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A descriptive study on prescription pattern of antihypertensive medications in a tertiary care hospital in Northern Sri Lanka.

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Abstract

Background: Hypertension is a major public health problem globally and it accounts for a significant health burden to developing countries like Sri Lanka. The prescribing patterns of antihypertensive medications are highly dynamic due to the invention of new medications and regular update in the existing guidelines.

Objective: To study on prescription pattern of antihypertensive medications, factors influencing the choice and its effect on the blood pressure control in a tertiary care hospital.

Methods: This cross-sectional study was carried out in medical outpatient clinics of teaching hospital, Jaffna. The interviewer administered questionnaire was used to collect data. Data were analysed using SPSS 26.

Results: Most of the patients were on monotherapy (46.7%) followed by two medications regimens (33.8%). Among the monotherapy group, "Angiotensin Converting Enzyme Inhibitors" (ACEI) (30.1%) were the most widely prescribed medication. Commonly used medications for the treatment of hypertension either as monotherapy or combination therapy were ACEI (72.6%), CCB-DP (35.9%), thiazide diuretics (32%), ARB (19.8%), and alpha-blockers (11.7%). Factors such as age (P-0.012), family income (P<0.001), place of residence (P-0.016) and diabetes mellitus (P-0.026) were significantly associated with choice of antihypertensive medications. Further type of medication regimen (P-0.014) showed significant influence on the SBP control.

Conclusion: This study revealed prescription pattern of antihypertensive medications was largely complied with published international guidelines and was rational. Systolic blood pressure control significantly influenced by type of medication regimen. Despite published hypertension management guidelines, the choice of anti-hypertensive medications should be tailored to each patient depending on the socio-demographic and clinical factors.

Keywords: Antihypertensive medication pattern, Northern Sri Lanka, Blood pressure control, Hypertension

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INTRODUCTION

Hypertension is a major public health concern as it is an underlying cause for cardiovascular morbidity and mortality globally[1,2]. The prevalence of hypertension of adults is rising globally hence treatment of hypertension is the most common reason for clinic visits and long term use of prescribed medication[3,4] . Recent developments provided the opportunity to choose different classes of anti-hypertensive medications to treatment of hypertension and evidences showed those are equally effective[2]. Further a study conducted on the effectiveness of anti-hypertensive medications in controlling blood pressure among Sri Lankan adults concluded that hypertension can be controlled within three months[5]. However, many patients' factors can affect the way a patient may respond to one treatment over another[2].

The prescribing patterns of antihypertensive medications are highly dynamic due to the invention of new medications and update in the existing guidelines. It varies among the countries even within the country as well due several factors such prevalence of hypertension, cost and availability, physicians' preferences and patient's compliance to treatment[1]. Based on previous studies in primary care setting 75.7% received mono therapy[6] and similarly in an Ethiopian tertiary care centre 50% of patients were on mono therapy[7]. In contrast study in South Indian tertiary care hospital[8], showed that 51% were on multi medications therapy and calcium channel blockers (49%) were the commonest medication class prescribed. But study carried out in Mexico City in 2012 showed 86.4% of the patients with hypertension receiving medications and of that 63.8% on Angiotensin-converting enzyme inhibitors[9.]

The regular monitoring and evaluation of the prescription pattern of antihypertensive medication are necessary to modify the prescribing practices of the prescribers in addition it gives an insight into prescribing patterns and if there is a suboptimal prescription which will then warrant further evaluation[10-12]. Although the prescribing pattern of antihypertensive medications is a leading cause of uncontrolled hypertension there were very limited number of researches has been done. In the Sri Lankan context, only one study was done in the eastern province to date. Current study particularly focused on the prescription pattern of antihypertensive medications and factors influencing the prescription pattern, and also compares their effect on the blood pressure control in the tertiary care hospital in Northern Sri Lanka.

MATERIALS AND METHODS

Study design and setting

This cross-sectional descriptive study was carried out in medical outpatient clinics of Teaching Hospital, Jaffna of Northern Sri Lanka. Teaching Hospital, Jaffna is the only tertiary care centre in the region and hypertensive patients from all over the northern province of Sri Lanka usually attend the general medical clinics of Teaching Hospital, Jaffna.

Sample size

The Sample size was estimated using estimate a proportion formula [14]

$n = Z^2 x\ P\ (1-P)/\ d^2$

z -value at the confidence level = 95% is 1.96 Acceptable difference (d) = 0.03(3%) and we have taken 10.5% from the previous study in same setting [13] in order to give sample size (n) and with assumed 5% not response rate sample size was inflated 421.

Inclusion criteria

Adult male and female patients with hypertension with or without other co-morbid diseases who were attending general medical clinics of Teaching Hospital Jaffna were considered for this study. Participants who consented to participate in the study were included, whereas mentally handicapped patients, under 18 years, and pregnant were excluded.

Study instrument and techniques

Data were collected from patients who fulfill the inclusion criteria by using an interviewer administrative questionnaire. The principal investigator collected the data during the study period from 1st of April 2020 to June 2020.

According to records available 1500 patients were expected to attend to outpatient clinic settings. So every 3rd patient was interviewed starting from randomly selected number between numbers 1 to 3 over the 3 months to reflect entire population.
The Tamil version of the questionnaire was evaluated by five consultant physicians for consensual, face and content validity by expert judgment. Then the questionnaire pre-tested and participants included in the pre-test were not included in the study proper. Following pre-test necessary changes were made. The questionnaire covered patients' demographics, clinical details including chronic medical conditions (diabetes, Chronic kidney disease(CKD), Ischaemic Heart Diseases (IHD), Peripheral vascular Diseases(PVD), Bronchial Asthma (BA)/ Chronic Obstructive Pulmonary Disease (COPD), Cerebrovascular Accidents (CVA)) and number of anti-hypertensive and other medications. Anti-hypertensive medication details extracted from clinic records by principal investigator. Drug compliance was assessed by principal investigator by cross checking of use of pills.

Definition of Blood Pressure control

Definition of hypertension varies according to the guidelines. 2017 ACC/AHC guideline defines hypertension as systolic blood pressure equal to or more than 130mmhg and/ or diastolic pressure equal to or more than 80mmhg [15] Blood pressure control was defined as "good control" if a systolic blood pressure (SBP) below 130 mmHg and/or diastolic blood pressure (DBP) below 80 mmHg

Ethical Approval

The ethical approval was obtained from the Ethical Review Committee, postgraduate institute of medicine, University of Colombo, Sri Lanka.

Statistical Data Analysis

Data were entered and analysed using SPSS (version 26). Descriptive and summary statistics were presented in tables and figures. Data were expressed as a percentage and bivariate analysis was done to identify which variables associated with antihypertensive medications therapy (Single therapy/Combined therapy) and also with blood pressure control by using Chi-square test. P-value less than 0.05 was considered as statistically significant. Multivariable logistic regression was used for controlling the possible effects of confounders to identify the factors influenced on antihypertensive medication pattern (Single or Combined therapy). Factors included in the model were age**,** family income, place of residence**,** co-morbidities such as diabetes, duration of hypertension, duration of treatment and medication started by(Consultants/non-specialist medical officer).Similarly backward stepwise logistic regression analysis done by including significant factors identified in the bivariate analysis(civil status, current occupation, Chronic Kidney Disease, duration of hypertension, duration of treatment, medication adherence, number of medications (Mono/Two/Three/ Four or More medications) to see the influence on blood pressure control.β coefficient (standard error) and Wald statistics were calculated. Finally, the variables independent associated with identified based on the P-values.

RESULTS

The mean age of the 435 patients was 63.67±9.75. Nearly three-fourths of patients were above the age 50 (76.6%) and the majority study population were female (65.1%). Approximately two-third of the participants were living in rural area (60.7%) (Table 1). The majority of them completed secondary education (63.9%) and belongs to the lower income group (60%).Most of them were married and 22.8% were widowed. Small proportion of participants reported consuming alcohol (6.4%) and 4.1% were consuming in unsafe levels. Similarly, only 4.8 % of them reported smoking and on average they smoke 3 Pack year+_2.31.

Table 1: Socio demographic characteristics of the participants (n-435)

Socio demographic Character	Categories	Number	Percentage
Gender	Male	150	34.5
	Female	283	65.1
	Transgender	2	0.5
Age	<40Years	12	2.8
	40-60Years	90	20.7
	Above 60Years	333	76.6
Place of Residence	Urban/Sub Urban	171	39.3
	Countryside	264	60.7
Educational Status	No Formal Schooling	12	2.8
	Primary Education(up to Year 6)	143	32.9
	Secondary Education (Year 6-A/L)	278	63.9
	Tertiary	2	0.5
Civil Status	Married	310	71.3
	Unmarried	16	3.7
	Divorced/Separated	10	2.3
	Widowed	99	22.8
Current Occupation	Night Duty	39	9.0
	No Night Duty	396	91.0
Religion	Hindu	361	83.0
	Buddhist	7	1.6
	Christian	65	14.9
	Muslim	2	0.5
Ethnicity	Tamil	427	98.2
	Sinhalese	5	1.1
	Muslim	3	0.7
Family Income	<Rs25000	261	60.0
	Rs25001-Rs50000	26	6.0
	>Rs50001-Rs75000	148	34.0
Smoking	Yes	21	4.8
	No	414	95.2
Alcohol	No	407	93.6
	Safe Level	10	2.3
	Not Safe Level	18	4.1

Clinical Characteristics related to Hypertension

Significant proportion (31.5%) of patients is having hypertension more than 10 years, 26.9% of them having it 1-5 years and similarly 26.9% for 6-10 years. One hundred and sixty-four (37.7%) were diagnosed at age between 51 and 60, followed by 33.6% of them were diagnosed after age 60 and another 21.4% between age 40 and 50. The SBP was well controlled in the majority (57.2%:52.6-61.8) but DBP was not well controlled (71.7%:67.4-75.8) in most of them. Majority (95.4%) showed good compliance with medication and most of them on medications for more than 5 years (58. 2%).All patients were getting medications free of charge from the state health sector. The majority of the time medication was initiated by specialists (67.4%) and medication dose was changed or increased in most (60.2%) of the patients and 74 patients (17%) reported either medications were decreased or withheld. The main reasons for either dose decreased or withheld were side effects (16.1%) or co-morbidity (0.9%) (Table 2)

Table 2: Clinic Characteristics related to hypertension (n-435)

Clinical Character	Categories	No	%
Duration of Hypertension	Lessthan1year	64	14.7
	1-5 Years	117	26.9
	6-10Years	117	26.9
	More than 10 Years	137	31.5
Age at Diagnosis	Age18-30 Years	6	1.4
	31-40 Years	26	6.0
	41-50 Years	93	21.4
	51-60Years	164	37.7
	>60Years	146	33.6
SBP (Systolic Blood Pressure) Controlled	Yes	249	57.2
	No	186	42.8
DBP(Diastolic Bl0od Pressure)Controlled	Yes	123	28.3
	No	312	71.7
Medications Compliance	Good	415	95.4
	Poor	20	4.6
Duration of Medication	Less Than 1 Year	64	14.3
	1-5 Years	120	27.6
	Above 5 Years	253	58.2
Medication Free Charge	Yes	435	100
Medication Started by	Consultant	293	67.4
	Non Consultant Medical Officer	6	1.4
	Consultant & Non Consultant Medical Officer	136	31.3
Change medication or dose from the start	No Change	109	25.1
	Dose Increased	262	60.2
	Dose Decreased	4	9
	Withheld	38	8.7
	Dose Decreased & Withheld	22	5.1
Reason for decreased/With held	Side Effects	70	16.1
	Due to coexisting Morbidity	4	0.9

Comorbid conditions among patients with hypertension and medications (other than anti-hypertensive medications) prescribed among study participants

Dyslipidemia (75.9%), diabetes mellitus (48.5%), IHD (22.1%) chronic lung disease (15.2%), CKD (6%) and cerebrovascular disease (5.2%) are the most common co-morbidities among hypertensive patients. Table 3 shows the gender differences with co-morbidities. Only CVA showed significant differences between males and females (P-0.023). Further the common medications other than anti-hypertensive medications prescribed among the patients were statins namely atorvastatin (76.8%), followed by metformin (39.5%), sulphonylureas (24.8%) and aspirin 23.2%. Further 3.7% were on DPP4i, 0.5% were taking clopidegral and 8.3% were on insulin.

Table 3: Comorbid conditions among participants according to the gender (n-435)

Co Morbidities	Male (n,%)	Female (n, %)	Trans gender (n, %)	Total (n, %), P value
Diabetes Mellitus (DM)	67(15.4%)	142(32.6%)	2(0.5%)	211(48.5%);P-0.190
Chronic Kidney Disease (CKD)	15(3.4%)	11(2.5%)	0	26(6%);P-0.071
Ischaemic Heart Disease (IHD)	42(9.7%)	76(17.5%)	0	118(22.1%);P-0.616
Peripheral Vascular Disease (PVD)	0	0	0	0
Chronic Lung Disease (BA/COPD)	20(4.6%)	46(10.6%)	0	66(15.2%);P-0.604
Dyslipidaemia	111(25.5%)	217(49.9%)	2(0.5%)	330(75.9%);P-0.599
Cerebrovascular Disease(CVA)	14(3.2%)	9(2.1%	0	23(5.2%);P-0.023

As showed in the Table 4, most of the patients prescribed by mono-therapy (46.7%) for the control of blood pressure followed by two medications regimen (33.8%), three medications (15.6%), and four or more medications regimens (3.9%). Among the mono-therapy group ACE-I (Angiotensin-Converting Enzyme Inhibitors) (30.1%) are the most widely prescribed medications followed by Angiotensin Receptor Blocker (ARB) (10.8%), Calcium Channel Blockers, Non-dihydropyridine (CCB-NDP) (3.2%) and Thiazide diuretics (1.2%). Among the two medications regimen ACEI + CCB-DP (13.3%) was commonly used followed by ACEI+ Thiazide Diuretic (8.5%). Similarly, among the three drug regimens, ACEI + CCB-DP+ Thiazide Diuretic (6.7%) was the common combination used and among four or more or medications combination ACEI + CCB-DP+ Thiazide Diuretic + Beta Blockers & others (2.3%) was the commonly used combination. Fig. 1, shows the commonly used medications for the treatment of hypertension either single therapy or combination therapy. ACEI (72.6%) group was most commonly prescribed medications by physicians for the treatment of hypertension followed by CCB-DP (35.9%), Thiazide diuretics (32%), ARB (19.8%), alpha-blockers (11.7%), others include beta-blockers (5.8%) and CCB-DP-0.5%.

Table 4: Anti-Hypertensive Medication used by patients in Mono and combination therapy (n=435)

Medications	Frequency	Percent
Mono Therapy (Single Therapy)	**203**	**46.7%**
ARB	47	10.8
ACEI	131	30.1
Thiazide Diuretic	5	1.2
Alpha Blockers	6	1.4
Two Medications Regimen	**147**	**33.8%**
ARB+ACEI	2	0.5
ARB+CCB-DP	5	1.2
ARB + Thiazide Diuretic	16	3.7
ACEI + CCB-DP	58	13.3
ACEI+CCB-NDP	2	0.5
ACEI+ Thiazide Diuretic	37	8.5
ACEI+ Alpha Blockers	8	1.8
ACEI+ Others (Beta Blockers & others)	2	0.5

CCB-DP+ Thiazide Diuretic	9	2.1
CCB-NDP+ (Beta Blockers & others)	6	1.4
Thiazide Diuretic+ Alpha Blockers	2	0.5
Three Medications Regimen	**68**	**15.6%**
ARB+ACEI+ CCB-DP	1	0.3
ARB+ACEI+ Thiazide Diuretic	2	0.5
ARB+CCB-DP+ Thiazide Diuretic	8	1.8
ARB+CCB-NDP+ Beta Blockers & others	2	0.5
ARB+ Thiazide Diuretic+ Alpha Blockers	1	0.3
ARB+ Alpha Blockers+ Beta Blockers & others	2	0.5
ACEI + CCB-DP+ Thiazide Diuretic	29	6.7
ACEI + CCB-NDP+ Alpha Blocker	6	1.4
ACEI + CCB-NDP+ Beta Blockers & others	1	0.3
ACI+ Thiazide Diuretic+ Alpha Blockers	13	3.0
ACEI+ Thiazide Diuretic+ Beta Blockers & others	3	0.7
Four/More Medications	**17**	**3.9**
ACEI + CCB-DP+ Thiazide Diuretic+ Alpha Blockers	4	1.0
ACEI + CCB-DP+ Thiazide Diuretic+ Alpha Blockers+ Beta Blockers & others	2	0.5
ACEI + CCB-DP+ Thiazide Diuretic+ Beta Blockers & others	10	2.3
ACEI + CCB-DP+ Alpha Blockers+ Beta Blockers & others	1	0.3

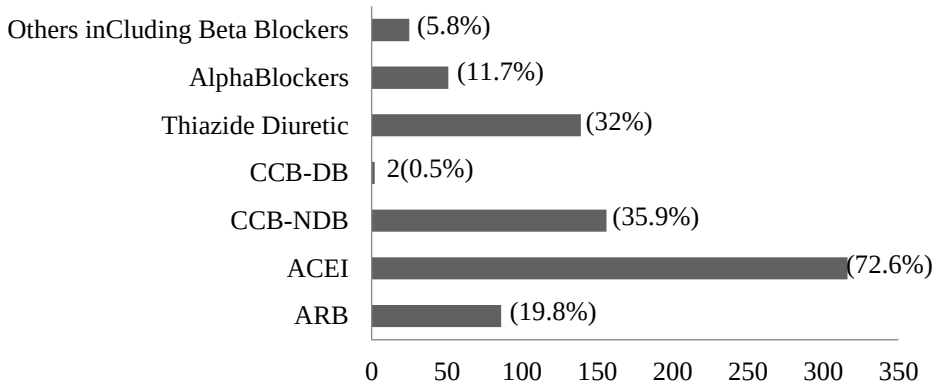

Figure 1: Anti-hypertensive medication use

Factors associated with the type of medications therapy (Single therapy /combined therapy)

Socio-demographic and clinical factors analyzed separately to see the association with a selection of medications therapy (Mono-therapy/Combined therapy), and results were summarized in Table 5 and 6. Among the socio-demographic factors age (P-0.019), family income (P-0.001) and place of residence (P-0.028) were associated with the choice of antihypertensive medications. Similarly, analysis of clinical factors revealed co-morbidities such as diabetes (P-0.043), and BA/COPD (P-0.028), duration of hypertension (P-0.007), duration of treatment(P-0.004) and medication started by (Consultants/non-specialist medical officers) (P<0.0001) were associated with the choice of antihypertensive medications. Further logistic regression analysis showed age (P-0.012), family income (P<0.001) and place of residence (P-0.016) and diabetes mellitus (P-0.026) significantly influenced the medications choice.

Table 5: Socio-demographic factors associated with the type of medications therapy

Variable	Type of Medications Therapy		Statistics
	Single	Combine	
Gender-			
Male	74(49.3%)	76(50.7%)	P-0.215
Female	127(44.9%)	156(55.1%)	
Educational Status-			
No formal schooling	6(50%)	6(50%)	
Primary Education	71(49.7%)	72(50.3%)	P-0.344
Secondary Education	124(44.6%)	154(55.4%)	
Tertiary Education	2(100%)	0	
Civil Status			
Married	149(48.1%)	161(51.9%)	
Unmarried	7(43.8%)	9(56.3%)	P-0.076
Divorced/Separated	8(80%)	2(20%)	
Widowed	39(39.4%)	60(60.6%)	
Current Occupation			
Night Duty	18(46.2%)	21(53.8%)	P-0.948
No Night Duty	185(46.4%)	21(53.3%)	
Place of Residence			
Urban/Sub Urban	90(53.2%)	80(46.8%)	P-0.028**
Countryside(Rural)	112(42.4%)	152(57.6%)	
Family Income			
<Rs25000	138(52.9%)	123(47.1%)	P-0.001***
Rs25001-Rs50000	15(57.7%)	11(42.3%)	
>Rs50001-Rs75000	50(52%)	98(66.2%)	
Age			
<40Years	2(16.7%)	10(83.3%)	P-0.019**
40-60Years	35(38.9%)	55(61.1%)	
Above 60Years	166(49.8%)	167(50.2%)	

Table 6: Clinical factors associated with the type of medications therapy

Variable	Type of Medication therapy		Statistics
	Single	Combined	
Diabetes			P-0.043**
Yes	109(51.7%)	102(48.3%)	
No	94(42%)	130(58.0%)	
Chronic Kidney Disease			P-0.245
Yes	15(57.7%)	11(42.3%)	
No	188(46.0%)	221(54.0%)	
IHD			P-0.818
Yes	54(45.8%)	69(54.2%)	
No	149(47.0%)	168(53.0%)	
CVA			P-0.586
Yes	12(52.2%)	11(47.8%)	
No	191(46.4%)	221(42.5%)	
BA/COPD			P-0.028**

Yes	39(59.1%)	27(53.6%)	
No	164(44.4%)	205(55.6%)	
Duration of Hypertension			
Less than1year	37(57.8%)	27(42.2%)	
1-5Years	65(55.6%)	52(44.4%)	P-0.007**
6-10Years	44(37.6%)	73(62.4%)	
More than 10 years	57(41.6%)	80(58.4%)	
Duration of Treatment			P-0.004**
Less than 1 Year	35(56.5%)	27(43.8%)	
1-5 Years	67(55.8%)	53(44.2%)	
Above 5 Years	101(39.9%)	152(60.1%)	
Medication Started by			P<0.0001***
Consultant	199(67.9%)	94(32.1%)	
Consultant & Non Consultant Medical Officer	0	136(100%)	
Non Consultant Medical Officer	4(66.7%)	2(33.2%)	

Influence of type of anti-hypertensive therapy and other factors on blood pressure control

Among the socio-demographic and clinical factors civil status (P-0.014), current occupation (Night duty /no night duty) (P-0.024), CKD (P-0.016), duration of hypertension (P<0.001), duration of treatment (P<0.001), type of medication regimen (Single, two medications/3 medications/4 medications or more) (P-0.014) and medication adherence (P<0.001) were significantly influenced the SBP control in bivariate analysis as showed in Table 7 & 8. Further logistic regression analysis revealed current occupation (P-0.002), CKD (P-0.024), type of medication regimen (0.007), duration of hypertension (P-0.001) and medication adherence (P<0.001) were independently associated with of SBP control.

Similar bivariate analysis for DBP control showed socio-demographic such as age and educational status (P<0.05) and of clinical variables showed duration of hypertension (P<0.001), the duration of treatment (P<0.001) and medication compliance (P<0.001) were showed association. Further logistic regression analysis showed the only duration of hypertension (P-0.002) and medication adherence (P<0.001) were associated with DBP control.

Table 7: Socio demographic Factors associated with SBP control

Variable	SBP Control		Statistics
	Yes	**No**	
Gender			ChiSquare-1.748;P-0.417
Male	88(58.7%)	62(41.3%)	
Female	154(56.2%)	124(43.8%)	
Transgender	2(100%)	9	
Educational Status-			ChiSquare-6.685; P-0.083
No Formal Schooling	10(83.3%)	2(16.7%)	
Primary Education	85(59.4%)	58(40.6%)	
Secondary Education	154(55.4%)	124(44.6%)	
Tertiary Education	0	2(100%)	
Civil Status			ChiSquare-10.643;
Married	168(54.2%)	142(45.8%)	P-0.014**
Unmarried	8(50%)	8(50%)	
Divorced/Separated	10(100%)	0	

Widowed	63(63.6%)	36(36.4%)	
Current Occupation			ChiSquare-5.129;
Night Duty	29(74.4%)	10(25.6%)	P-0.024**
No Night Duty	220(55.6%)	176(44.4%)	
Place of Residence			ChiSquare-0.594; P-0.441
Urban/Sub Urban	94(55%)	77(44%)	
Countryside (rural)	155(58.7%)	109(41.3%)	
Family Income			
<Rs25000	158(60.5%)	103(39.5%)	ChiSquare-0.594; P-0.441
Rs25001-Rs50000	14(53.8%)	12(46.2%)	
>Rs50001-Rs75000	77(52%)	71(48%)	
Age			
<40Years	6(50%)	6(50%)	ChiSquare-3.685; P-0.158
40-60Years	44(48.9%)	46(51.1%)	
Above 60Years	199(59.8%)	134(40.2%)	

Table 8: Clinical factors associated with SBP control

Variable	**SBP Control**		**Statistics**
	Yes	**No**	
Diabetes			ChiSquare-1.256;P-0.262
Yes	115(54.5%)	96(54.5%)	
No	134(59.9%)	90(40.2%)	
Chronic Kidney Disease (CKD)			ChiSquare-5.784;
Yes	9(34.6%)	17(65.4%)	P-0.016**
No	240(58.7%)	169(41.3%)	
IHD			ChiSquare-0.594;
Yes	64(54.2%)	54(45.8%)	P-0.440
No	185(58.4%)	132(41.6%)	
CVA			ChiSquare-0.255;
Yes	12(52.2%)	11(47.8%)	P-0.614
No	237(57.5%)	175(42.5%)	
Duration of Hypertension			
Less than1 year	20(31.3%)	44(68.8%)	
1-5Years	72(61.5%)	45(38.5%)	ChiSquare-21.427;
6-10Years	69(59%)	48(41%)	P<0.001***
More than 10 years	88(64.2%)	49(35.8%)	
Medications Compliance			ChiSquare-19.115;
Good	247(59.5%)	168(40.5%)	P<0.001***
Poor	2(10%)	18(90%)	
Duration of Treatment			ChiSquare-18.521;
Less than 1 year	20(32.3%)	42(67.7%)	P<0.001***
1-5 years	75(62.5%)	45(37.5%)	
Above 5 years	154(60.9%)	99(39.1%)	
Medications Therapy			ChiSquare-10.574;
Mono therapy	127(62.6%)	76(37.4%)	P-0.014**
Two Medications	86(58.5%)	61(41.5%)	
Three Medications	30(44.1%)	38(55.9%)	
Four/More Medications	6(35.3%)	11(64.7%)	

DISCUSSION

Most of the anti-hypertensive medications are freely available in Sri Lankan Government hospitals. Angiotensin system inhibitors (ACEI /ARB), Thiazide diuretics, CCB, alpha-blockers, methyldopa, beta-blockers and potassium-sparing diuretics are the five major classes of antihypertensive medications which are available to treat hypertension in this centre. Nearly half of patients were on a single medication regimen (46.7%) this is similar to the findings in a previous international study[8]. Among the patients receiving single medication, the most frequently used class was ACE-I (30.1%), followed by ARB 10.8%), CCB (3.2%), Alpha-Blockers (1.4%), and diuretics (1.2%). Notably beta-blockers were not prescribed as single medication. However, Alpha-Blockers were prescribed (1.4%) even though it is not recommended as first-line treatment in AHA guidelines [16]. This may be due to intolerance to other standard first-line medication or due to co-morbid conditions.

33.8% of patients were on two medications regimens and among them, ACE-I and CCB (40.8%) were the most commonly prescribed combination which is consistent with international standards[17]. Furthermore, there was a significant number of patients were on three or more medications (19.5%) and 17 patients (3.9%) were on four or more medications which indicates resistant hypertension. In the three medications regimen, the most commonly used medication combination (8.5%) was ACE-I or ARB, CCB and diuretics, which is in accordance with the standard international guidelines [16].

Most commonly being used as either monotherapy or combination therapy were ACE-I (72.6%), followed by CCB (35.9%), Thiazide diuretics (32%) and ARBs (19. 8%).This finding also is in line with a study done in Mexico City [9]. Furthermore, in multi medication regimens alpha-blockers (11.7%), centrally acting methyldopa (4.8%) and Beta-blockers or spironolactone (altogether less than 0.5% of patients) had been prescribed as alternatives when there was a contraindication or in toleration to standard antihypertensive medications.

The use diuretics and CCB was low when considering the age, indicates CCB and Thiazide diuretics were under-prescribed, even though the international guidelines recommend diuretics in the treatment of hypertension in elderly. The same results were observed in a study carried out in Serbia which study concluded that in spite of effectiveness of diuretics in the treatment of hypertension in the elderly, it was under utilized[17].

Following Table 9 concept was adopted and modified from previous study [18] comparing the prescription pattern of antihypertensive medications in different studies which have done internationally.

Table 9: different studies conducted to evaluate prescribing pattern of antihypertensive medications

Author Name	Number of Participants	Single /Combine therapy	Anti-hypertensive medication class	Remarks/Observation
Caceres *et.a l*[19]	100 % of the Extremadura Spanish Population (1.1Million)	Single Therapy	ARBs, ACEIs	Use of ARBs increased over ACEIs
Xu *et al*. [20]	59 hospitals' databases in China	Single therapy	CCBs, ARBs, ACEIs, BBs, and diuretics	The top-prescribed antihypertensive medications classes were CCBs and ARBs

Beg *et al*. [21]	645 prescription were analyzed in tertiary care teaching hospital at Dehradun, Uttara hand, India	Two or more	ARB	225 (32.28%) anti-hypertensive medication from total.
Gu*est al*. [22]	9320 hypertensive aged ≥18 years from the National Health and Nutrition Examination Survey 2001 to 2010 in US	Multiple	ARB	ARB With Single pill combination 55 % likelihood of BP control
Kuma nan *et.al* [23]	406hypertensive aged ≥18 years from Cardiology Outpatient Department of a Tertiary Care Centre in Northern Sri Lanka	Multiple	ARB	No significant association between any class of hypertensive medication and SBP VVV.
Current study	435hypertensive aged ≥18 years	Multiple(Majority Mono)	ACEIs	About half of our patients were on single medications therapy (46.7%)
Al-Dra bah *et al*. [24]	416 family medicine clinics at Jordan University Hospital in Jordan	Majority mono-therapy(192)	ACEIs	Most patients did not achieve target BP

Essential hypertension is usually diagnosed in the 5th decade. However, in the current study majority (92.7%) of the patients were diagnosed after 5th decades. This might be due to the possible late in the diagnosis of hypertension in our population. The majority of the patients' medication changed or dose increased (60.2%) but 74 patients (17%) reported either medication was decreased or withheld. The main reasons for either dose decreased or withheld were side effects (94.7%) or co-morbidity (5.3%). A study carried out in India revealed that, adverse effects are highly regarded as significant obstacles of the prescribed medications to the successful treatment [21].

Socio-demographic factors and clinical factors were implicated in the prescription pattern. In the current study there were no observed differences between men and women in the type, number and combination of antihypertensive medications. Interestingly, patients with young (<40years) (83.3%) and middle age (40– 60 years) (61.1%) groups when compared to the elderly age group (50.2%) received combination therapy rather than single medication therapy. Similarly, study conducted at the United States concluded that selection of antihypertensive agents showed limited variation by age, gender, race, and insurance type [25].

In addition, nearly equal distribution of combination (48.3%) and single medication therapy (51.7%) were noted among diabetic patients. At the same time, more non-diabetic patients were on the combination therapy than single medication (P-0.026). Likewise, the majority of the obstructive airway disease (BA/COPD) patients were on single medication (59.1%) compare to without disease those more on combination treatment (55.6%). This may be to avoid poly pharmacy in patients who are taking multiple medications due to their co-morbid illness.

Furthermore, duration of hypertension (P-0.007), duration of treatment (P-0.004) and person who initiated the medication (Consultants/non specialist medical officers) (P<0.0001) were associated with the prescription pattern. Most of the patients who were treated for hypertension for more than 5 years were on combination treatment (60.1%). Similar line of findings was found in a

study at secondary care hospital in the United Arab Emirates which reported choice of antihypertensive treatment influenced by co-morbidities, concomitant medications, and physician's preference as per the patient characteristics as well as the availability of medicines[26].

A strong epidemiological interaction exists between CAD and hypertension that accounts for 25%–30% of acute myocardial infarctions [27]. Furthermore, Hypertension is the most important risk factor for ischemic or hemorrhagic stroke[28]. Stroke can be largely prevented by strict BP control. Blood pressure should be lowered to a target <130/80 mmHg (<140/80 in elderly patients) [28].

The proportion with controlled blood pressure among diabetics, patients with CVA, stroke and for no co-morbidities was 62.6%, 58.5% 44.1% and 35.3% respectively. Suboptimal control of blood pressure from mono-therapy towards multi medication therapy may be due to the resistant nature of hypertension and medication adherence. Along with other clinical factors such as co-existing CKD (P-0.016), duration of hypertension (P<0.001), medication adherence (P<0.001) and duration of treatment (P<0.001), type of medication regimen (Single/Two/three/4 or more) (P-0.014) was significantly influenced the SBP control but not on DBP control.

Limitation and recommendation

This study could have been improved by collecting data regarding specific side effects related anti-hypertensive medications. Further expanding study to multicenter level would have been beneficial to generalize the findings to whole country.

In spite of these data and published hypertension management guidelines, anti-hypertensive treatment should be individualized based on the socio demographic factors such as age, family income and place of residence and clinical factors such as co-morbidities and patient adherence to the treatment. A review of these prescribing patterns can give better insights into the concept of personalized, yet cost-effective pharmacological management of hypertension.

CONCLUSION

Achieving blood pressure targets among hypertensive patients has always been a challenge for clinicians. The initial choice in prescription of anti-hypertensive treatment varied from diuretic to ACEI/ ARB/ CCB and from mono-therapy to low dose combination single-pill therapy. This study found that the most frequently prescribed antihypertensive medication classes are ACEI and ARB, which is consistent with the global prescription trend of antihypertensive medications.

Socio-demographic factors such as age, family income and place of residence and clinical factors such as diabetes mellitus independently influenced the number of medications (Single/Combined). Further analysis showed medication regimen (single/two/three/four or more) significantly influenced SBP control along with other factors such as occupation, CKD and medication adherence. Based on these findings and published hypertension management guidelines, the socio-demographic factors and clinical factors should be taken into account in tailoring treatment regimens. A regular review of prescribing patterns of antihypertensive medications helps to create good insight among clinicians to adopt an individualized and cost-effective approach to manage hypertension.

Abbreviations

ACE-I -Angiotensin Converting Enzyme Inhibitors
ARB-Angiotensin Receptor Blocker
CCB-NDP-Calcium Channel Blockers –Non Dyhyropyridine
CCB-DP -Calcium Channel Blockers – Dyhyropyridine
SBP-Systolic Blood Pressure
DBP-Diastolic Blood Pressure
VVV-Visit to Visit Variability
CVA- Cerebro Vascular Accident
MI-Myocardial Infraction
DM- Diabetes Mellitus
COPD- Chronic Obstructive Pulmonary Disease
BA-Bronchial Asthma
IHD-Ischaemic Heart Disease
CVD-Cardio Vascular Disease
CAD-Coronary Artery Disease
PVD-Peripheral Vascular Disease

Author declaration
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Authors' contributions
KS, SG and TK conceived the study. KS involved in the data and sample collection. NR did analysis. KS, NR, TK and SG wrote the manuscript. All authors read and approved the manuscript.

Conflict of interests- The authors declare that none of the authors has competing interests.

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Ethics approval and consent to participate
Ethical clearance was obtained from the Ethical Review Committee of the Post Graduate Institute of Medicine, University of Colombo. Permission to carry out this study was obtained from the Director, TH, Jaffna and written consent was obtained from the participants after explaining the purpose and the nature of the study.

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