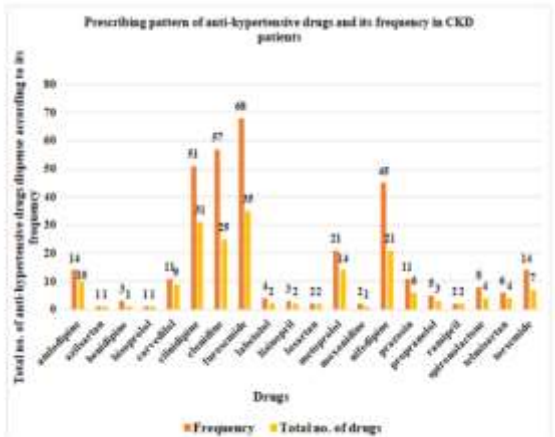


Fig. 2. Prescribing pattern of anti-hypertensive classes and its frequency in CKD patients

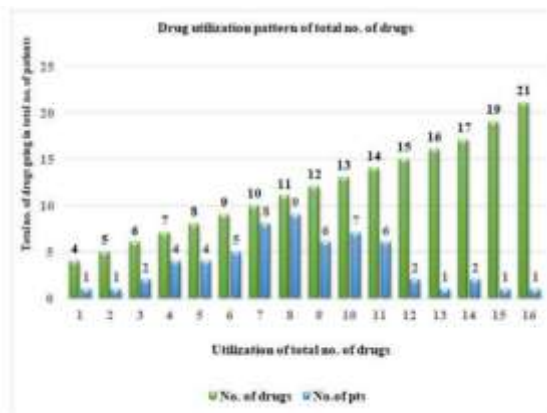


Fig. 3. Drug utilization pattern of total no. of drugs

total frequency was 329. It was found that amlodipine 5.52% (n=10) having frequency of 4.26% (n=14), Azilsartan 0.55% (n=1) having frequency of 0.30% (n=1), Benidipine 0.55% (n=1) having frequency of 0.91% (n=3), bisoprolol 0.55% (n=1) having frequency of 0.30% (n=1), carvedilol 4.97% (n=9) having frequency of 3.34% (n=11), cilnidipine 17.13% (n=31) having frequency of 15.50% (n=51), clonidine 13.81% (n=25) having frequency of 17.33% (n=57), furosemide 19.34% (n=35) having frequency of 20.67% (n=68), labetalol 1.10% (n=2) having frequency of 1.22% (n=4), lisinopril 1.10% (n=2) having frequency of 0.91% (n=3), losartan 1.10% (n=2) having frequency of 0.61% (n=2), metoprolol 7.73% (n=14) having frequency of 6.38% (n=21), Moxonidine 0.55% (n=1) having frequency of 0.61% (n=2), nifedipine 11.60% (n=21) having frequency of 13.68% (n=45), prazosin 3.31% (n=6) having frequency of 3.34% (n=11), propranolol 1.66% (n=3) having frequency of 1.52% (n=5), ramipril 1.10% (n=2) having frequency of 0.61% (n=2), spironolactone 2.21% (n=4) having frequency of 2.43% (n=8), % (n=9) having frequency of 3.34% (n=11), % (n=9) having frequency of 3.34% (n=11), telmisartan 2.21% (n=4) having frequency of 1.82% (n=6) and torsemide 3.87% (n=7) having frequency of 4.26% (n=14) were the various antihypertensive drugs prescribed to the study population.

The average total number of drugs was found to be 11.2 (± 3.3). Total no. of drugs 4, 5, 16, 19, 21 respectively was found to be 1.67% (n=1) followed by total no. of drugs 6, 15 and 17 respectively was found to be 3.33% (n=2) followed by total no. of drugs 7 and 8 respectively were found to be 6.67% (n=4) followed by total no. of drugs 9 was found to be 8.33% (n=5) followed by total no. of drugs 12 and 14 was found to be 10% (n=6) followed by total no. of drugs 13 was found to be 11.67% (n=7) followed by total no. of drugs 10 was found to be 13.33% (n=8) followed by total no. of drugs 11 was found to be 15% (n=9). The average total number of drugs was found to be 3.01% (± 1.13). Total no. of anti-hypertensive drugs 1, 6 and 3 respectively were found to be 5% (n=3) followed by total no. of anti-hypertensive drugs 4 respectively were found to be 15% (n=9) followed by total no. of anti-hypertensive drugs 2 respectively was found to be 28.33% (n=17) followed by total no. of anti-hypertensive drugs 3 respectively was found to be 41.67% (n=25).

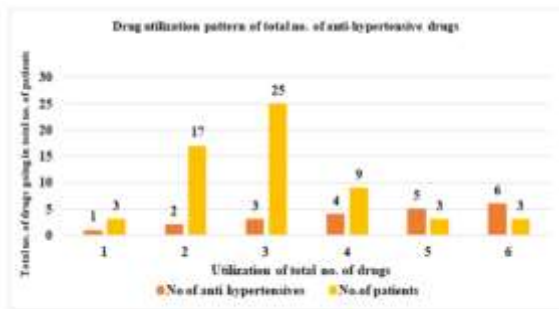


Fig. 4. Drug utilization pattern of total no. of anti-hypertensive drugs

IV. DISCUSSION

This study includes data of 60 CKD patients from the general medicine and Nephrology ward with an evaluation of antihypertensive drugs in CKD patients were analysed. The demographic results of the study revealed gender distribution of male and female with age between 18- 65 years are 64.29% (N=36) and 37.5% (N=21) respectively, similar to the study conducted in Bangalore, India in which a total number of 105 renal failure patients are participating, out of

which 65 (61.9%) were male and 40 (38.09%) were female [9]. Another study was carried out at Chitradurga, India; where 72.5% were males and 27.5% were females [10]. Hence, the susceptibility of hypertension with CKD could be more probable in males as compared to the female. However, considering the age distribution of patients by three groups i.e., 18-30 age, 31-45 age, and 46-65 age, the percentage of hypertension with CKD patients were 3.51%, 24.56%, and 71.93% respectively. Hence, the majority of study participants were in the group of geriatrics (age 46-65 years), similar to the study performed at Mysore Medical College and Research Institute, Mysore, India having 49.47% of the patients belonged to the age group of 40 – 60 years followed by 31 – 40 years (26.32%) [11]. The mean age of CKD patients prescribing antihypertensive drugs is around 52.32 years, same as the study carried out by ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) in which average age was 54 years [12]. Similarly, another study conducted in Japan reported that CKD is more prevalent in the elderly as compared to young/middle-aged individuals having hypertension for 2 or more years. Moreover, Indiana University and VAMC, Indianapolis, had the same results including the mean number of antihypertensive agents used was 2.66 in CKD patients. The utilization of antihypertensive drugs per prescription is a significant index of the prescription audit. Despite, the use of multi antihypertensive drugs in hypertensive patients with CKD, achieving the optimal BP control is challenging. Antihypertensive therapy recommended as monotherapy in the present study is 4 (7%) and polytherapy is 56 (93%) was comparable to the study carried out at Bangalore, India which antihypertensive drugs were prescribed as monotherapy in 5 (4.76%) patients, two-drug combinations were prescribed to 55 (52.38%) patients whereas 3 drug combinations were

prescribed to 45 (42.85%) patients [9]. Same study performed at Assam, India; monotherapy (65%), receiving two drugs therapy (80%), and polytherapy (20%). It was stated that ACEIs (angiotensin-converting enzyme inhibitors) and ARBs (angiotensin receptor blockers) are recommended as 1st line antihypertensive therapy for CKD patients, followed by CCBs (calcium channel blockers) and diuretics. It is concluded that 16% of the patients are been prescribed with ACEIs/ARBs according to the national kidney foundation/kidney diseases outcomes quality guideline. A total of 60 hypertensive patients with CKD were observed for anti-hypertensive prescribing pattern, out of which CCBs are mostly prescribed agents(34.80%), followed by loop diuretics(23.20%), central α_2 agonist (14.36%), β -blockers (8.28%), angiotensin receptor blockers (3.86%) and angiotensin converting enzyme inhibitors (2.20%), relevant to the study carried out at Assam, India; which includes CCBs have mostly used drugs despite their fewer side-effects and patient who are follow-up are commonly recommended combination antihypertensive therapy. Another relevant study carried out at Chitradurga, India; 74.16% of patients have been prescribed calcium channel blockers, and the most commonly prescribed in CCBs is Amlodipine (50%) [9,10]. Similarly, in a study performed in Israel, diuretics recommended controlling the expansion of intravascular volume caused by fluid retention [13]. Another study carried out at Philadelphia; a combination of the selective antihypertensive drug along with appropriate diuretics and non-pharmacological therapy is the rational use for hypertension with CKD [14]. In the present study, diuretics specifically furosemide is highly prescribed agents in the patients (19.34%) was comparable to the study carried out in the US; 70% of patients recommended multidrug antihypertensive therapy including ARBs/ACEIs, and 37% prescribed as diuretics

[15]. The study conducted in Tokyo; Japan suggested that diuretics may be better than CCBs for urinary excretion of protein [16]. The targeted BP control achieving in CKD patients is difficult and challenging despite the recommended guidelines and antihypertensive drugs. The study conducted at Chitradurga, India showed that a total of 120 CKD patients were analysed for prescribing patterns of antihypertensive agents, in which the recorded value of systolic blood pressure was 172.17 ± 21.309 and diastolic blood pressure was 97.33 ± 13.704 . [10] In the present study, the recorded systolic and diastolic BP in 60 patients were 152.1333 ± 27.02194 and 93.61667 ± 15.80184 respectively. Moreover, the relevant study conducted in Spain record the ABPM (Ambulatory BP Monitoring) 24-hr systolic blood pressure (SBP), awake SBP, and sleep SBP. Thus, ABPM hypertension is considered to be more severe due to increasing sleep systolic BP [17]. Another study carried out in Japan showed that the average BP of elderly and young/middleage patients were $134 \pm 10 / 71 \pm 9$ mmHg and $131 \pm 11 / 78 \pm 9$ mmHg, respectively [18]. CKD is more potent in elderly patients and failed to achieve the targeted BP goal. Despite the hypertension leading cause and sequel of chronic kidney diseases, the other most associated co-morbidity is diabetes mellitus along with hypertension. The group 2 patients having two associated co-morbidities along with CKD are highest i.e., 40.35%. The other comorbidity along with CKD in patients is dyslipidaemia, pulmonary TB, obstructive uropathy, ischemic heart diseases, sepsis, etc. Creatinine is the predominant diagnostic marker in the evaluation of CKD in hypertensive patients. The estimated GFR and creatinine in patients with CKD have a significant effect on diagnosis. As compared to the study carried out by ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial), mean serum creatinine was 2.2 mg/dL in

men and 1.8 mg/dL in women [12]. The resultant mean \pm SD creatinine of our study was 7.55 ± 6.72 . Among the CKD stages I- V, the highest prevalence of hypertension is associated in stage IV and stage V with 26.31% and 59.64% respectively as compared with the study by the American Journal of Kidney Diseases having 9%-39% in individuals with stage 5 CKD [19]. Another study carried out at Yale University School of Medicine, New Haven showed that the prevalence of CKD is highest in stage 4 and stage 5 [20]. Moreover, cardiovascular mortality and morbidity increase in higher rates in stage 5 before progressing into dialysis/transplantation. However, patients with hypertension with stage IIIA and stage IIIB have similar prevalence i.e., 6.67% and there is significantly low data of hypertensive patients with stage II CKD. Therefore, patients with stage IV and stage V require more intensive care and treatment in comparison to other stages. Therefore, physicians should prescribe agents considering independent criteria of age, stagespecific, identification of hypertensive CKD patients, and other risk factors associated with CKD.

V. CONCLUSION

This study represents prospectively the pattern and use of antihypertensive medications in patients with CKD with HTN, where the most affected age group was found to be 31-45 in both males and females. This is due to the increased use of anti-hypertensive drugs in CKD patients with HTN at tertiary care hospital. This research shown that patients were administered the maximum amount of Anti-HTN medications, with an average of 3.01 HTN medications per individual, resulting in polypharmacy. Where the highest

Hadia et al.; JPRI, 33(35B): 9–18, 2021; Article no.JPRI.69770 17 Calcium channel blockers were found to be the most often used antihypertensive class, while non-selective beta-blockers were the lowest antihypertensive class

that was recommended. It is followed by a breakdown of medication frequency: furosemide had the highest use, while roxonidine, bisoprolol, benidipine, and acilartan exhibited the lowest utilization. Clinical parameters were also emphasized in this research, with the most data coming from patients with Stage 5 CKD and the least amount from those with Stage 1 CKD. Additionally, blood pressure was measured at several phases, with the majority of patients having moderate systolic and diastolic blood pressure in both groups.

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