



Study of Pattern of Antihypertensive Use in Subjects with Chronic Kidney Disease in A Tertiary Care Hospital

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Received: 10-05-2023; Revised: 20-07-2023; Accepted: 26-07-2023; Published on: 15-08-2023.

ABSTRACT

Chronic Kidney Disease (CKD) is an emerging health problem and is one of the major causes of mortality. Hypertension is closely linked with CKD and both these conditions cause severe cardiovascular events. Hence, blood pressure control is imperative in all stages of CKD and this plays a major role in preventing its CKD progression to end stage kidney disease and death.

Objectives: To determine the pattern of antihypertensive prescribing among hypertensive CKD patients, with or without other comorbid conditions and to assess the proportion of hypertension in CKD patients.

Methodology: 100 consecutive CKD subjects of either gender, attending the outpatient nephrology were included into the study. Using predesigned case record form data was collected about – the antihypertensives used, single and fixed dose combinations, concomitant medications and about number and type of comorbidities.

Results: CKD was seen more prevalent in males (72%) compared to females (28%), and majority of the study subjects were in the age group 41-60 years. 93% of the study subjects were hypertensives and more than 50% of subjects were not following both physical exercise and dietary measures. In our study most prescribed hypertensive medication as monotherapy was calcium channel blockers (Amlodipine/Cilnidipine/Nicardipine) and fixed dose combination was ARBs + Thiazides and CCBs + Thiazides.

Conclusion: The study concluded that though treatment regimen used in our study was not in accordance to the 2021 KDIGO guidelines, (According to 2021 KDIGO guidelines, ACEI/ARB are the first line drugs to treat HTN in CKD patients without dialysis), prescribed antihypertensives were effectively controlled systolic and diastolic blood pressure.

Keywords: Antihypertensives, Chronic kidney disease, Prescribing pattern, Kidney Disease Improving Global Outcomes (KDIGO) guidelines.

INTRODUCTION

Hypertension and chronic kidney disease (CKD) are interrelated and increasingly recognized as a serious global public health concern.¹ CKD is defined as the presence of reduced kidney function (an estimated glomerular filtration rate [eGFR] <60 mL/min/1.73 m²) or kidney damage (often indicated by the presence of proteinuria) for ≥3 months duration.² Hypertension, defined by the European Society of Cardiology and the European Society of Hypertension (ESC/ESH) as a blood pressure of ≥140/80 mmHg, affects ~ 30% of the general adult population and up to 90% of those with CKD.² Globally, the prevalence of CKD is significantly rising, and it is associated with major morbidity and mortality that demands special attention as one of the growing public health problems. The estimated worldwide prevalence of CKD is 8% to 16%.¹ Its prevalence is not only high in developed countries but is also on the rise in developing countries.¹ The prevalence of CKD in India is approximately 13%.³ Detection of CKD and its important risk factors/comorbidities, particularly at early stages, is essential because therapeutic interventions are likely to be effective if they are implemented early in the

course of the disease process.⁴ Antihypertensive 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 CKD⁵ (Hypertension is both a risk factor and comorbidity for CKD). Additionally, hypertensive CKD patients often require treatment with multiple antihypertensive drugs. Various clinical guidelines, including the American College of Cardiology (ACC)/American Heart Association (AHA) hypertension treatment guidelines, the Kidney Disease Improving Global Outcomes (KDIGO) guidelines and JNC-8, provide consensus recommendations about optimal antihypertensive therapy for CKD patients with regard to both BP-lowering and renal protection.⁵ These recommendations include angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) as first-line therapy for CKD patients, particularly for those with proteinuria and/ or reduced renal function.⁵ However, it is not known to what extent these guidelines are recommended or preferred/used in the real- world clinical setting.⁵ Despite the recognition of hypertension and CKD as a major public health concern, epidemiologic



research to provide insights into public health approaches on prevention and treatment of hypertension in patients with CKD is limited and very few studies have been conducted in India to evaluate the percentage/proportion of hypertension in CKD patients, and the prescribing pattern of antihypertensives in CKD patients. Therefore, the present study was taken up.

MATERIALS AND METHODS

Following approval and clearance from the Institutional Ethics Committee (KIMS/IEC/A009/M/2022), present observational study was conducted to determine the pattern of antihypertensive prescribing among hypertensive CKD patients, with or without other comorbid conditions and to assess the proportion of hypertension in CKD patients. 100 consecutive CKD subjects visiting the outpatient Nephrology department at Kempgowda Institute of Medical sciences, Hospital and Research Centre, Bangalore were included into the study by the investigator after coordinating and confirming the diagnosis with Nephrologist. Study subjects were recruited by purposive sampling method from October 2021 – March 2022 (6 months). Written informed consent was obtained from all the study subjects after fully explaining the study procedure to their satisfaction, in both English and vernacular language. **Subjects fulfilling the following inclusion criteria were included into the study;** Willingness to give written informed consent, Study subjects of either gender aged between 18 to 80 years, diagnosed as per KDIGO classification guidelines to have chronic kidney disease (irrespective of the cause), CKD subjects with single or multiple comorbidities, CKD subjects on immunotherapy and with any acute infections, and all grades of CKD subjects not on dialysis. **Patients with the following conditions were excluded from the study;** Subjects with end stage renal disease (renal dialysis), Subjects with surgical conditions like tumors of genitourinary system, Subjects with terminal illnesses due to malignancy, Subjects planned for or post-renal transplant, CKD subjects with chronic infections like tuberculosis, leprosy, HIV, HBsAg or HCV status, Pregnant and lactating women.

A detailed present and past medical, personal (including life style), family and drug history, was recorded from all the study subjects. The available medical records of the subjects were thoroughly scrutinized to obtain any relevant information about the comorbid conditions, previous and ongoing drug therapy. In hypertensive CKD subjects, the details of the ongoing antihypertensive therapy including the number of drugs or drug combinations used, the therapeutic class, dose, frequency, and duration of administration were documented. Proportion of hypertension in CKD was calculated from the total number of CKD subjects recruited and number of CKD patients associated with hypertension. The results were depicted in the form of tables and graphs. Microsoft Word and Excel are used to generate graphs and tables.

RESULTS

The demographic data of the study subjects is presented in the **Figure-1**. The mean age for males was 54.53 ± 12.6 years and for females was 55.11 ± 13.37 years. In this study CKD was seen more prevalent in males (72%) compared to females (28%) and majority of the study subjects were in the age group 41-60 years, with CKD Stage 3. **Table 1 summarizes CKD staging and comorbidities.** 93% of the study subjects were hypertensives followed by diabetes (54%), anemia (11%) and IHD (10%). Hypertensives were more in Stage 3. **Table-2 summarizes the lifestyle measures taken by the study subjects.** Among the study subject's 41% of the study subjects were following the dietary measures and only 23% of the subjects following exercise (walking). **prescribed medications/ongoing therapy for hypertension in subjects with CKD** are presented in **Table-3.** 54 % of the subjects received calcium channel blockers (Amlodipine, Cilnidipine, Nicardipine), 35% β -blockers (Propranolol, Metoprolol, Atenolol, Carvedilol, Bisoprolol), 18% α -blockers (Prazosin), 9% α -agonists (Clonidine) 7% Diuretics (Spironolactone, Chlorthiazide), 7% ARBs (Losartan, Telmisartan, Olmesartan) and only 1% were on ACEIs (Ramipril, Enalapril). Fixed dose combinations were used in 13% of study subjects.

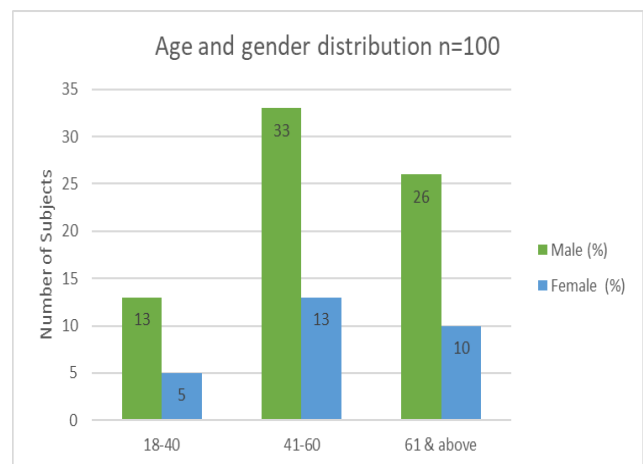


Figure 1: Age & Gender Distribution (n=100)

Table 1: CKD staging and comorbidities (n=100)

Staging and Co morbidities	HTN (%)	DM (%)	ANEMIA (%)	IHD (%)	Proportion of HTN
Stage 2	8	3	0	0	$\frac{8 \times 100}{100} = 100\%$ 8
Stage 3	42	25	4	4	$\frac{42 \times 100}{48} = 87.5\%$ 48
Stage 4	31	19	4	4	$\frac{31 \times 100}{32} = 96.8\%$ 32
Stage 5	12	7	3	2	$\frac{12 \times 100}{12} = 100\%$ 12
Total	93	54	11	10	$\frac{93 \times 100}{100} = 93\%$ 100

Table 2: Lifestyle Measures (n=100)

Lifestyle measures		n (%)
Diet modification	Not follow	59
	Follow	41
Physical activity	Walking	23
	No regular physical activity	77
Smoking	Yes	2
	No	98
Alcohol consumption	Yes	1
	No	99

Table 3: Prescribed medications/ongoing therapy for hypertension in subjects with CKD (n=100)

MEDICATIONS	n (%)
ANTIHYPERTENSIVES	
Diuretics (Spirinolactone, Chlorthiazide)	7
ACEIs (Ramipril, Enalapril)	1
ARBs (Losartan, Telmisartan, Olmesartan)	7
CCBs (Amlodipine, Cilnidipine, Nicardipine)	54
β -blockers (Propranolol, Metoprolol, Atenolol, Carvedilol, Bisoprolol)	35
α -blockers (Prazosin)	18
α -agonists (Clonidine)	9
FIXED DOSE ANTIHYPERTENSIVES	
Telmisartan + Hydrochlorothiazide	2
Losartan + Hydrochlorothiazide	2
Telmisartan, + Medoxonil + Amlodipine + Hydrochlorothiazide	1
Amlodipine + Metoprolol	1
Cilnidipine +Metoprolol	2
Cilnidipine, + Chlorthalidone	2
Amlodipine + Bisoprolol	1
Olmesartan + Hydrochlorothiazide	1
Metoprolol + Ramipril	1

DISCUSSION

In the present study, the pattern of antihypertensive prescribing and proportion of hypertensive CKD subjects were assessed in 100 CKD hypertensive subjects who attended the Nephrology outpatient department at KIMS Hospital and Research Centre, a tertiary care teaching hospital. In this study, CKD was seen more prevalent in males compared to females. The male predominance is probably because of the better awareness about health and economic independence compared to females. This result was similar with the study done by Hiroshi Kimura and etal⁶ which showed male preponderance of 56%. Majority of the study subjects were in the age group 41-60 years; this result was consistent with study conducted by

Avez Ali.⁷ Majority of subjects were under CKD stage 3 and stage 4 CKD. The stage of CKD in the study subjects was categorized as per kidney disease improving global outcome (KDIGO) classification. Our results are like study conducted by Hilda O Hounkpatin and etal.⁸ In other study conducted by Sowmya Santra⁹ showed that majority (28%) had CKD stage 3, 20% stage 4, 14% had CKD stage 5. 93% of the study subjects were hypertensives followed by diabetes, anemia and IHD, almost all the patients had more than one comorbidity. Study conducted by Latha Kamath and etal¹⁰ shown hypertension was commonest comorbidity in 40% of the subjects. In other study done by Sourav Chakraborty and etal¹¹ shown anemia to be the most common comorbidity in 89% of the subjects followed by Hypertension in 85% of the subjects. Calcium channel blockers (Amlodipine, Cilnidipine, Nicardipine) and β -blockers (Propranolol, Metoprolol, Atenolol, Carvedilol, Bisoprolol) were the most prescribed antihypertensive agents in the present study and similar observation was made in many other studies, like study conducted by Rajesh Hadia etal,¹² showed CCB were prescribed in 34.18% patients and it was the most prescribed antihypertensive. Next most prescribed antihypertensive agent in the study found to be Beta blockers followed by alpha blocker. In study conducted by C.S. Shastri etal¹³ where CCBs were prescribed in 27.6% patients followed by Diuretics 19.6%, beta blockers 8.5%, alpha blockers 5.5%, ARBs 1.9%, ACEI in 1.9%. Hypertension is both a cause and effect of CKD and contributes to its progression. Several mechanisms contribute to the development of hypertension in CKD and these influence its management. Antihypertensive medications have direct BP-lowering effect and, they provide additional reno protective and/or cardioprotective action, which may be independent of their BP-lowering effects.

CONCLUSION

In our study most prescribed hypertensive medication as monotherapy was calcium channel blockers (**Amlodipine/Cilnidipine/Nicardipine**) and fixed dose combination was ARBs + Thiazides and CCBs + Thiazides. The study **concluded** that though treatment regimen used in our study was not in according to the 2021 KDIGO guidelines, (According to 2021 KDIGO guidelines, ACEI/ARB are the first line drugs to treat HTN in CKD patients without dialysis), prescribed antihypertensives have effectively controlled systolic and diastolic blood pressure. Also helped to reduce cardiovascular risk associated with the progression of CKD.

ACKNOWLEDGEMENT

We are grateful to all the patients and department of Nephrology from KIMS hospital who contributed to this study.



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Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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