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Original Research Article

**Drug utilization, adherence and occurrence of Resistant Hypertension among hypertensive patients visiting community based screening and management program in Eastern Nepal**Bhawesh Koirala<sup>\*1</sup>, Gajendra Prasad Rauniar<sup>2</sup>, Anup Ghimire<sup>3</sup> and Sanjib Kumar Sharma<sup>4</sup><sup>1</sup>Assistant professor, Department of Pharmacology, BPKIHS, Dharan, Nepal<sup>2</sup>Head of Department and Professor, Department of Pharmacology BPKIHS, Dharan, Nepal<sup>3</sup>Head of Department and Professor, School of Public Health and community Medicine, BPKIHS, Dharan, Nepal<sup>4</sup>Head of Department and Professor, Department of Internal Medicine, BPKIHS, Dharan, Nepal

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Hypertension is a global health problem with almost quarter of adults estimated to have high blood pressure [1]. Studies have indicated high prevalence of hypertension in Nepalese population. One such study done in Dharan, Eastern Nepal 2005 found a prevalence of almost 23% (according to JNC VII guidelines) [2].

Treatment with antihypertensive drugs reduces the morbidity and mortality related to hypertension [3]. Various guidelines on hypertension treatment are available[4-5].

The Joint National Committee (JNC) in 2003 published a series of guidelines recommend the appropriate  
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antihypertensive therapy based on the best available evidence. At present we have JNC 8 guidelines for the treatment of hypertension. The study of prescription pattern is the part of medical audit that monitors and evaluated the prescribing practices and recommends necessary modifications to achieve rational drug use[6].

Poor drug adherence may play a crucial role in the success of management of any disease. It is more important in case of chronic disease in hypertension[7].

Some patients with hypertension despite multiple medications and proper life style modification are not able

to control their high blood pressure. This increases the risk of adverse cardiovascular events.[8], such patients are said to have a resistant hypertension.

Resistant hypertension is defined in the 2008 American Heart Association guideline as blood pressure that remains above goal in spite of concurrent use of three antihypertensive agents of different classes, one of which should be a diuretic[9]. Patients whose blood pressure is controlled with four or more medications are considered to have resistant hypertension[10].

The current study aims to assess the drug utilization pattern, drug adherence and occurrence of resistant hypertension in hypertensive patients visiting community based program for early detection and management of Kidney disease, Hypertension, Diabetes and Cardiovascular diseases.

## 2. Methods

In this prospective crossover study, 140 hypertensive patients were enrolled after getting written informed consent. This study was performed after obtaining the ethical clearance from Institutional Research Committee (IRC), B.P. Koirala Institute of Health Sciences (BPKIHS), and Dharan. The study duration was of 6months starting, June 2017.

Data was collected using structured self-constructed questionnaire (translated in Nepali also) which have been prepared after reviewing multiple literatures [11-13] from the hypertensive patients visiting community program (KHDC) held on first Saturday of every month for follow-up. KHDC is a community based program for early detection and management of Kidney disease, Hypertension, Diabetes and Cardiovascular diseases[14].

The information regarding sociodemographic data, Blood pressure (measured value in mm Hg), Drug utilization, Drug adherence and adverse effects was entered in the questionnaire. For assessing the assessing the drug adherence patients were asked if they take the drug regularly. What was the cause of not taking the drug regularly? In past one month how many times did they miss taking the drugs? All the drugs patients were taking were listed. The patients were considered having resistant hypertension if they have uncontrolled BP in spite of taking antihypertensive from 3 different groups (one being diuretics). Those patients were also considered to have resistant hypertension if they were taking antihypertensive from four different groups irrespective of their Blood Pressure. The data was then entered in MS Excel and then analyzed using SPSS 17.0 version. For descriptive statistics, percentage, mean, Standard deviation was calculated along with graphical and tabular presentation. Mean BP among adherent and non-adherent patients was compared using independent sample t test.

## 3. Results

Out of 140 patients enrolled 52.1% (73) were male. Majority of the patient were aged between 40-59 years of age 50.7 % (71). Most of them were Aryans 55.7 % (78) followed by Mongolians 44.3% (62). Mean of Systolic Blood Pressure was 131.48(SD± 16.57) and Mean of Diastolic Blood Pressure was 81.7(SD±9.57). The Mean Drug prescribed per patients was 2.16(1.321) with maximum number of drug prescribed to be 7 and minimum 1. Eighty patients (57.1%) were taking single antihypertensive drugs. Others were taking two or more antihypertensive. Amlodipine was commonly prescribed antihypertensive 57.8. The other commonly prescribed antihypertensives were Losartan 26.424 % (37), Hydrochlorothiazide 17.1 % (Table 1).

**Table 1: Prescription pattern of antihypertensive drugs**

Drugs
<b>Diuretics</b>
Hydrochlorothiazide 24(17.1%)
Chlorthalidone 2
<b>ACE Inhibitors</b>
Enalapril 19(13.57%)
Ramipril 9(6.4%)
<b>Angiotensin(AT1) blockers</b>
Losartan 37(26.4%)
Omlsartan 8(5.7%)
Telmesartan 7(5%)
<b>Calcium channel Blockers</b>
Amlodipine 81(57.8%)
<b>Beta Adrenergic blockers</b>
Atenolol 20(14.2%)
Metoprolol 3
Bisoprolol 2
Nevivolol 1

Diabetes mellitus was the most frequent comorbidity. Metformin was the most common drug prescribed among non-antihypertensive drugs (Table 2).

**Table 2: List of Non- antihypertensive drugs prescribed**

<b>Anti-hyperglycemic Drugs</b>
Metformin(31)
Glimepiride(19)
Insulin(4)
Sitagliptin (3)
Linagliptin (1)
Tenegliptin(1)
Voglibose(1)
<b>Statins</b>
Atorvastatin (10)
<b>Antiplatelet Drugs</b>
Aspirin (9)
Clopidrogel(1)
<b>Thyroid Hormone</b>
Levothyroxine(4)
<b>Anti-Asthmatics</b>
Salbutamol (2)
Doxyfylline (1)

Drug adherence was seen among 76.4% of patients. (Figure 1) The most common cause of non-adherence was forgetfulness (Figure 2). There was significance difference in mean Systolic Blood Pressure among the adherent and non-adherent patients (Table 3). The common adverse seen among these patients was fatigue (Figure 3). The occurrence of other adverse effects was low (Table 4). Resistant hypertension was seen in 2 out of 140 patients enrolled.

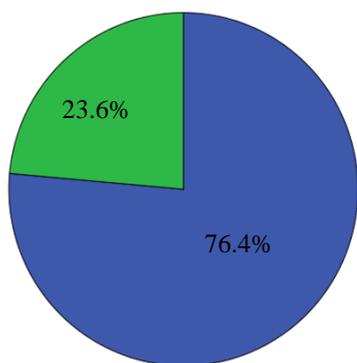


Figure 1: Drug Adherence

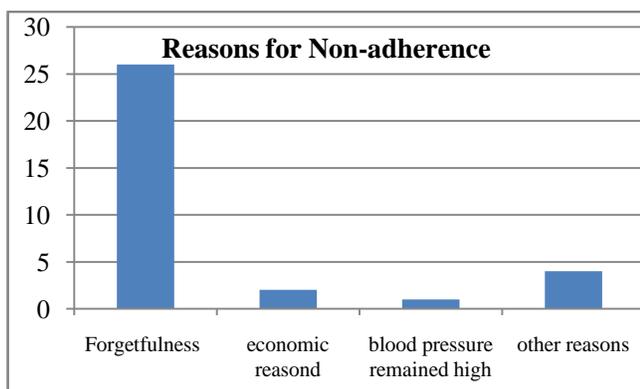


Figure 2: Reasons for the non-adherence

Table 3: Difference in Mean SBP and DBP amongst adherent and non-adherent patients

	Adherent Patients (N=109)	Non-Adherent Patients (N= 31)	P value
Mean Systolic BP	129.88	136.64	P=0.04*
Mean Diastolic BP	81.12	84.73	P=0.96

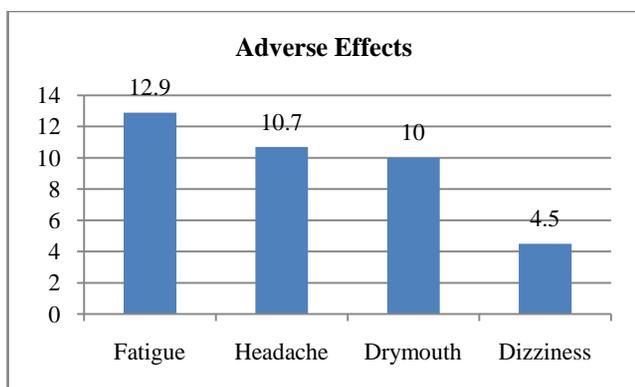


Figure 3: Common adverse effects

Table 4: Occurrence of adverse effects amongst patients on antihypertensive medications

Adverse Effects	Occurrence N (%)
Fatigue	18(12.9%)
Dry mouth	14(10%)
Drowsiness	12(8.6%)
Nausea	7(5%)
Diarrhea	6(4.3%)
Constipation	10(7.1%)
Swollen feet or legs	13(9.3%)
Muscle pain	12(8.6%)
Cramps	7(5%)
Headache	15(10.7%)
Dizziness	14(10%)
Anxiety	8(5.7%)
Shortness of breath	7(5%)
Persistent dry cough	6(4.3%)
Itching	7(5%)
Skin rashes	5(3.6%)
Increase in sweating	7(5%)
Frequent urination	9(6.4%)
Decreased sexual desire	1(0.7%)

#### 4. Discussions

Hypertension is common disease and is on rising trend. The occurrence of hypertension in age group of > 40 years is consistent with the study done in china[15]. Most of the patient had their blood pressure controlled.

The Mean Drug prescribed per patients was just above 2. In a study done by Hesse in which he studied the pattern of outpatient drug treatment of hypertension, the mean drug prescribed per prescription was 2.2[16] which is very similar to our study. Number of medicine prescribed may have implication on adherence. This was reflected in our study where the adherence was good.

Eighty patients (57.1%) were taking single antihypertensive drug. One retrospective study showed that the monotherapy (48.94%) was leading trend in hypertensive therapy[17], which is similar to our study.

Amlodipine (Calcium channel blocker) was prescribed in 57.8% of patients followed by losartan (ARB) (26.4 %) and Hydrochlorothiazide (Diuretics) (17.1%) One cross-sectional study conducted in Nigeria showed that the common antihypertensive drugs used were diuretics and calcium channel blockers [18].

Other study in India showed the common antihypertensive used was Amlodipine (37%) followed by Losartan (11%) and Telmisartan (10%) and hydrochlorothiazide was prescribed in 15% of the patients [19]. So our findings in this regard are somewhat similar to previous studies.

Metformin (Biguanides) and Glimperide (Sulphonylureas) were commonly prescribed non antihypertensive drugs. The above mentioned cross sectional study done in Nigeria also showed metformin and Glimperide were the commonly prescribed non-

antihypertensive drugs [17]. Other study done by P Das showed similar results in regard with antidiabetic drugs[20]. Further, diabetes mellitus was seen in 25% of our patient. Studies have shown that hypertension and diabetes mellitus coexist commonly and is the leading cause of polypharmacy[21]. This might be one of the reasons why the mean prescription in our study was more than 2 as antidiabetic drug had to be given along with antihypertensive.

In our study 76.4% patients were adhere to medicines .One Institutional based cross sectional study conducted in Ethiopia revealed found adherence to antihypertensive medication to be 67.2% (22). Further study conducted in Malaysia also observed that the patients' adherence to antihypertensive medication was good (53.4%)[7].

The adverse effects were not that common among patients. Fatigue, headache, dryness of mouth and dizziness were common among seen adverse effects. Headache and dizziness is associated with amlodipine[23] which was the most commonly used drug in our patients. Moreover adverse effects were mild and not affecting the therapy whatsoever.

The resistant hypertension was seen in 2patients out of 140. Studies have shown the prevalence of resistant hypertension to be 15 to 30% while the incidence rate of the same to be 1.9%[24]. So although our study showed the occurrence of resistant hypertension to be low, more extensive studies involving larger group of cohort is required to reach any conclusion.

The common group of antihypertensive prescribed was CCB, ARB and Diuretics, so the prescription pattern is consistent with guidelines provided by JNCVII for the treatment of hypertension. The adherence to the prescribed drugs was good amongst the patients. The occurrence of resistant hypertension was low.

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