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Prescribing patterns of antihypertensive drugs by clinicians at the National Referral Hospital outpatient department, Thimphu, Bhutan

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ABSTRACT

Introduction: Around 1.28 billion adults aged 30-79 years have hypertension, globally. Of these, two-thirds are in low and middle-income countries, with only 21% having it under control. In Bhutan, there are 362.4 people per 10,000 population with hypertension. Antihypertensive medications must be appropriately prescribed to prevent the complications of hypertension. **Methods:** A cross-sectional study of the prescriptions of antihypertensive medications at Jigme Dorji Wangchuck National Referral Hospital was undertaken to characterize the current prescribing patterns. **Results:** Nine monotherapy, 18 dual therapy, 19 triple therapy and 2 multiple combination therapy with antihypertensive drugs were noted during the study period spanning April to December 2023. Nearly half (59.1%) of the hypertensive patients were treated with monotherapy, 36.3% with dual therapy, 4.3% with triple therapy and 0.3% with multiple combination therapy. The proportion of patients who had their blood pressure under control was 42.45%, with females slightly outnumbering males (26.66% versus 15.79%). However, there was no statistically significant difference in blood pressure control between females and males and also between patients who received monotherapy or combination therapy. **Conclusion:** The study found the prescription of a wide range of drugs, both alone and in combination, to treat hypertension. The proportion of patients with controlled blood pressure was 42.45%.

Keywords: *Antihypertensive drugs; Bhutan; Blood pressure control; Hypertension; Prescribing pattern*

INTRODUCTION

Globally, 1.28 billion adults in the age group of 30-79 years have hypertension and 66% of them are in low and middle-income countries. Of these, only 21% have their blood pressure under control[1]. In the Southeast Asia Region where 25% of adults have hypertension, only one in three are treated and only 10% have their hypertension under control[2]. Hypertension is defined as a systolic blood pressure of >= 140 mmHg or a diastolic pressure of >= 90 mmHg[1,3]. Despite advances in medical therapy, hypertension remains a major risk factor for stroke, heart failure, renal failure, atherosclerosis, and dementia[4]. In Bhutan, there are 352.4 people per 10,000 population (3.52%) with hypertension, an increase from 301.2/10,000 (3.01%) in 2019[5]. Among other complications, hypertension (20.85%) was the most common cause of end stage renal disease in Bhutan[6].

The treatment and control of hypertension is essential to prevent the development of complications, as well as control the worsening of associated complications. Similarly, patients's optimal adherence to anti hypertensive drugs is essential to prevent complications of hypertension[7]. Effective hypertension management and compliance with medications will bring about better health and economic benefits. It will reduce burdens on acute-care services, increase the integration of health care systems, and most importantly, reduce deaths, suffering, and costs arising from complications such as heart failure, stroke and kidney failure[1]. Patients often require a combination of antihypertensive drugs for the control of hypertension.

Although there are several guidelines for treating hypertension such as the Joint National Committee guideline, WHO guidelines for the pharmacological treatment of hypertension in adults and the recent hypertension protocol of Bhutan, clinicians may not be aware of the latest updates on treatment guidelines[3,8,9]. These could lead to outdated prescription practices and suboptimal control of blood pressure leading to complications of hypertension.

Over 10 antihypertensive drugs of various classes are available for prescription in Bhutan. The objective of the study was to characterize the current prescribing patterns of antihypertensive drugs.

METHODS

Study design

This cross-sectional study was carried out at the outpatient departments of JDWNRH over a period of nine months spanning 18 April 2023 to 31 December 2023.

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Study setting

JDWNRH is the apex tertiary teaching hospital in Bhutan, where 593,290 patients were seen in the outpatient department in 2023[10]. The hospital has 1,530 staff with 20 clinical departments. The departments provide general clinical services as well as superspeciality services including cardiology, nephrology, gastroenterology, maternal fetal medicine, urology, neurosurgery, pediatric surgery, and pediatric ophthalmology among others.

Study participants

The study included patients over the age of 18 years who were on antihypertensive treatment. Patients under the age of 18 years, pregnant women, and those with comorbidities were excluded from the study.

Data collection

The prescriptions of patients who were diagnosed with hypertension and on antihypertensive drugs were retrieved from the electronic Patient Information System (ePIS). ePIS is a system for recording, storing and sharing patient information for patient care, research and quality management through an online electronic system. The system was launched at JDWNRH on 18 April 2023 and is being rolled out to other hospitals. Details including demographic information, names of antihypertensive medications and blood pressure readings were extracted by the author from the ePIS record.

Data analysis

Data was checked for duplication by using Microsoft Excel and analyzed using SPSS version 25. Demographic information of patients is presented as percentages, median, and mean values. The types of drugs prescribed and the proportion of controlled blood pressure are analysed as frequencies and percentages. The significance of the association of blood pressure control between females and males and between monotherapy and combination therapy was determined using a chi square test, with a p value of < 0.05 being statistically significant.

Ethical clearance

Ethical clearance was obtained from the Institutional Review Board of KGUMSB (IRB/Approval/PN/2023-021/1134). Administrative clearance for the study was obtained from Ministry of Health and JDWNRH.

RESULTS

A total of 1150 prescriptions were obtained for the study, where 61.65 % were females. The median age was 55 years with a range of 19-94 years. Nearly 40% of the patients were above the age of 60 (Table 1).

More than half of the patients were treated with monotherapy (59.1%), followed by dual therapy (36.3%) as depicted in Table 2. Among the antihypertensive regime, losartan is the most prescribed drug (45.9%) among the monotherapy drugs and a combination of losartan with amlodipine is the most frequent drug prescribed for dual therapy (16.2%). The combination of losartan, hydrochlorothiazide, and amlodipine was prescribed most frequently (1.7%) in the triple therapy group (Table 3).

Table 1. Demographics of patients taking antihypertensive drugs at JDWNRH outpatient departments, 2023.

Age group (years)	Females n(%)	Males n(%)
15-19	1 (0.09)	0 (0)
20-24	4 (0.35)	2 (0.17)
25-29	5 (0.43)	10 (0.87)
30-34	25 (2.17)	11 (0.96)
35-39	68 (5.91)	16 (1.39)
40-44	76 (6.61)	39 (3.39)
45-49	91 (7.91)	62 (5.39)
50-54	117(10.17)	44 (3.83)
55-59	68 (5.91)	60 (5.22)
60-64	64 (5.57)	53 (4.61)
65-69	70 (6.09)	46 (4.00)
70-74	66 (5.74)	42 (3.65)
75-79	41 (5.57)	26 (2.26)
80-84	8 (0.70)	21 (1.83)
85-89	3 (0.26)	8 (0.70)
90-94	2 (0.17)	1 (0.09)
Total	**709 (61.65)**	**441 (38.35)**

Table 2. Distribution of antihypertensive drug therapy prescribed to hypertensive patients during the study period at JDWNRH in 2023.

Therapy type	N (%)
Mono Therapy	680 (59.1)
Dual Therapy	417 (36.3)
Triple Therapy	50 (4.3)
Multi Therapy	3 (0.3)
Total	**1150 (100)**

Table 3. Prescription pattern of antihypertensive drugs among hypertensive patients during the study period at JDWNRH in 2023.

Antihypertensive drugs	Number of patients n (%)
Monotherapy	
Losartan	528 (45.9)
Hydrochlorothiazide	73 (6.3)
Amlodipine	38 (3.3)
Nifedipine	22 (1.9)
Enalapril	7 (0.6)
Propranolol	7 (0.6)
Atenolol	3 (0.3)
Carvedilol	1 (0.1)
Hydralazine	1 (0.1)
Dual therapy	
Losartan, amlodipine	186 (16.2)
Losartan, hydrochlorothiazide	123 (10.7)
Losartan, nifedipine	59 (5.1)
Losartan, propranolol	16 (1.4)
Nifedipine, hydrochlorothiazide	6 (0.5)
Losartan, atenolol	5 (0.4)
Amlodipine, enalapril	5 (0.4)
Losartan, metoprolol	3 (0.3)
Losartan, carvedilol	2 (0.2)
Losartan, enalapril	2 (0.2)
Nifedipine, metoprolol	2 (0.2)
Hydrochlorothiazide, amlodipine	2 (0.2)
Hydrochlorothiazide, propranolol	2 (0.2)
Losartan, captopril	1 (0.1)
Amlodipine, carvedilol	1 (0.1)
Amlodipine, hydralazine	1 (0.1)
Amlodipine, propranolol	1 (0.1)
Enalapril, atenolol	1 (0.1)
Triple therapy	
Losartan, hydrochlorothiazide, amlodipine	20 (1.7)
Continued...	
Losartan, nifedipine, hydrochlorothiazide	7 (0.6)
Losartan, amlodipine, propranolol	3 (0.3)
Losartan, nifedipine, atenolol	2 (0.2)
Losartan, hydrochlorothiazide, propranolol	2 (0.2)
Losartan, amlodipine, metoprolol	2 (0.2)
Losartan, nifedipine, atenolol	1 (0.1)
Losartan, hydrochlorothiazide, hydralazine	1 (0.1)
Losartan, hydrochlorothiazide, enalapril	1 (0.1)
Losartan, hydrochlorothiazide, metoprolol	1 (0.1)
Losartan, hydrochlorothiazide, atenolol	1 (0.1)
Losartan, amlodipine, carvedilol	1 (0.1)
Losartan, amlodipine, atenolol	1 (0.1)
Losartan, enalapril, carvedilol	1 (0.1)
Nifedipine, amlodipine, carvedilol	1 (0.1)
Nifedipine, amlodipine, captopril	1 (0.1)
Hydrochlorothiazide, amlodipine, atenolol	1 (0.1)
Hydrochlorothiazide, enalapril, carvedilol	1 (0.1)
Amlodipine, atenolol, propranolol	1 (0.1)
Multiple therapy	
Losartan, hydrochlorothiazide, amlodipine, metoprolol	2 (0.2)
Losartan, nifedipine, hydrochlorothiazide, propranolol	1 (0.1)
Total	**1150 (100)**

Among those patients on medications, 42.45% of the patients had their blood pressure under control. Blood pressure control is defined as systolic blood pressure and diastolic blood pressure <140/90 mmHg. There was no significant difference in the blood pressure control between patients receiving monotherapy or combination therapy, neither between females and males on antihypertensive drug treatment (Table 4).

DISCUSSION

A total of 1150 prescriptions were obtained in the study, wherein 61.65% of the prescriptions were of females with hypertension, in contrast to a study in India with 82.5% males[7]. The difference could be due to the selection of patients in the two studies. In the Indian study, patients were selected only after three visits and maybe male patients could make it to all three visits. The lesser number of males with hypertension in this study could be attributed to their higher physical activity levels, while higher in-

take of salt by females may explain their higher prevalence of hypertension[11]. The mean age of 55.80 years (± 13.67) in this study is similar to two studies conducted in India, where the mean age of the study participants was reported as 57.13±10.94 years and 56.96±14.60 years, respectively[7,12]. This similarity in mean age amongst hypertensive patients could be due to the similarities of the population, both belonging to the Southeast Asia region with similar dietary habits.

It is concerning that nearly 40% of the patients are aged 60 years and above, as hypertension is an important risk factor for cardiovascular morbidity and mortality amongst the elderly[13]. A possible reason for this increased prevalence of hypertension in the older age group could be due to arterial stiffness along with neurohormonal and autonomic dysregulation, which develops with advancing age [1,14].

The majority of hypertensive patients in this study were treated with monotherapy (59.1%) followed by dual therapy (36.3%), triple therapy (4.3%) and multiple therapy (0.3%). Monotherapy as a treatment for hypertension has been noted to be the most common type of drug therapy in the region. Three studies conducted in India have reported monotherapy in 47.5%, 34.6% and 50.8% of their participants respectively. Dual therapy is the next most commonly used therapy in these three studies as well[7,12,15]. Similar findings have also been reported by studies in Taiwan and South Korea where 53% and 63% of hypertensive participants respectively, were on single drug therapy[16,17]. Contrary to this study's findings, a study conducted in the United Arab Emirates reported that dual therapy was the most common prescription (35.5%) followed by monotherapy (23.1%)[19]. A possible cause for this difference may be because they included both admitted patients and those availing outpatient department services.

Losartan, an angiotensin receptor blocker, was the most commonly used monotherapy agent (45.9%) in this study. Losartan features in the top 3 commonly used antihypertensive drugs when used as a single drug therapy in studies in India and South Korea[7,12,15,17]. A combination of losartan and amlodipine, a calcium channel blocker, was the most frequently prescribed dual therapy (16.2%) in this study. Similar findings have been reported by studies conducted in India, South Korea and Singapore[7,17,18].

Although losartan is the most commonly prescribed medication both as monotherapy and in combination, it is not the recommended first line agent as per Bhutan's first national hypertension protocol. The guideline recommends hydrochlorothiazide as the first line agent. This deviation from the recommendation may be due to the fact that the guideline was launched only in September 2023, and thus, prescribers are unaware of this recommendation.

A significant finding is that only 42.45% of patients had their blood pressure under control, with females slightly outnumbering males (26.66% versus 15.79%). A similarly low rate of blood pressure control was reported by the 5th National Health Survey 2023 where only 7.9% had their blood pressure under control[11]. The difference in the blood pressure control rates between this study and the National Health Survey would be due to the large sample size of the Nationwide Health Survey. A study in South India, with exclusion criteria similar to this study, reported that 39.5% of their participants had controlled blood pressure[21]. An analysis that compared national surveys from 20 countries reported varying rates of controlled hypertension ranging from 4.4% in Albania to 15.7% in Thailand and 43.2% in Bangladesh[20]. Despite the availability of several antihypertensive drugs worldwide, blood pressure control remains suboptimal[22, 23].

Table 4. Blood pressure control among hypertensive patients, by types of therapy and gender, visiting outpatient departments of JDWNRH, 2023.

Status of Blood pressure	Controlled n (%)	Un-controlled n (%)	Chi-square	p-value
Types of therapy				
Combination therapy	163 (16.40)	243 (24.44)		
Monotherapy	259 (26.06)	329 (33.10)	1.495	0.221
Gender				
Male	157 (15.79)	219 (22.03)		
Female	265 (26.66)	353 (35.51)	0.121	0.728

There was no statistically significant difference in blood pressure control between females and males, neither between patients on monotherapy or combination therapy in this study. However, a Sri Lankan study has reported a significant association between systolic blood pressure and the type of drug therapy[24]. The contrasting findings in the two studies could be due to the inclusion of hypertensive patients with co-morbidities in the Sri Lankan study.

Limitations

This study was conducted at the National Referral Hospital and may not represent the findings from the whole country. Furthermore, blood pressure control was based on a single visit and thus, may vary from other studies.

CONCLUSION

This study found that losartan and hydrochlorothiazide were the most commonly prescribed antihypertensive drugs, either alone or in combination. Policymakers should promote the National Hypertension Protocol for consistent prescribing. Targeted interventions for those aged 60 years or older, and general interventions for improving controlled blood pressure rates must also be planned. As these findings are specific to the national referral hospital, further studies are needed to explore prescribing patterns across the country.

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AUTHORS CONTRIBUTION

DS formulated the concept, collected data, wrote up, edited and reviewed the manuscript. He agrees to be accountable for all respects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

None

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