

Antihypertensive Drug Use Pattern in a Tertiary Care Hospital of Western Region of Nepal: A Cross-Sectional Study

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ABSTRACT:

Introduction: Assessing antihypertensive drug use pattern always plays an important role to mitigate the burden of hypertension and also helps doctors to prescribe the drugs rationally. This study was conducted to assess antihypertensive drug use pattern in a tertiary care hospital. **Methods:** An observational cross-sectional study was conducted in the Internal Medicine department of Lumbini Medical College and Teaching Hospital from July 2021 to December 2021 for the duration of five months after ethics approval. Hypertensive patients who were prescribed one or more antihypertensive drugs irrespective of age and gender were included. Socio-demographic profiles, clinical characteristics and antihypertensive drug use related data were collected. Convenience sampling technique was used. Categorical variables were expressed as frequency and percentage while continuous variables were reported as mean \pm standard deviation. **Results:** A total of 224 patients were included. The average number of antihypertensive drugs per patient was 1.7 ± 0.8 . Combination drug therapy (54.5%) was commonly used. Calcium channel blockers (Amlodipine) were commonly prescribed (66.5%). Moreover, 98.7% and 41.5% patients were prescribed drugs from Essential Drug List of Nepal (Revised 2016) and in Fixed Dose Combination respectively. Use of combination drug therapy was higher among male patients ($p = 0.003$) and patients with stage II hypertension ($p < 0.001$). **Conclusion:** Calcium channel blockers were commonly used as monotherapy and in combination therapy as well. In approximately all of the patients, antihypertensive drugs were used from the essential drug list of Nepal which is an essential component of rational use of medicine.

Keywords: Antihypertensive, Calcium Channel Blockers, Drug Use, Hypertension, Tertiary Care.

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INTRODUCTION:

Hypertension is a serious public health problem and a major cause of deaths globally.[1] The adverse consequences of hypertension are increased risk of development of chronic kidney disease, cardiovascular disease, stroke and eye disease. The factsheet of WHO in 2019 reported that approximately one billion people throughout the world have hypertension.[2] Of them, about two-third of the patients are

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living in low- and middle-income countries.[2] Similarly, the data of Department of Health Services of Nepal in 2020 also revealed that approximately one million of population are suffering from hypertension.[3]

The use of antihypertensive drugs is the mainstay of treatment and they should be used on the basis of efficacy, safety and cost-effectiveness. Inadequate treatment of hypertension with antihypertensive drugs may increase its complications and financial burden of treatment.[4] The risk of occurrence of hypertensive complications and subsequent mortalities can be minimized if patients are treated rationally with antihypertensive drugs.[4,5] The assessment of antihypertensive drug use in hospitals at regular time intervals always plays an important role to mitigate the burden of hypertension and may help healthcare providers prescribe the drugs rationally.[5,6]

Many studies have been published worldwide related to the pattern of use of antihypertensive drugs. Some studies have been also conducted in low-income countries including Nepal.[5,6,7] Thus, this study attempted to add the data to previous studies with the general objective to provide an understanding of antihypertensive drug use pattern in a tertiary care hospital of the western region of Nepal. Whereas, the specific objectives were to identify antihypertensive drug use pattern, to assess socio-demographic and clinical characteristics of the patients, and to analyze the association of single drug and combination drug used for hypertension with socio-demographic and clinical characteristics of the patients.

METHODS:

A hospital based observational, cross-sectional study was carried out in the Internal Medicine Out-patient Department

(OPD) of Lumbini Medical College and Teaching Hospital (LMCTH), Tansen, Palpa after approval letters were received from the Institutional Review Committee (Protocol No: IRC-LMC 04-C/021) and the Internal Medicine Department of LMCTH. The duration of the study was five months from July 2021 to December 2021. The study included data of hypertensive patients who visited the Internal Medicine OPD and were prescribed one or more antihypertensive drugs irrespective of age and gender. The study excluded data of hypertensive patients who were not prescribed any antihypertensive drug and the follow up patients who had been encountered by the researcher previously. The sample size calculated was 191 using the sample size formula $N = Z^2 p (1-p) / d^2$ [4,8], where N = Minimum sample size required for accuracy in estimating proportions, Z = Standard normal value for 95 % confidence interval (1.96), p = Proportion of the study population estimated to have hypertension from a previous study, which was 14.5% as per the study by Adejumo et al.[4], d = Margin of sampling error tolerated, 0.05 (5%).

A convenience sampling technique was used for data collection. The required data were collected from the patients' prescription forms and entered in the pre-designed case proforma. The case proforma consisted of socio-demographic characteristics of patients (age, gender, hospital number, domicile and ethnic group), clinical characteristics of patients (diagnosis, number of diagnosis, stage of hypertension, presence of complications and name of complications) and information related to antihypertensive drug use pattern (number of drugs used, class of antihypertensive drugs, name of antihypertensive drug, route of administration, use of monotherapy or combination therapy, number of drugs used in combination therapy,

Table 1: American Heart Association classification of blood pressure

Blood Pressure Category	Systolic Blood Pressure (mm Hg)	And	Diastolic Blood Pressure (mm Hg)
Normal	< 120	And	< 80
Elevated	120-129	And	< 80
Stage 1 Hypertension	130-139	Or	80-89
Stage 2 Hypertension	≥ 140	Or	≥ 90
Hypertensive Crisis	More than 180	and / or	More than 120

Table 2: Anatomical Therapeutic Classification of Antihypertensive Drugs

Anatomical Therapeutic Classification (Main Group C : Cardiovascular System) Code	Class of Drug
C02AB	Centrally Acting Anti-adrenergics (Methyldopa)
C03	Diuretics
C07	Beta Blockers
C08	Calcium Channel Blockers
C09	Renin-Angiotensinogen-Angiotensin Inhibitors
C09A	Angiotensin Converting Enzyme Inhibitors
C09C	Angiotensin II Receptor Blockers

generic prescription, presence of fixed dose drug combinations and use of drugs from essential drug list of Nepal).

Hypertension was classified as stage 1 hypertension, stage 2 hypertension and hypertensive crisis on the basis of American Heart Association classification of blood pressure as shown in Table 1.[9] Similarly, Anatomical Therapeutic Classification (ATC) of Antihypertensive Drugs was used for

classifying drug groups in code as C02AB, C03, C07, C08 and C09 [10] as shown in Table 2. Moreover, Essential Drug List of Nepal (Revised 2016) was also used to find out the number of the antihypertensive drugs used from that list.[11]The data of the patients were kept confidential by using code numbers used in place of name and address of the patients. However, hospital numbers were

recorded to make sure that the data were original.

Data were entered in and analyzed by Statistical Package for Social Sciences (SPSS), version 18. Basic socio-demographic variables, clinical characteristics and findings related to antihypertensive drug use were described. Categorical variables were expressed as frequency and percentage while continuous variables were reported in terms of mean \pm standard deviation (SD). The associations of socio-demographic characteristics and co-morbidities with the use of mono therapy or combination therapy were analyzed. For inferential statistics, independent t-test and chi-square test were used as appropriate. p value less than 0.05 was considered as statistically significant.

RESULTS:

A total of 224 patients were included, of which, 54% were male and 78.6% were above 50 years of age (Table 3). The mean age of the patients was 59.7 ± 12.3 years. Similarly, the mean age of the female and male was 60.3 ± 11.8 and 59.2 ± 12.7 respectively ($t=0.674$, $df=220.202$, $p=0.501$). The average number of antihypertensive drugs used per patient was 1.7 ± 0.8 . In 55.8% of the patients, comorbidities were present. Diabetes mellitus was the most common comorbidity present (38.4%) as shown in Table 3. The majority of the patients belonged to Stage I hypertension (63.4%). Only, 25.9% patients were prescribed antihypertensive drugs in generic name (Table 3)

Table 3: Socio-demographic and clinical characteristics of hypertensive patients (N = 224)

Variables		Frequency (%)
Age (in years)	21-30	01 (0.4)
	31-40	13 (5.8)
	41-50	34 (15.2)
	51-60	70 (31.2)
	61-70	58 (25.9)
	>70	48 (21.5)
Gender	Female	103 (46)
	Male	121 (54)
Presence of complications		125 (55.8)
Presence of Diabetes		86 (38.4)
Stage of Hypertension	Stage 1	142 (63.4)
	Stage 2	82 (36.6)
Number of diagnosis	One	67 (29.9)
	More than one	157 (70.1)
Generic prescriptions	Yes	58 (25.9)
Fixed Dose Combination	Yes	93 (41.5)
Prescription from Essential Drug List of Nepal (Revised 2016)	Yes	221 (98.7)

Table 4: Prescription pattern of monotherapy and combination therapy (N = 224)

Pattern of monotherapy and combination therapy	Number of prescriptions n (%)
Monotherapy	102 (45.5)
Combination therapy	122 (54.5)
Two drug-combination	86 (38.4)
Three drug-combination	27 (12.1)
Four drug-combination	9 (04.0)

Table 5: Association of socio-demographic and clinical characteristics with monotherapy or combination therapy of hypertension (N = 224)

Characteristics		Mono-therapy	Combination Therapy	Statistics
Age (in years)	≤50	22	26	$\chi^2=0.002$, df=1, p=0.96
	>50	80	96	
Gender	Male	44	77	$\chi^2=8.926$, df=1, p=0.003
	Female	58	45	
Number of diagnosis	One	30	37	$\chi^2=0.022$, df=1, p=0.881
	More than one	72	85	
Presence of complications	Yes	57	68	$\chi^2=0.0004$, df=1, p=0.983
	No	45	54	
Presence of diabetes	Yes	48	38	$\chi^2=5.946$, df=1, p=0.015
	No	54	84	
Stages of hypertension	Stage 1	84	58	$\chi^2=29.011$, df=1, p<0.001
	Stage 2	18	64	

Nearly in all of the patient's prescription forms (98.7%) drugs were prescribed from Essential Drug List of Nepal (Revised 16). In less than half of the patient's prescription forms (41.5%) drugs were prescribed in Fixed Dose Combinations (Table 3).

The majority of the patients were prescribed combination drug therapy (54.5%). Regarding the combination drug therapy used, 38.4%, 12.1% and 4% of patients were prescribed two drugs, three drugs and four drugs respectively (Table 4). In 66.5% of total patients, calcium channel blockers were used. Amlodipine was the most commonly used drug followed by Losartan. Likewise, 66.5% of the patients were prescribed drugs from C08 class of Anatomical Therapeutic Classification of Antihypertensive Drugs followed by C09. Amlodipine 5 mg + Losartan 50 mg (25.4%) was the most common fixed dose combination followed by Losartan 50 mg + Hydrochlorothiazide 12.5 mg (10.7%).

Use of antihypertensive drugs in combination therapy was more likely among male patients ($\chi^2[N = 224, df = 1] = 8.926, p = 0.003$) and patients with Stage II hypertension ($\chi^2[N = 224, df = 1] = 29.011, p < 0.001$) respectively as shown in Table 5.

DISCUSSION:

The aim of our study was to assess the antihypertensive drug use pattern in a tertiary care hospital of western region of Nepal. Assessment of antihypertensive drugs is an essential tool to promote rational and appropriate use of drugs.[5,6] Rational use of drugs is the process of appropriate use of drugs for prevention, diagnosis and treatment of disease.[6] They provide good contribution in reduction of morbidity, mortality and burden of treatment that may lead to medical, social and economic benefits.[6]

In our study, hypertension is distributed commonly among male gender. Few other

studies also showed that the distribution of hypertension was common in male gender.[7,12,13,14,15,16].The possible reason for this finding may be that in Nepalese society males are excessively exposed to some risk factors of hypertension like excessive smoking, excessive consumption of alcohol, stress and obesity. In few other studies, it was found that hypertension was similarly distributed to both gender.[5,6,9,17] Our study also demonstrated that more than two-thirds of hypertensive patients were above 50 years of age. This similar finding was also found in other studies.[13,15,18,19,20] Hypertension commonly belongs to the middle to elderly aged population.[12,18] The possible reasons are increased arterial stiffening leading to increase vasoconstriction, progressive declining of the capacity of kidney to excrete sodium and increased prevalence of diabetes mellitus that further enhances blood vessel injury and reduces renal function.[12]

Moreover, in this study, the average number of antihypertensive drugs used per patient was found to be approximately two. This value was similar to WHO standard value two.[21,22] It was also observed that combination drug therapy was commonly used. This finding was comparable with other studies.[4,5,6,14,18] While, few studies demonstrated that single drug was commonly used for hypertension treatment.[7,13,15,16.] Hypertension was also associated with other comorbid diseases like diabetes, coronary artery disease, renal diseases and dyslipidemia. This could be a possible cause of the use of two or more drugs for better control of blood pressure in hypertensive patients with comorbid diseases. The synergistic action of two or more drugs increases efficacy and reduces frequency of adverse effects.[7] Besides this, fixed dose combination of drugs also reduces doses of drugs and cost of treatment compared to when they are given separately.[7] However, in our

study it was found that the tendency of use of combination therapy was significantly lower in hypertensive patients with diabetes mellitus. Related to Anatomical Therapeutic Classification of Antihypertensive Drugs (ATC), the highest numbers of drugs were used commonly from C08 class followed by C09. Calcium channel blockers and renin-angiotensinogen-angiotensin inhibitors are represented by ATC codes C08 and C09 respectively.[10] ATC is a drug classification that “classifies the active ingredients of drugs according to the organ or system on which they act and their therapeutic, pharmacological and chemical property.”[10] It is an important tool to compare drug use at local, national or international level.[10]

Our study also showed that calcium channel blockers (amlodipine) were used in more than half of the patients included. The similar findings were found in other studies.[6,7,13,14,15,16,18] A possible reason for the common use of this drug is that the calcium channel blockers effectively lower the blood pressure to achieve the target level with better safety and tolerability profile. However, Alkabi and Busari et al. demonstrated that diuretics were preferred for treatment of hypertension.[4,5] Calcium channel blockers control the blood pressure by producing coronary and / or peripheral arteriolar dilation via inhibition of voltage-gated L-type of calcium channels. They do not dilate veins. Among calcium channel blockers, amlodipine (dihydropyridines) are commonly used worldwide. Diuretics act by reducing re-absorption of sodium at different levels of nephrons. They are also the preferred drugs for hypertensive patients with renal disease. Furthermore, our study also found that almost every patient was prescribed from the essential drug list of Nepal (Revised 2016). This finding showed that the practice of prescribing antihypertensive drugs by doctors was rational. Cost effectiveness, improved

drug use in terms of safety and effectiveness are the advantages of using medicines from international or national essential drug list.[21,22] However, if drugs are not used from essential drug list, it does not mean that the prescriptions are irrational because essential drug lists do not contain the medicines used for common and/or uncommon diseases. There are also some limitations in our study like small sample size, short duration of the study and convenience sampling technique. Beside this, the study was not able to assess adherence of the patients to antihypertensive drugs.

CONCLUSION:

In this study calcium channel blockers (amlodipine) were commonly used as combination drug therapy as well as single drug. The prevalence of use of calcium channel blockers was comparable with the findings of some other similar studies done in international settings. In almost all of the patients, antihypertensive drugs were used from the essential drug list of Nepal which is an essential component of rational use of medicine.

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