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Research Article

STUDY OF ANTIHYPERTENSIVE DRUG UTILIZATION PATTERN IN CHRONIC KIDNEY DISEASE PATIENTS

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ABSTRACT

Introduction: Hypertension is a chronic illness associated with high morbidity & mortality, with a rising number of patients with hypertension and chronic kidney disease, achieving blood pressure of less than 140/90 mm of Hg is challenging. Hence, there is a need for appropriate, safe, effective and economical study to find out the patterns of drug therapy.

Objectives: To evaluate utilization patterns of antihypertensive agents in chronic kidney disease patients.

Methodology: A prospective observational study was conducted for a period of 6 months in Jayanagar General Hospital, Bengaluru. We included 70 hypertensive CKD patients. Detailed patient information data were noted, and data entered in a preformed proforma in Microsoft Excel sheet for compilation and subjected to statistical analysis.

Results: Total 70 case records of patients having chronic kidney disease were analysed. Mean age was 52.08 ± 15.14 . CKD was more prevalent in males 38 (54.2%) and 32 (46.8%) females with male to female ratio of 2.3:2. Most of the patients (52.80%) belonged to age group of 41-60 years. Among the anti-hypertensive agents, most frequently used was calcium channel blockers (91.4%), followed by diuretics (54.2%), Beta blockers (31.4%), alpha blockers, ACE inhibitors and ARB.

Conclusion: Dual and triple therapy were prescribed which was according to ESH guidelines. This study highlights some therapeutic rationality in this health centre. However,

targeted education of the prescription-givers and dissemination of treatment guideline could facilitate rational use of drugs and adherence to treatment guidelines.

Keywords: Hypertension; Chronic kidney disease; Drug utilization; ESH Guidelines; Treatment.

INTRODUCTION

According to WHO, Hypertension is defined as a systolic blood pressure (SBP) of 140 mmHg or more, or a diastolic blood pressure (DBP) of 90 mmHg or more. Hypertension is a common disease that is simply defined as persistently elevated arterial blood pressure (BP). Although elevated BP was perceived to be “essential” for adequate perfusion of essential organs during the early and middle 1900s, it is now identified as one of the most significant risk factors for cardiovascular (CV) disease. Increasing awareness and diagnosis of hypertension, and improving control of BP with appropriate treatment, are considered critical public health initiatives to reduce CV morbidity and mortality. Hypertension is an important public health challenge in both economically developing and developed countries. In India, cardiovascular diseases (CVDs) are estimated to be responsible for 1.5 million deaths annually. Hypertension is a major risk factor for CVDs, including stroke and myocardial infarction, and its burden is increasing disproportionately in developing countries as they undergo demographic transition.

Complications of Hypertension

- Stroke
- Cerebral/brainstem infarction
- Cerebral haemorrhage
- Lacunar syndromes
- Multi-infarct disease
- Hypertensive encephalopathy/ malignant hypertension

- Dissecting aortic aneurysm
- Hypertensive nephron-sclerosis
- Peripheral vascular disease (Walker R et al., 2012)

Globally CKD is a major threat because of an increasing incidence, long term hospital stay, high cost of treatment and poor outcome associated with various complications and co-morbidities. CKD is an array of heterogeneous disorders affecting renal architecture and function as well. The Kidney Disease Outcomes Quality Initiative (KDOQI) of the National Kidney Foundation defines CKD as kidney damage and/or a decreased glomerular filtration rate of less than 60 mL/min/1.73 m² for three months or more. Hypertension (HTN) has been reported in most of patients with CKD (Stages III-V). (Kearney PM et al., 2004)

In India, the incidence of CKD is rising, and as per estimates from 006, the age-adjusted incidence rate of end-stage renal disease (ESRD) is 229 per million populations. Further, the number of new patients entering renal replacement programs annually is >100,000. The rising incidence of CKD in India is likely to burden healthcare and the economy in the future (Walker R et al., 2012).

Study Criteria

Inclusion Criteria:

- Patients treated for hypertension and chronic kidney disease with or without other co morbid conditions like Diabetes mellitus, and other associated cardiovascular diseases.

Exclusion Criteria:

- Pregnant and lactating patients.
- Age below 18 and above 90 years.
- Terminally ill patients co-infected with HIV or Hepatitis or with any infective conditions or with any autoimmune diseases or continuing medications for the same.
- Patients with renal transplant.

MATERIAL AND METHODS

A descriptive, prospective and hospital-based study was conducted in Jayanagar General Hospital, Bangalore over a period of 6 months, after obtaining the clearance and approval from the Institutional Ethics Committee, 70 in-patients were included in the study. The patients were diagnosed of having Chronic Kidney Disease by the consultant Nephrologist according to KDOQI guidelines.

Statistical analysis

Descriptive statistics is done by measuring different proportions. statistical measurement was done in SPSS trial version 24.0. Graphical representation was done in using Microsoft Excel.

RESULTS

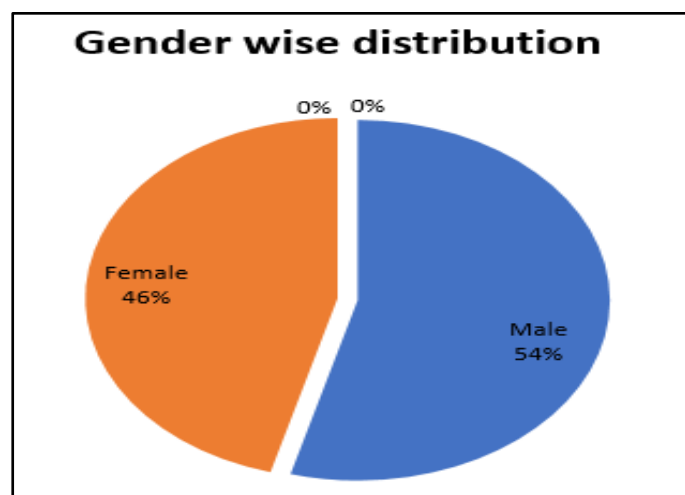
Gender wise distribution

During the study period, a total of 70 hypertensive patients were included. Out of 70 patients, 38 (54.2%) were male and 32 (45.8%) were females (Table 1 and Figure 1).

Table 1: Gender wise distribution of patients

S. No	Gender	Numbers	Percentage (%)
1	Male	38	54.2
2	Female	32	45.8

Figure 1: Gender wise distribution of patients.



Age wise distribution

Out of 50 patients, 37 (52.8%) belonged to age group of 41-60 years, followed by 17 (24.2%) belonged to 61-80 years and 12 (17.1%) belonged to 21-40 years. Mean age in study subject was 52.08 ± 15.14 years (Table 2).

Table 2: Age wise distribution of hypertension

S. No	Age group	Total No	Males	Females	Total percentage (%)
1	18-20	2	1	1	2.8
2	21-40	12	6	6	17.1
3	41-60	37	23	14	52.8
4	61-80	17	7	10	24.2
5	>80	2	1	1	2.8

Distribution of patients based on social habits

Out of 70 patients, we found that 13 (18.5%) patients were smokers alone in which 8 (61.5%) were males and 5 (38.4%) were females and 14 (20%) patients were alcoholic in which 8 (57.1%) were males and 6 (42.8%) were in females. Patients having habit of both alcoholic and smoking were found to be 23 (32.8%) in which 19 (82.6%) were males and 4 (17.3%) were females. 20 patients have not had any habits mentioned (Table 3).

Table 3: Social habits of the patients

S. No.	Social Habits	Total	Male	Female
1	Smokers	13	8	5
2	Alcoholics	14	8	6
3	Both	23	19	4
4	None	20	3	17

Comorbid conditions

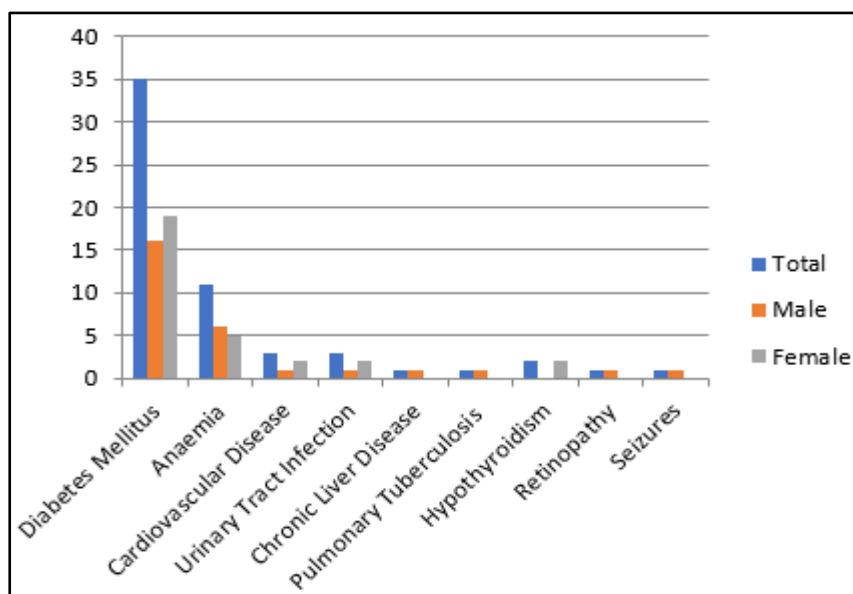
Majority of the patients were suffering from concurrent diabetes mellitus (50%). Other commonly associated conditions were Anaemia (15.7%), Cardiovascular Disease (0.42%), Urinary Tract Infection (0.57%), Chronic Liver Disease (0.14%), Pulmonary Tuberculosis

(0.14%), Hypothyroidism (0.28%), Retinopathy (0.14%) and Seizures (0.14%) (Table 4 and Figure 2).

Table 4: Co-morbid conditions.

S. No	Co-morbid conditions	Total	Male	Female
1	Diabetes Mellitus	35	16	19
2	Anemia	11	6	5
3	Cardiovascular Disease	3	1	2
4	Urinary Tract Infection	3	1	2
5	Chronic Liver Disease	1	1	0
6	Pulmonary Tuberculosis	1	1	0
7	Hypothyroidism	2	0	2
8	Retinopathy	1	1	0
9	Seizures	1	1	0

Figure 2: Co-morbid conditions.



Antihypertensive drugs use pattern

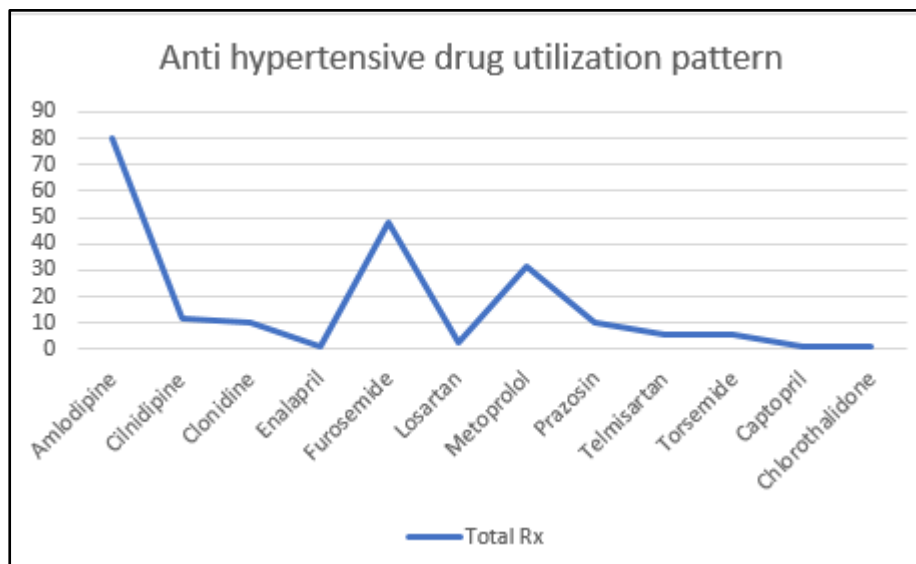
In our study, out of 70 patients we concluded that 39 patients had received two anti-hypertensive drugs (55.7%), followed by both one and three anti-hypertensive drugs (25.7%) and four antihypertensive drugs. Among the antihypertensive drugs, amlodipine (CCB) was

the most commonly prescribed drug (80%) followed by furosemide (loop diuretic) (48.5%), metoprolol (beta blocker) (31.4%), cilnidipine (CCB) (11.4%), torsemide (diuretic) (5.7%) telmisartan (ARB) (5.7%), losartan (ARB) (2.85%), prazosin (alpha blocker) (10%), clonidine (centrally acting alpha-agonist) (10%), metoprolol (beta blocker) (4%) and enalapril (ACEI) (1.42%), chlorothalidone (thiazide diuretic) (1.42%),captopril (ACEI) (1.42%) (Table 5 and Figure 3).

Table 5: Number of prescriptions with anti-hypertensive drugs.

S. No	Anti-Hypertensive Drugs either given alone or in Combinations	Percentage of Prescriptions
1	Patients treated with Calcium channel blocking agents	91.4
2	Patients treated with Beta - Adreno receptor Blocking agents	31.4
3	Patients treated with Diuretics	54.2
4	Patients treated with ACE inhibitors	2.85
5	Patients treated with Alpha – adreno receptor Blocking agents	10
6	Patients treated with Angiotensin Receptor Antagonist	8.5
7	Patients treated with Centrally acting anti-hypertensive agent (Clonidine)	10

Figure 3: Anti-hypertensive agents use pattern.



Combination therapy (Table 6)**Table 6:** Number of combination therapy.

Therapy	No. of Prescription	Percentage (%)
Mono therapy	18	25.7
Dual Therapy	29	41.4
Triple Therapy	18	25.7
Combination of four	5	7.14

Percentage adherence to ESH 2018 GUIDILINES: HT+CKD

Out of 70 patients 47 were prescribed in accordance to the ESH guidelines European society of hypertension. Percentage adherence to ESH guideline in relation to treatment of hypertensive patients with compelling indication (s) was found to be 67.1% (Table 7).

Table 7: Percentage adherence to European society of hypertension.

Variables	No. of prescriptions	Percentage (%)
Adherence	47	67.1
Nonadherence	23	32.9

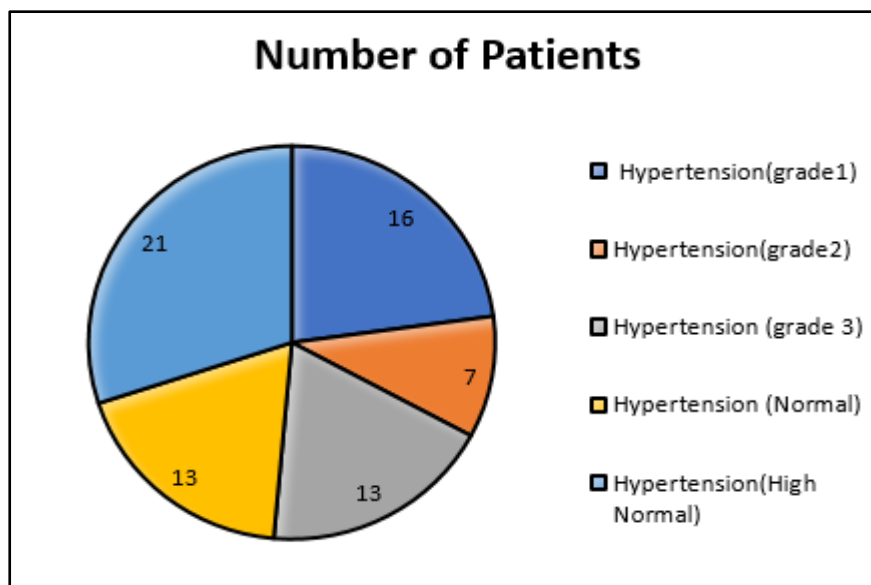
Categorization of hypertensive patients based on blood pressure reading

In our study that included 70 hypertensive CKD patients, 5 were having severe hypertension requiring intensive anti-hypertensive therapy with more than one antihypertensive agent, 13 were having moderate hypertension requiring pharmacological intervention and remaining 32 were in controlled blood pressure. The categorization is done based on ESH Guidelines 2018 (Table 8 and Figure 4).

Table 8: Categorization of hypertensive patients based on blood pressure reading.

S. No.	Blood Pressure Reading	No. of Patients
1	Hypertension (Grade 1)	16
2	Hypertension (Grade 2)	7
3	Hypertension (Grade 3)	13
4	Hypertension (Normal)	13
5	Hypertension (High Normal)	21

Figure 4: Categorization of hypertensive patients based on blood pressure reading (ESH Guidelines 2018).



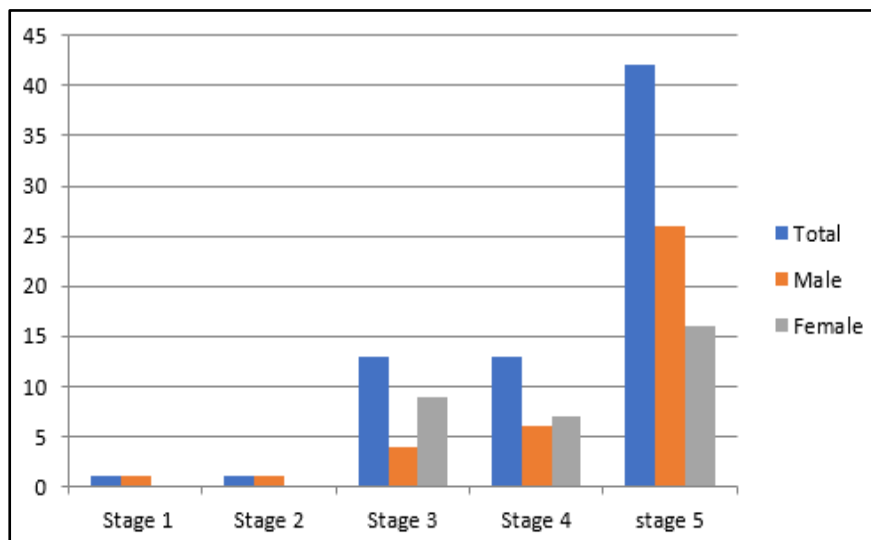
Categorization chronic kidney disease patients according to eGFR with MDRD Method

Out of the 70 patients, 42 patients were in stage 5 (60%) among them 26 (61.9%) were male and 16 (38.09%) were female. 13 were in stage 4 (18.5%) among them 6 (46.1%) were male and 7 (53.85) were female. 13 patients were in stage 3 (18.5%) among that 4 (30.7%) were male and 9 (69.2%) were female. 1 patient in stage 1 and 1 patient in stage 2 which of them were male (Table 9 and Figure 5).

Table 9: Categorization chronic kidney disease patients according to eGFR with MDRD method.

S. No.	Stages	Total patients	Male	Female
1	Stage 1	1	1	0
2	Stage 2	1	1	0
3	Stage 3	13	4	9
4	Stage 4	13	6	7
5	Stage 5	42	26	16

Figure 5: Categorization chronic kidney disease patients according to eGFR with MDRD method.



DISCUSSION

Drug utilization study is described as “The marketing, distribution, prescription and utilization of drugs in the society, with special attention to the resulting medical, social and economic consequences” and has the main objective of facilitating the rational use of drugs which is very important in decision making for healthcare set ups. A prescription survey is one of the most effective methods to evaluate the prescribing attitude of doctors. It is also important to consider the guidelines of international regulatory associations on the management of hypertension that will improve prescribing practice of the physicians and ultimately, the clinical standards. This practice will eventually, help to promote rational use of drugs (Abhisek PA et al., 2017).

The study on antihypertensive drug utilization pattern in presence of chronic kidney disease included 70 patients. According to gender wise distribution it was found that males were slightly more predisposed to the HTN with CKD than females. A similar study concluded that male population was (58.4%) slightly at the higher end for the condition than the females, which was like our study (Sarafidis PA et al., 2012; Verberne WR et al., 2019).

Another study in Odisha reveals the mean age of the hypertensive CKD patients was 49.26 ± 11.46 years somewhat close to our study results that is 52.08 ± 15.14 years (Abhisek PA et al., 2017).

In our prescription-based survey, the prominent findings were, out of 70 prescriptions, most of the subjects were of the age group between 41-60 years of age. Two patients were found between 18-20 and two above 80 years of age, this distribution shows that the age group of 41-60 were more prone to have CKD along with hypertension. According to a study conducted in Cuttack, majority of the patients were in the age group of 41-60 years compared to other age groups reflecting the similar pattern with our study years (Abhisek PA et al., 2017).

In our survey, combination therapy was most widely prescribed regimen by the physicians. Earlier studies have revealed that an ideal combination must have antihypertensive drugs possessing complementary modes of action that provide a synergistic effect with minimal adverse effects. Most hypertensive diabetic patients with normal renal function require a combination of two to three antihypertensive agents to lower blood pressure to $<130/80$ mmHg; patients with concomitant chronic kidney disease may require three or more agents. Combination therapy is required for optimal blood pressure control and prevention of cardiovascular, renal and neurological complications.

Out of 70 patients, we found that 13 (18.5%) patients were smokers alone in which 8 (61.5%) were males and 5 (38.4%) were females and 14 (20%) patients were alcoholic in which 8 (57.1%) were males and 6 (42.8%) were in females. Patients having habit of both alcoholic and smoking were found to be 23 (32.8%) in which 19 (82.6%) were males and 4 (17.3%) were females. 20 patients have not had any habits mentioned.

In this survey, most commonly prescribed monotherapy was calcium channel blocker (80%) in our study corroborate with the study (Bailie GR et al., 2005). In our study the second most used mono therapy was by loop diuretics (48.5%) however in another study, the most prescribed drug class was ACE inhibitors /ARB which is not similar with our results. In elderly patients, the preferred antihypertensive by the physicians were calcium channel blockers (Magvanjav O et al., 2019).

Our study elicited that most of the patient who were hospitalized were in Stage V (60%) followed by stage 4 (18%) and stage 3 (18%).

Co-morbidities associated with hypertension and CKD were seen in all 52 patients, Diabetes mellitus in 67.3%, anaemia in 21% and other conditions included urinary tract infection and those related to CVS. Most of the studies have shown diabetes mellitus as the favourite co-morbidity in the similar patients.

These findings indicate that medication use was consistent with the international recommendations from JNC 8 and European Society of Hypertension among hypertensive CKD patients (James PA et al., 2014).

CONCLUSION

Amlodipine and furosemide were the most frequently prescribed antihypertensive drugs. Prescription of antihypertensive drugs for some patients with compelling indications (specifically CKD), were very much congruent with ESH guideline. This study highlights some therapeutic rationality in this health centre. However, targeted education of the prescription-givers and dissemination of treatment guideline could facilitate more rational use of drugs and better therapeutic outcomes.

Control of hypertension and maintenance of ideal blood pressure is the root point that would benefit the CKD patients most maintaining their renal health and related complications. Pharmacists must become more vigilant about current guidelines for the treatment as well as the ADR detection of some antihypertensive which can impact renal functions on patients with concomitant hypertension and Chronic Kidney Disease.

Strategies such as patient education and medication assessment can help to optimize care for these patients and slow the progression to chronic kidney disease. Many patients with CKD and hypertension are still out of reach of specialized care. Specific risk factors determined may aid in identifying patients at high-risk for inadequate treatment. Patient and education provider, public health approaches, and health system changes are needed to address these issues. As the population grows older renal function also tend to decrease proportionally,

hence kidney injuries becomes more prominent at the same time condition as hypertension tend to double the risk factor for such age group.

LIMITATIONS

In spite of several limitations like inadequate sample size, study duration, point prevalence nature of the collected data and being unicentric, this study provided a profile of drug utilisation pattern in hypertensive CKD patients compared by class and also individualistic comparison of drugs in the same class. This study will serve as a basis for future comparison. Certain areas like potential drug-drug interaction, AEs and adherence are needed to be explored further.

Fair portion of the drugs were prescribed from the prescribers and all the available medication in hospital were written in generic name. So, it is the need of the hour to avail all the required medication in the institution to prescribe rationally. Continuous prescription audit from the clinical pharmacists in government sector will improve the utilization pattern and therapeutic outcomes in economically challenged hypertensive CKD patients.

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