

Prescription Pattern of Antihypertensive Drugs in Chronic Kidney Disease Patients Attending - A Tertiary Care Hospital

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Abstract:

Background: Chronic kidney disease exists both as a common cause of hypertension and complication of uncontrolled hypertension. This complex interplay of hypertension and CKD further increases the risk of adverse cardiovascular and cerebrovascular outcomes. Blood pressure control is pertinent in all stages of chronic kidney disease. **Method:** An observational descriptive cross-sectional study was conducted in Nephrology Department of Dhaka Medical College Hospital from January 2022 to December 2022. Total 264 hypertensive CKD patients were included in this study according to selection criteria. Collected data were processed and analyzed by using SPSS26.0.p value of < 0.05 was taken as statistically significant. **Result:** Among 264 CKD patients 58% male, 42% female and mean age was 49.43±13.87 years. Only 67% patient achieved control of BP with

antihypertensive. 53.8% patient were in stage-5 and 18.2% in stage-4 CKD. 85.6% patient received combination therapy. Among them 58.3% patients received two drug combination therapy. CCBs was prescribed in 169 patients. Amlodipine was 41.42% the preferred CCB and the combination of ARBs+CCBs was (28.7%) the frequently prescribed. Control of blood pressure was achieved in CKD patients taking monotherapy (p = 0.039) and on three drug combination therapy (p = 0.006). **Conclusion:** Calcium channel blocker is the treatment of choice in CKD patients with hypertension and commonly prescribed CCB is amlodipine. Combination of antihypertensive therapy is a better choice for control of hypertension.

Keywords: Chronic kidney disease (CKD), Antihypertensive drug.

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Introduction:

Worldwide chronic kidney disease (CKD) is considered as one of the major public health problem with adverse outcome of kidney failure, cardiovascular disorder, and premature death¹. The prevalence of CKD in Bangladesh is 22% in the year 2020 and the global estimated prevalence of CKD is 13.4%.^{2,3} CKD is associated with a multitude of complications including electrolyte imbalance, mineral and bone disorder, anemia, dyslipidemia, and HTN⁴. Once kidney impairment sets in, it progresses to ESKD and this population is very much vulnerable to cardiovascular events⁵. A meta-analysis showed that every 10 mm Hg reduction in systolic BP significantly reduces the risk of major CVD by 20%, IHD by 17%, stroke by 27%, heart failure by 28% and all-cause mortality by 13%⁶. The relationship between CKD and hypertension is cyclic as CKD can contribute to or cause hypertension. Proper control of BP in CKD patients is necessary for slowing the progression of CKD⁷.

Antihypertensive drugs are recommended in hypertensive patients as they offer cardio-protective and reno-protective benefits. Antihypertensive drugs serve three major purposes in CKD patients, it lowers BP, reduces the risk of CVD, slows the progression of kidney disease and reduces proteinuria. Thus improve health outcomes and reduce health care cost⁸. In order to achieve and maintain adequate BP control, most patients with CKD require combination of antihypertensive therapy. According to JNC-8 guideline, patients of any age with CKD with or without diabetes have BP goal of <140/90 mm Hg⁹. According to national guidelines for the management of hypertension in Bangladesh, 2013 patients with CKD and diabetes have BP goal of <130/80 mm of Hg¹⁰. KDIGO 2012 guideline recommended a BP goal of <140/90 mm of Hg for both diabetic and non-diabetic adults with CKD with urine albumin excretion of <30 mg/24 hours and BP goal of <130/80 mm of Hg with urine albumin excretion of >30 mg/24 hours¹¹.

Method:

Following approval and clearance from the Institutional Ethical review Committee this observational cross-sectional study was conducted in the Nephrology Department of Dhaka Medical College Hospital, Dhaka. The aim of this study was to determine the utilization pattern of antihypertensives among CKD patients of different stages with or without comorbidities. The study was conducted from January 2022 to December 2022. Total 264 patients of either gender aged between 18 to 78 years, diagnosed as per KDIGO 2012 guideline to have CKD with hypertension with or without other comorbidities but not on dialysis were enrolled to the study. Aims, objectives and procedures of the study was explained with understandable language to the patient. Risks and benefits were also made clear to the patient. Patients were encouraged for voluntary participation and they were allowed being free to withdraw themselves from the study. Informed written consent was taken from each patient. A structured data collection tool was used to collect data. Patient's record including socio-demographic characteristics, clinical history, examination findings, laboratory data, antihypertensive medication and other relevant data were collected according to the objectives of the study. Staging of CKD was performed by using estimated glomerular filtration rate (e-GFR). e-GFR was calculated by using CKD-EPI equation with the help of e-GFR calculator. Blood pressure was measured as per JNC 8 guideline.

Two readings of BP one to two minutes apart were taken and the average of two reading was recorded. Collected data were processed and analyzed by using SPSS(Statistical Package for the Social Sciences) 26.0.p value of <0.05 was taken as statistically significant.

Result:

Among 264 CKD patients 58% were male 42% were female and mean age was 49.43±13.87 years (Table-I). Mean systolic BP (SBP) was 132.1±18.9 mm of Hg and 35.2% patient had SBP range of 130-139 mm of Hg (Table-II). Mean diastolic BP (DBP) was 83.2±9.7 mm of Hg and 30.7% patient had DBP range of 80-89 mm of Hg (Table-III). 67% patients achieved control of BP(<140/90 mm Hg) with antihypertensives (Fig-1). 53.8% patients were in stage and 18.2% in stage-4 CKD. Common comorbidities were DM (45.8%), IHD (27.3%) and Stroke (11.7%) (Fig-2). 85.6% patients received combination therapy and 38.3% patient received two drug combination therapy. Mostly prescribed antihypertensive drug was CCBs prescribed in 169 patient followed by β -blockers in 135 patients, α -blocker in 126 patients, Diuretics in 98 patients and ARBs in 80 patients. Amlodipine was the preferred CCB (41.42%) and combination of ARBs+CCBs (28.7%) was frequently prescribed combination therapy. Control of blood pressure was achieved in CKD patients taking monotherapy (p = 0.039) and on three drug combination therapy (p = 0.006).

Table-I: Gender and age distribution of patients (n=264)

Gender distribution	Frequency	Percentage	Mean±SD
Male	153	58	
Female	111	42	
Age distribution (years)			
18-30	37	14	Mean age 49.43±13.87 years
31-40	41	15.5	
41-50	55	20.8	
51-60	72	27.3	
61-70	52	19.7	
71-80	07	2.7	

Table-II: Systolic Blood Pressure (mm of Hg) of patients (n=264)

Systolic pressure (mmHg)	No. of patients	Percentage (%)	Mean±SD
100-119	63	23.9	132.1±18.9 (100-190)
120-129	21	8.0	
130-139	93	35.2	
140-160	69	26.1	
>160	17	6.4	
Total	264	100.0	

Table-III: Diastolic Blood Pressure (mm of Hg) of patients (n=264)

Diastolic blood pressure (mmHg)	No. of patients	Percentage (%)	Mean±SD
70-79	68	25.8	83.2±9.7 (70-110)
80-89	81	30.7	
90-99	90	34.1	
>100	25	9.5	
Total	264	100.0	

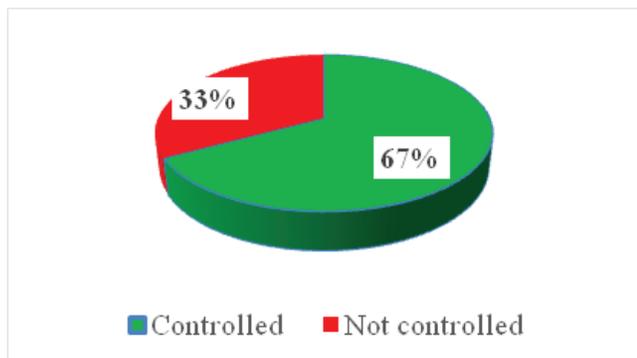


Fig-1: Distribution of CKD patients according to control of BP (<140/90 mm of Hg)

Table-IV: Distribution of patients according to stages of CKD (n=264)

Stages of CKD	Frequency	Percentage(%)
Stage-1	2	0.8
Stage-2	13	4.9
Stage-3	59	22.3
Stage-4	48	18.2
Stage-5	142	53.8

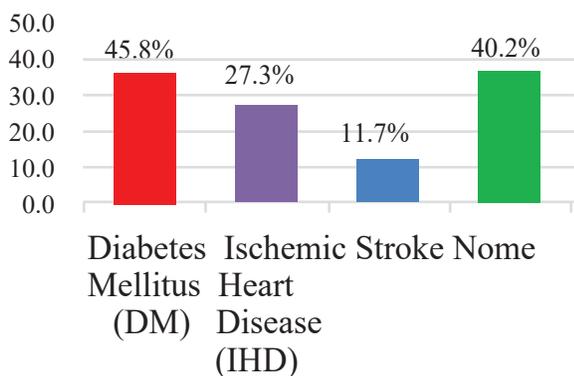


Figure-2: Comorbidities associated with CKD patients

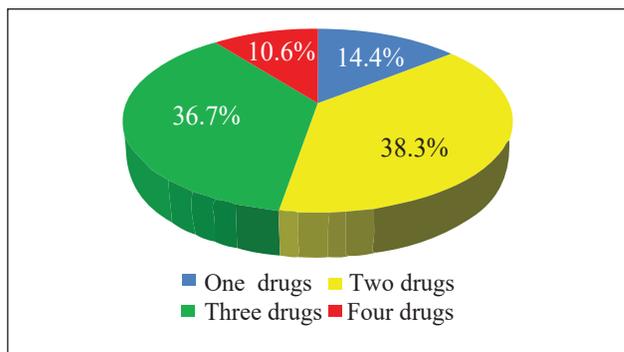


Figure-3: Distribution of number of antihypertensive drug prescribed

Table-V: Antihypertensive Drugs prescribed in CKD Patient (n=264)

Class of Antihypertensive	Name of Drug	Number of Prescriptions (%)	
CCBs(169)	Amlodipine	70(41.42%)	
	Nifedipine	51(30.1%)	
	Cilnidipine	40(23.6%)	
	Diltiazem	8(4.7%)	
β-blockers(135)	Bisoprolol	105(77.7%)	
	Carvedilol	10(7.49%)	
	Atenolol	15(11.1%)	
	Nebivolol	5(3.7%)	
α-blocker(126)	Prazosin	126(100%)	
Diuretics(98)	Furosemide	90(91.8%)	
	Indapamide	6(6.1%)	
	Spironolactone	2(2.1%)	
ARBs(80)	Olmesartan	40(50%)	
	Losartan	30(37.5%)	
	Telmisartan	10(12.5%)	
ACE inhibitor(19)	Ramipril	19(100%)	
Monotherapy		Three drug combination	
Drug Regimen	No (%)	Drug Regimen	No (%)
CCBs	12(31.6)	CCBs+BB+ Alpha Blocker	29(29.9)
ARBs	10(26.3)	CCBs+BB+D	21(21.7)
BB	6(15.7)	CCBs+D+ Alpha Blocker	17(17.5)
Diuretics	5(13.2)	D+BB+ Alpha Blocker	13(13.4)
Two Drug Combination		ARBs+CCBs+ Alpha Blocker	11(11.3)
ARB + CCBs	29(28.7)	ACEIs+BB+D	6(6.2)
CCB+Alpha Blocker	21(20.8)	Four Drug Combination	
CCB + BB	18(17.8)	ARB+CCB+BB+ Alph Blockera	12(42.8)
ARB+ Diuretics	15(14.9)	CCBs+BB+ Alpha Blocker+D	9(32.2)
BB+Diuretics	10(9.9)	ARBs+CCBs+BB+D	5(17.9)
BB + Alpha Blocker	8(7.9)	ARB+CCB+BB+Alpha 2 agonist	2(7.1)

Table VI: Relation of number of antihypertensive drug prescribed to control of blood pressure (<140/90 mm Hg) in CKD patients

Number of drugs	Control of BP		p-value
	Controlled (n=177) No. (%)	Not controlled (n=87) No. (%)	
One drug	31(17.5%)	7(8.0%)	0.039*
Two drugs	73(41.2%)	28(32.2%)	0.155
Three drugs	55(31.1%)	42(48.3%)	0.006*
Four drugs	18(10.2%)	10(11.5%)	0.742

Chi-square (χ^2) test were applied to see the level of significance, *significant, $p < 0.05$ considered as significant.

Discussion:

This study shows that CKD with HTN occurs more in men (58%) than in women (42%), which resembled to the study conducted by Singh et al, 2022, Prabitha et al, 2019, Thomas et al, 2020^{12,13,14}. Study by Halbesma et al, 2008 shows that systolic BP in women was 10 mm Hg lower than in men¹⁵. In this study 27.3% patients were in 51-60 years age group and mean age was 49.43+13.87 years, which was similar to the study of Bharani et al, 2018 and Prabitha et al, 2019^{13,16}. In my study 51-60 years age group patients commonly suffering from CKD. Kidney function deteriorates with aging. Study offseki K, 2008 states that longitudinal studies in USA and Norway revealed a decline in GFR of 0.75-1.03 ml/min/1.73 m²/year¹⁷. In my study 67% CKD patients of all ages with or without DM had achieved BP goal of <140/90 mm Hg with antihypertensive therapy. Patients having BP of <140/90 mm of Hg with therapy considered to have controlled BP. This study coincides with the study of Singh et al, 2022 and Malpani et al, 2018^{12,18}.

In current study, 60% patients had comorbid conditions like DM (45.8%), IHD (27.3%) and stroke (11.7%). Thomas et al, 2020, Bharani et al, 2020 and Prabitha et al, 2019 supported this study^{13,14,16}. It differs from the study done of Malpani et al, 2018¹⁸. Here most of the patients were in later stage of CKD, 142 (53.8%) patients in stage-5, 48 (18.2%) patients in stage-4, and 59 (24.3%) patients in stage-3 CKD. Here no significant association was evident between stages of CKD and control of BP according to JNC-8 guideline. In this study, 85.6% patients were on antihypertensive combination therapy, which was similar to the study conducted by Sing et al, 2022, Thomas et al, 2020, Prabitha et al, 2019^{12,13,14}. Here frequently prescribed combination therapy was two-drug combination therapy (38.3%) followed by three- drug combination

therapy (36.7%), four-drug therapy (10.6%). Combination therapy evoke synergistic antihypertensive effect with sustained BP control in hypertensive CKD patients. JNC-8 guideline recommended the use of combination therapy when BP is greater than 20/10 mm of Hg above goal blood pressure⁹. In this study BP was controlled (<140/90 mm of Hg) with single drug therapy ($p=0.039$) and with three drug combination therapy ($p=0.006$).

In present study commonly prescribed antihypertensive was CCB prescribed in 169 patients followed by Beta-blockers in 135, Alpha-blockers in 126, Diuretics in 98, ARBs in 80, ACEIs in 19 patients. Combination of ARBs+ CCBs was taken by 29 (28.7%) patients and commonly prescribed three-drug combination was CCBs+ Beta-blockers+ Alpha-blocker combination taken by 29(29.9%) patients. Both JNC-8 guideline and Bangladesh national guideline recommended ACEIs/ARBs as first line therapy for treatment of hypertension in CKD patient^{9,10}. Utilization of ARBs in present study was 26.3% as monotherapy and combination therapy. ARBs utilized in combination with CCBs in 28.7% patients, which is greater than other combination therapy and the pattern supports JNC-8 guideline. This study coincides with the study of Rajasekhar et al, 2016¹⁹. Use of other drugs in combination with ACEI or ARBs were recommended in JNC-8 guideline⁹.

Among CCBs Amlodipine was the preferred drug and prescribed in 41.42% patient followed by Nifedipine in 30.1% and Cilnidipine in 23.6% patients, which coincides with the study of Thomas et al, 2020 and in contrast with the study of Sing et al, 2022 and Prabitha et al, 2019 where frequently prescribed CCBs was Nifedipine and Cilnidipine respectively^{12,13,14}. CCB scanbeused as first-line therapy in combination with ACEIs/ARBs in CKD patient with or without DM according to JNC-8 guideline⁹.

Conclusion:

Blood pressure control is pertinent in all stages of CKD to reduce cardiovascular risk associated with the progression of CKD and to decrease mortality. CCBs was the drug of choice for treatment of hypertension in CKD patients both as monotherapy and combination therapy. Amlodipine was the mostly prescribed CCB. ARBs+CCBswas the preferred combination therapy. There is statistically significant control of BP in different stages of CKD with one drug therapy ($p=0.039$) and with three drug therapy ($p=0.066$).

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