



CORRELATION OF PRESCRIBING PATTERN OF ANTIHYPERTENSIVE MEDICATION AND JNC8 GUIDELINE IN HYPERTENSION WITH CHRONIC KIDNEY DISEASE IN A TERTIARY CARE HOSPITAL IN BANGLADESH

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Abstract:

Background: Hypertension is a cardiovascular disease condition. If it is untreated, it may cause severe morbidity and mortality. Hypertension is both a cause and effect of Chronic Kidney Disease (CKD) and affects the vast majority of CKD patients. So effective blood pressure control is necessary. The risk and progression of CKD may reduce by controlling HTN. Control of HTN plays a major role in preventing its progression to end stage kidney disease and death. The objectives of the study were to evaluate the class, dosing schedule of anti hypertensive prescribed in CKD and the percentage of mono therapy and combination therapy.

Material and methods: A cross-sectional, observational study conducted in the Department of Pharmacology in collaboration with the Department of Nephrology out patients' Department in Mymensingh Medical College Hospital, Mymensingh.

Results: Most commonly used single drug is CCB (13.27%) and most commonly used combination therapy is CCBs + ARB.

Conclusion: It is concluded that in CKD with HTN, majority of patients were treated with combination therapy. CCB was found to be the commonest prescribed anti hypertensive in mono therapy and in combination therapy. According to JNC8 guideline majority of the blood pressure (BP) goals were achieved.

Keywords:

Anti-hypertensive drugs, Chronic Kidney Disease, Mono therapy, Combination therapy, Prescription pattern.

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Introduction:

Chronic Kidney Disease (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. Hypertension (HTN) is defined by the European Society of Cardiology

and the European Society of Hypertension (ESC/ESH) as a blood pressure (BP) of ≥140/80 mmHg affects ~ 30% of the general adult population and up to 90% of those with CKD¹. Hypertension is not a disease but an important risk factor for development of CKD. The risk of development of hypertension is especially related to the elderly people². Now a days CKD is

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globally increasingly prevalent condition and is strongly associated with circumstance of cardiovascular disease (CVD). CKD is a rising health problem and one of the major causes of mortality³. The incidence and severity of hypertension may be increased due to a decline in eGFR. On the other hand, CKD is the most common cause of secondary HTN and also an independent risk factor for cardiovascular morbidity and mortality¹. The mechanisms of HTN in CKD include volume overload, sympathetic over activity, salt retention, endothelial dysfunction, and alterations in hormonal systems that regulate blood pressure (BP). The prevalence of HTN is higher among patients with CKD, progressively increasing with the severity of CKD. Many guidelines discuss the importance of BP control to decrease the progression of renal disease and decrease cardiovascular morbidity and mortality. However, in order to maintain adequate BP, it requires combination of anti hypertensive agents often up to three or four classes. But many clinicians practice their own prescribing pattern according to their clinical experiences. This study is designed to assess the prescribing pattern of anti hypertensive agents among CKD patients to control BP in the outpatient Department of Nephrology in Mymensingh Medical College Hospital. Findings of this study will give some idea about prescribing patterns in Bangladesh.

Method and Materials:

It was a cross sectional descriptive type of observational study. The study was carried out in the Department of Pharmacology & Therapeutics in collaboration with the Department of Nephrology, Mymensingh Medical College Hospital, Mymensingh, during the period from January 2021 to December 2021. All the data were collected from Department of Nephrology, Mymensingh Medical College Hospital, Mymensingh. Data were collected by interviewing the patients and reviewing patients' prescription. Data were collected ensuring the privacy and confidentiality as far as possible. After completion of data collection, data analysis was done using SPSS version 20.

Inclusion Criteria:

- Patient of either sex.
- Patient of adult age group.
- Patient with diagnosed CKD with HTN with or without DM and Cardio Vascular Disease (CVD).
- Willing to be enrolled in the study with informed consent.

Exclusion Criteria:

- Patient not willing to give consent.
- Patients associated with some comorbidity other than DM, CVD, IHD. Other comorbidities were excluded from this study because of those were no or less related with CKD.

Results:

This study was carried out to determine the pattern of drugs used for the hypertension with chronic kidney disease patients attending outpatient Department of Nephrology in Mymensingh Medical College Hospital in Bangladesh. A total of 113 patients coming to outpatient department of MMCH were selected for the study. A cross-sectional descriptive type of observational study was conducted. Finding of the study are presented by graphs and tables.

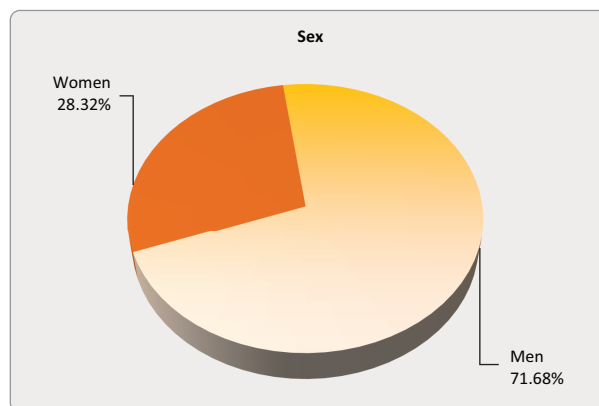


Figure 1: Sex distribution of patients in CKD with HTN

Here, majority of the patients suffering from CKD with HTN are males and they cover 71.68% of total patients and 28.32% were female patients suffering from CKD with HTN.

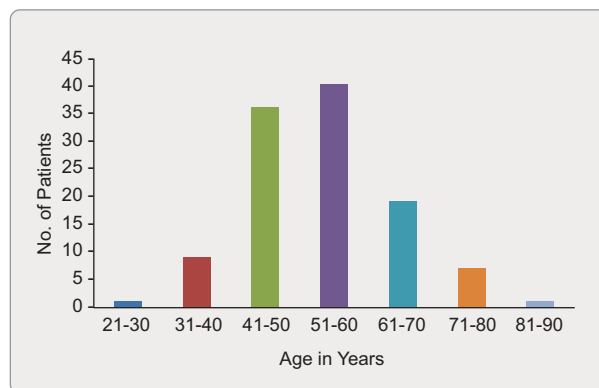


Figure 2: Age distribution of patients in CKD with HTN

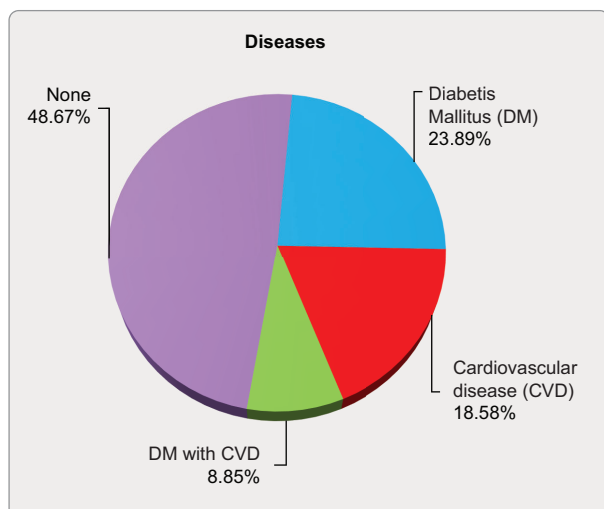


Figure 3: Comorbidity associated with HTN with CKD

Out of 113 patients CKD without any co-morbidity was 55 (48.67%), DM 27(23.89%), IHD 21(18.58%), DM with IHD 10 (8.85%).

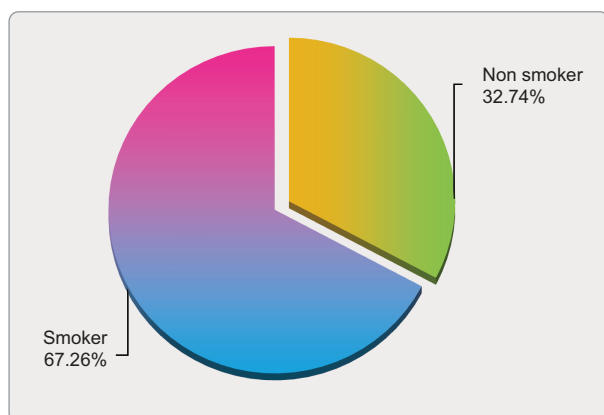


Figure 4: Personal factor (smoking) of the participants

Figure 4 shows that all the male patients are smoker. Systolic Blood Pressure (mmHg)

Table-I
Systolic Blood Pressure (mmHg) of the participants (n=113)

	No. of patients	Percentage	Mean	SD
100-109	60	53.1		
110-130	53	46.9	123.32	7.00
Total	113	100.0		

Table I shows that systolic blood pressure 100-109 mmHg had 53.1% participants and 110-130 mmHg had 46.9% participants

Diastolic Blood Pressure (mmHg)

Table-II
Diastolic Blood Pressure (mmHg) of the participants (n=113)

	No. of patients	Percentage	Mean	SD
60-69	81	71.7		
70-80	32	28.3	80.62	7.11
Total	113	100.0		

Table II shows that Diastolic blood pressure 60-69 mmHg had 71.7% and Diastolic Blood Pressure 70-80 mmHg had 28.3%.

Table III
Distribution of anti hypertensives according to drug prescribed

Drug prescribed	Total number of patients having anti-hypertensive drugs	Percentage
Calcium channel blocker	76	33.48%
Angiotensin II receptor blocker	65	28.63%
Beta blocker	56	24.67%
Alpha blocker	16	7.04%
Diuretics	12	5.29%
Both Alpha and Beta blocker	2	0.88%

Table-IV
Different therapy used in prescription (n=113)

Different therapy	No. of prescription	Percentage
Mono therapy	29	25.66
Combination therapy	84	74.34
Total	113	100.0

Table-V
Anti hypertensive drugs prescribed in hypertension with CKD patients as mono therapy and combination therapy

Name of drugs	Number of patients	Percentage
Angiotensine II receptor blocker + Calcium channel blocker	26	23.01
Calcium channel blocker	15	13.27
Angiotensine II receptor blocker + Beta blocker	14	12.39
Calcium channel blocker + Beta blocker	12	10.62
Calcium Channel blocker + Beta blocker + Alpha blocker	7	6.19
Beta blocker	6	5.31
Angiotensine II receptor blocker + Diuretics	6	5.31
Angiotensine II receptor blocker + Calcium Channel blocker + Beta blocker	6	5.31
Angiotensine II receptor blocker	5	4.42
Angiotensine II receptor blocker + Calcium channel blocker + Beta blocker + Alpha blocker	5	4.42
Alpha blocker	3	2.65
Angiotensine II receptor blocker + Both Alpha & Beta blocker	2	1.77
Angiotensine II receptor blocker + Diuretics + Both Alpha & Beta blocker	2	1.77
Calcium Channel blocker + Diuretics	1	0.88
Calcium channel blocker + Diuretics+ Beta blocker	1	0.88
Angiotensine II receptor blocker + Calcium channel blocker + Diuretics + Beta blocker	1	0.88
Angiotensine II receptor blocker + Diuretics + Beta blocker +Alpha blocker	1	0.88

Discussion

The rationality of the prescription can be assessed and evaluated using a prescription based study, one of the methods available for such purpose. Recommendation of the various international bodies on CKD with HTN has enhanced the prescribing practice of the physicians; moreover, clinical standards are also now available. Prevalence of CKD is on the rise and hence its management is very relevant.⁴ So the main objective of the study is to assess the drug prescription pattern of anti-hypertensive in CKD considering the adherence to the JNC-8. According to JNC-8 patients of any age with diabetes or CKD have a goal of less than 140 mm Hg systolic and less than 90 mm Hg diastolic. The focus of the JNC-8 is to target on the BP values. However, it also provides recommendations to promote the safer use of specific anti-hypertensive agents. The objective of the current study was evaluating the prescription pattern for CKD with HTN at a tertiary care hospital. Besides this, the researcher also aimed to assess the pattern of using drugs in the treatment of CKD with HTN, use of drugs as mono therapy or combination therapy, route of administration and patient's knowledge regarding drug schedule. There were no cases of dialysis encountered

in the study. This study was conducted in the outpatient Department of Nephrology in MMCH.

This study analysis showed that CKD with HTN occurs more in men than in women, which is confirmed by demographic characteristics showing men to suffer more from CKD with HTN (71.68%) than women (28.32%) which was similar to the study conducted by Prabitha P et al.(2019), Neethu Joseph et al.(2017), and Thomas et al.(2020). Female appear to have protection against CKD and its progression to ESKD. The prevalence of CKD among female population is less in reproductive years and increase about 10 years later than in men. The unhealthy lifestyle and damaging effects of testosterone may lead to rapid deterioration of renal function in males whereas in females estrogen plays a protective role.^{5,6,7}

In this study, 35.4% patients were in 51-60 years age group which is similar to the study conducted by Saju AP et al. and which was in contrast with the study done by Neethu Joseph where the age group was 60-69 years of patients were affected more. In the study of Thomas et al. suffered age group was 60-69 years and 50-59 years are more prone to developed CKD.^{6,7,8}

This study revealed that tobacco use increases the risk of HTN and CKD which is similar to the study conducted by Neethu Joseph et al. where 50% of the patients were smokers and 67.26% patients were smokers from this study. Smoking seems to be an independent risk factor for development of nephropathy which increases the progression of renal disease. In the present study none of them were addicted to alcohol, which was one of the risk factor in the study conducted by Neethu Joseph⁶.

In this study 32.7% of patients had comorbidity of DM 2 which is supported by the study of Kalpana Bharani et al and Thomas et al. which showed DM-2 as major co-morbidity. DM seems to be a most important independent risk factor for development of nephropathy which accelerates the progression of renal disease. In this study 28.3% of patients had cardiovascular diseases which are the risk factor for development of CKD with HTN. Most of them were free from comorbidities (48.67%). In the present study 33.6% of patients had positive family history of CKD and HTN which is increase the risk of development of CKD and HTN.^{7,9}

HTN is a strong risk factor for CKD and the existing guidelines recommend strict anti hypertensive treatment. According to KDIGO (Kidney Disease Improving Global Outcomes) guidelines there is no strong evidence to support the preferential use of any class of anti hypertensive except in proteinuric CKD where angiotensin converting enzyme inhibitors (ACE-I)/ARBs are chosen. In non proteinuric patients targets currently recommended in the general population be extrapolated to those with CKD. In the present study the most commonly prescribed anti hypertensive were found to be CCBs (33.48%) which is similar to the study conducted by Neethu Joseph et al., Thomas et al., Prabitha P et al. and Venkataraman R et al.^{5,6,7,10} In this study the 2nd most common drug is ARB (28.63%) and the 3rd common is Beta blocker (24.67%). In this study Diuretic 5.29%, Alpha Blocker 7.04%, and Both Alpha and Beta blocker 0.88% were also used as anti hypertensive.

CCBs do not accumulate in patients with impaired kidney function. The most frequently prescribed CCB in this study was cilnidipine which is a new (fourth) generation DHP. Cilnidipine blocks both L-type/N-type voltage gated calcium channels whereas other DHPs are strictly L-Type CCBs. Cilnidipine significantly reduces urinary albumin creatinine ratio unlike other

DHPs which increases proteinuria. Additionally this drug reduces uric acid production without adversely affecting serum uric acid level and reduced urinary uric acid/ creatinine ratio. As hypertension causes sympathetic over activity, reduced nitric oxide production from vascular endothelium due to insulin resistance and this can lead on to unrestricted production of hypoxanthines which are uric acid precursors in the skeletal muscle causing myogenic hyperuricemia. There is no risk of hypotension or reflex tachycardia. Risk of pedal edema is also less with cilnidipine

In this study 74.34% of patients were on multiple drug therapy. Regarding on combination therapy patients were given multi drug therapy which is similar to the study conducted by Thomas et al., Ashok Kumar Malpani et al., Neethu Joseph et al. and Prabitha P et al. But in contrast with the study conducted by D.Giri Rajasekhar et al. however D.Giri Rajasekhar et al. showed mono therapy as most preferred type of therapy.^{5,6,7,11,12} Combination treatment is required for hypertension management in CKD according to the guidelines. In this study CCBs combined with Beta blocker 23.01% which is in contrast with the study conducted by Prabitha P et al. where CCBs + AA were frequently prescribed combination as alpha agonists interact minimally with other anti hypertensive and they are valuable as adjunct therapy for resistant hypertension in CKD patients.⁵ ARBs were used more regularly than ACE inhibitors may be because of the less tolerability of the latter. In this study 2nd most common combination was ARB + Beta blocker 12.39%. This prescribing trend may be attributed to the goals of anti hypertensive therapy to reduce blood pressure which is the major risk factor for CKD, to reduce the need for hospitalization and to reduce development of ESKD and prevent dialysis.

Conclusion

Hypertension and Chronic Kidney Disease are chronic diseases which are inter related to each other and cyclic in nature. The treatment of CKD is done by treating the associated diseases and associated factors. Treatment for HTN will help in the reduction of chances of development of cardiovascular complications, mortality rate and progression of CKD. Medical records of 113 patients were assessed in this study. The prevalence of CKD with HTN was more in males than in females and majority of the male patients were smokers. Some comorbidity like CVD and DM

were associated with development of CKD with HTN. The preferential drugs applied among the patients were CCBs and the most common CCB was Amlodipine & Cilnidipine followed by ARBs, Beta blockers, Diuretics, Alpha blockers, Both alpha & beta blocker, Centrally acting sympatholytic and vasodilators. This study revealed that multi drug therapy was more preferred than mono drug therapy. In multi-drug therapy dual therapy was the most preferred among the other multi drug therapy. The patients understanding about the disease and the importance of medication could be taking properly. CCBs were found to be the commonest prescribed anti hypertensive as mono therapy and in combination therapy.

Conflict of Interest:

None to disclose.

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