

## BLOOD PRESSURE CONTROL AMONG HYPERTENSIVE PATIENTS: ARE THEY ACHIEVING THE TARGET OF PHARMACOTHERAPY AT A TERTIARY CARE HOSPITAL IN NORTH CENTRAL NIGERIA?

Chioma Catherine Idoko<sup>1\*</sup>, Paul Otor Onah<sup>2</sup>, Kennedy Emeka Oluigbo<sup>3</sup>

<sup>1</sup>Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmacy, University of Benin, Edo State, Nigeria. <sup>2</sup>Department of Clinical Pharmacy and Pharmacy Administration, Faculty of Pharmacy, University of Maiduguri, Borno State, Nigeria. <sup>3</sup>Department of Clinical Pharmacy and Biopharmaceutics, Enugu State University of Science and Technology, Enugu, Nigeria.

\*Corresponding Author's E-mail: [pinkjewelone@yahoo.co.uk](mailto:pinkjewelone@yahoo.co.uk)

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### Abstract

**Background:** The prevention of hypertension-related complications is a major goal of antihypertensive therapy. While there is generally a significant reduction of blood pressure (BP) upon initiation of drug therapy, there are reported challenges with the long-term sustenance of blood pressure control over time. This study therefore aimed to evaluate the effectiveness of antihypertensive therapy in BP control among patients on long-term therapy and its sociodemographic determinants.

**Methods:** This was an observational cohort study involving 125 subjects recruited from among hypertensive patients receiving care at a tertiary healthcare facility. Patients who were  $\geq 30$  years of age and have been receiving therapy for at least four months participated in the study. The enrollees were followed up for six months on existing antihypertensive drug(s) and the BP control target was set at 140/90mm/Hg. Data was collected during physician consultations and analysed with SPSS version 21 using descriptive and inferential statistics. The chi-square test was used to determine the association between sociodemographic variables and achievement of the BP control target. P values  $\leq 0.05$  were considered statistically significant.

**Results:** The results showed that while patients on monotherapies achieved 63.9% and 88.1% of systolic blood pressure (SBP) and diastolic Blood pressure (DBP) targets respectively, those on dual therapies achieved 57.5% and 84% SBP and DBP target respectively. Several factors including long duration of therapy (P = 0.052) and high body mass index (BMI), (P = 0.016) were found to be significantly associated with the achievement of BP control targets. It was also observed that there were slightly more subjects on monotherapies who achieved BP control targets (76%) compared to those on dual therapies (72%).

**Conclusion:** Antihypertensive therapies remain effective in long term BP control, however monotherapies achieved slightly better outcome compared to dual therapies. It is clear that failure to achieve and sustain BP control over time should be an important consideration in drug selection and pharmaceutical care interventions.

**Keywords:** Antihypertensives, Blood pressure control, Dual therapy, long-term therapy, Monotherapy

### Introduction

Hypertension is a major risk factor for the development of cardiovascular diseases, and recent epidemiological studies suggest that it is responsible for rising morbidity and mortality among adults in developing countries<sup>[1]</sup>. It is among the leading cause of premature mortality and preventable disability in low and middle-income countries<sup>[2]</sup>. The global prevalence of hypertension in the adult population is reported to be on the increase and it is believed to be a major contributory factor in the rising incidence of heart diseases<sup>[3-5]</sup>. Recent epidemiological evidence from low and middle-income countries indicate that hypertension is an emerging epidemic as cases of secondary complications and life-long disabilities are more frequently reported<sup>[6,7]</sup>. The World Health Organization estimates that over one billion people are living with hypertension globally of which 10.4 million deaths have been reported annually to be directly attributed to the disease and its complications<sup>[4,8]</sup>.

In Nigeria, hypertension and its complications account for up to 25% of emergency hospitalizations in urban areas<sup>[9]</sup>, which makes it a significant contributory factor in cardiovascular disease-related deaths<sup>[10,11]</sup>. The prevalence of hypertension varies widely in the country<sup>[1,12]</sup>, although recent projections indicate an upward trend<sup>[6]</sup>. For instance, in a recent study, more than half of adult urban residents are believed to be living with hypertension<sup>[13]</sup>, although similar studies have reported a third of the adult population<sup>[10]</sup>. A recent review of pooled studies in Nigeria reported a steady rise in cases of hypertension-related hospitalizations from 8 – 22.5% up to 20.5 – 69.6% over a four decade period and 42.9% fatality rate.<sup>[14,15]</sup> A few studies in the country reported higher prevalence of hypertension among urban dwellers compared to rural residents.<sup>[16,17]</sup> A comparative review of studies around various parts of the country showed hypertension prevalence among the adult population to range between 38.8 – 44.5%, although high variability exists in different study settings<sup>[11,18]</sup>.

In most cases of hypertension, pharmacotherapy remains the cornerstone of long-term BP control and reduction in the risk of secondary complications and cerebrovascular accidents<sup>[19]</sup>. Antihypertensive therapy also significantly reduced the risk of mortality from stroke and coronary heart diseases<sup>[20,21]</sup>. There have been extensive literature reviews of antihypertensive therapies and clinical outcomes, some of which were used as the basis for development of treatment guidelines<sup>[22-25]</sup>. However, clinical evidence has shown that less than half of patients on long-term therapy achieve BP control target<sup>[26-28]</sup>. Global estimates have indicated that about 31% of patients on therapy achieved and sustained BP reduction targets<sup>[29]</sup>, which suggests that poor BP control is a global public health challenge<sup>[30-34]</sup>. Literature reviews have reported that 31 – 47% of patients achieve BP control target in countries such as Turkey<sup>[35]</sup>, Malaysia<sup>[36]</sup>, Tanzania<sup>[37]</sup>, Kenya<sup>[38]</sup>, Nigeria<sup>[39]</sup>, Uganda<sup>[40]</sup> and Zimbabwe<sup>[41]</sup>. In contrast, higher percentage of patients achieve BP control in other countries such as the USA<sup>[42,43]</sup>, South Africa<sup>[44]</sup> and Chile<sup>[45]</sup> although high variability exists within and between countries.

Several factors have been reported to affect the achievement and maintenance of BP control; some of which include diabetes mellitus, chronic kidney disease, nonadherence and presence of other comorbidities<sup>[46,47]</sup>. Other factors previously reported include older age, longer duration of therapy and poor glycaemic control among diabetics<sup>[48]</sup>. The presence of comorbidities further complicated adherence, drug affordability and increased risk of side effects, all of which are indicators of poor BP control. In many public health facilities, there is little structured monitoring of BP control during pharmaceutical care interactions with patients. This study is therefore aimed at assessing BP control among patients on long-term antihypertensive therapy and its demographic determinants.

## **Methods**

### ***Setting***

The study was carried out in the cardiology department of the Federal Medical Centre Makurdi, Benue State North central Nigeria. The hospital is a 400-bed federal government-owned tertiary healthcare facility providing care for patients with expertise in cardiology, nephrology, orthopaedics, and obstetrics/gynaecology. The cardiology department serves as a referral facility for patients from the State and nearby urban towns of neighbouring States. There are typically three days of clinical consultations per week and hospital data showed an average patient inflow of 180 per week and about 600 monthly.

### ***Study design***

This was a prospective observational cohort study involving hypertensive patients receiving long term therapy in the hospital.

### ***Enrolment***

Patients were approached during regular physician consultations and those who provided informed consent were enrolled after fulfilling the eligibility criteria. The sample size was determined using Taro Yamane's formula at 95% confidence interval and 5% level of precision. The average weekly patient

inflow of 180 was used to calculate the sample size of 125 for the study. A total of 137 patients were enrolled for the study, however only 125 of them successfully completed the six-month study which represent an 8.9% attrition rate.

### ***Eligibility criteria***

- Patients must be  $\geq 30$  years.
- They must have been receiving care at the facility for at least four months before enrolment.
- Women who are pregnant or planning pregnancy were excluded.
- Patients must attend not  $\leq 80\%$  of scheduled physician consultations.
- There will be no change in the antihypertensive drugs within the study period.

### ***Data collection***

The socio-demographic data of enrolees as well as medical and medication information was extracted from medical records. The blood pressure (BP) measured according to standard procedure on the date of enrolment was taken as the baseline and subsequent ones were obtained during clinical consultations.

### ***Data analysis***

The data was entered into SPSS version 21 for descriptive and inferential statistics. BP differences between pre-study and post-study values were compared using student t-test and association between BP reduction and demographic variables was carried out using Chi-square. P values  $\leq 0.05$  were considered statistically significant.

### ***Ethical approval***

The approval for the study was obtained from the human research ethics committee of the Federal Medical Centre, Makurdi (*Ref No: FMH/FMC/MED.108/Vol. I*).

## **Results**

Demographic data showed that two-thirds of subjects were males (65.6%) and a third were females (34.4%). Most of the subjects had no formal education (46.4%), were married (68.8%) and reside in urban areas (64.6%). The most frequently encountered comorbidity was type 2 diabetes mellitus (43.2%). The mean age of enrolees was  $52.4 \pm 5.1$  years (**Table 1**).

**Table 1:** Demographic data

<b>Demographic data</b>	<b>Number (%)</b>
<b>Gender</b>	
Male	82 (65.6)
Female	43 (34.4)
<b>Marital status</b>	
Single	2 (1.6)
Married	86 (68.6)
Divorced	2 (1.6)
Widowed	35 (28)
<b>Educational level</b>	
Illiterate	58 (46.4)
Primary	21 (16.8)
Secondary	9 (7.2)
Tertiary	37 (29.6)
<b>Occupation</b>	
Farming	32 (25.6)
Civil service	26 (20.8)
Self-employed	21 (16.8)
Unemployed	24 (19.2)
Housewife	5 (4)
Retired	17 (13.6)
<b>Residence</b>	

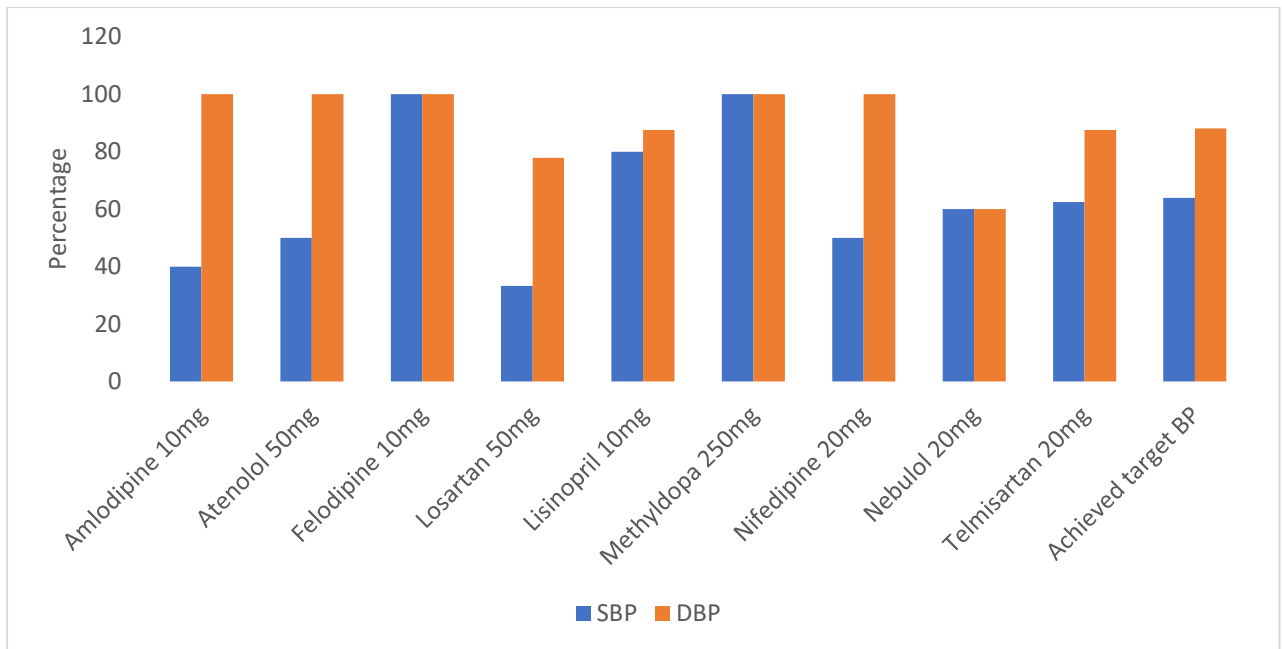
Urban	81 (64.8)
Rural	44 (35.2)
<b>Age (yrs.)</b>	
30 – 39	9 (7.2)
40 – 49	20 (16)
50 – 59	33 (26.4)
60 - 69	43 (34.4)
≥ 70	20 (16)
<b>Mean</b>	<b>52.4 ± 5.1</b>

Duration of antihypertensive therapy ranged between 2.8 – 13 years, however, majority of them have been on therapy for ≤ 10 years (73.6%). Diabetes mellitus type 2 was the most frequently encountered comorbidity (43.2%) for which less than a third of them were aware of a family history of the disease. The most commonly reported lifestyle factors were alcohol use (53.6%), smoking (10.4%) and only 12% reported that they regularly exercised (**Table 2**).

**Table 2:** Social and Medical data of subjects

<b>Variable</b>	<b>Number (%)</b>
<b>Duration of therapy [yrs.]</b>	
≤ 5	47(37.6)
6 – 10	45 (36)
≥ 11	33 (26.4)
<b>Mean</b>	<b>7.4 ± 4.1</b>
<b>Morbidity</b>	
Hypertension	71 (56.8)
Hypertension + Diabetes mellitus 2	59 (43.2)
<b>Family history of hypertension</b>	
Yes	33 (26.4)
No	59 (47.2)
Don't know	33 (26.4)
<b>Family history of diabetes mellitus 2</b>	
Yes	34 (27.2)
No	58 (46.4)
Don't know	33 (26.4)
<b>Alcohol use</b>	
Yes	67 (53.6)
No	58 (46.4)
<b>Regular exercise</b>	
Yes	15 (12)
Occasional	59 (47.2)
Never	51 (40.8)
<b>Smoking history</b>	
Yes	13 (10.4)
Occasional	18 (14.4)
Never	94 (75.2)

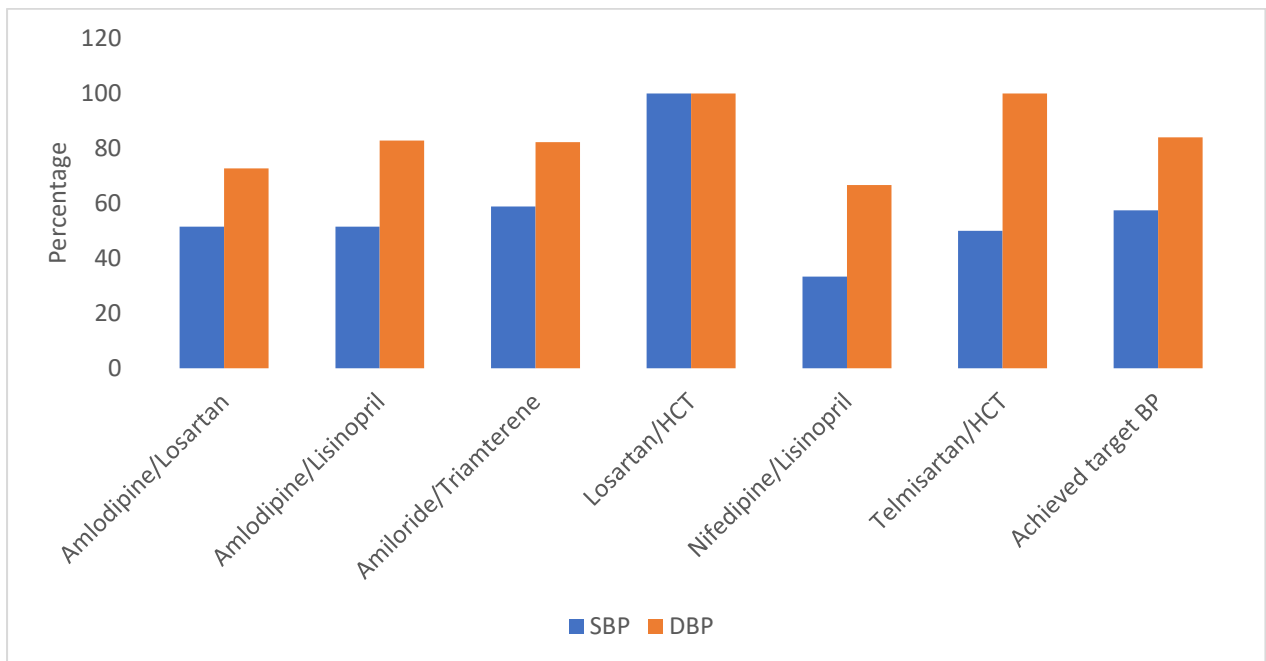
Patients who achieved BP control target of 140/90 mm/Hg with monotherapies were 63.9% and 88.1% for SBP and DBP respectively. While all patients on Felodipine and Methyldopa appeared to achieve BP control (100%), more patients appeared to achieve DBP target compared to SBP (**Figure 1**).



**Key:** SBP – Systolic blood pressure, DBP – Diastolic blood pressure

**Figure 1:** Percentage of patients who achieved BP target with monotherapies

Dual therapies did not appreciably improve BP control except with the Losartan/HCT combination (100%). Overall, about half of the subjects (57.5%) achieved the SBP target compared to 84% with DBP control (**Figure 2**).



**Key:** HCT - Hydrochlorothiazide

**Figure 2:** Percentage of subjects who achieved BP target with dual therapies

A comparison of BP reduction with monotherapies showed a 5.3 – 14.1% fall in SBP and a 0.8 – 11.8% fall in DBP. The greatest fall of SBP was observed with Nifedipine (14.1%), while that of DBP occurred

with Atenolol (15%). The fall in both SBP and DBP was not significant except with Lisinopril ( $P = 0.049$ ) (Table 3).

**Table 3:** Comparison of BP reduction produced by monotherapies

Drug	SBP pretest Mean [SD]	SBP Post-test Mean [SD]	P value	SBP [%] reduction	DBP pretest Mean [SD]	DBP Post-test Mean [SD]	P value	DBP [%] reduction
Amlodipine	152 (27.7)	140 (25.5)	0.496	7.9	90 (18.7)	84 (11.4)	0.557	8.5
Nifedipine	175 (7.1)	150.3 (14.1)	14.11	14.1	105 (21.2)	90 (0.1)	0.422	7.3
Felodipine	118.6 (29.1)	111.4 (13.4)	0.563	6.1	77.1 (13.4)	68.6 (4.9)	0.258	0.8
Telmisartan	146.2 (24.4)	135 (19.7)	0.321	7.7	78.7 (16.4)	77.5 (11.9)	0.869	6.1
Losartan	154.4 (21.8)	138.9 (21.4)	0.147	10.1	83.3 (11.2)	80 (11.8)	0.519	11.8
Lisinopril	145.7 (26.4)	127.2 (20.6)	0.049	12.7	81.7 (17.4)	80.8 (13.4)	0.879	5.8
Atenolol	150 (0.1)	135 (35.3)	0.609	10	85 (7.1)	80 (14.1)	0.698	15
Nebulol	150 (31.6)	142 (27.7)	0.682	5.3	86.8 (13.4)	88 (16.2)	0.924	7
Methyldopa	114.7 (27.7)	114 (14.3)	0.943	0.6	76 (11.6)	67 (8.4)	0.062	9

Patients on dual therapies had only a marginal fall in both SBP and DBP ranging from 1.6 – 2.9% and 1.8 – 18.8% from baseline respectively. The fall in DBP was highest with a combination of Losartan with Hydrochlorothiazide (18.8%). The fall in both SBP and DBP was not significant for any of the dual therapies (Table 4).

**Table 4:** Blood pressure reduction with dual therapies at the end of the study period

Drug combination	SBP pretest Mean [SD]	SBP post-test Mean [SD]	P value	SBP [%] reduction	DBP pretest Mean [SD]	DBP post-test Mean [SD]	P value	DBP [%] reduction
AML+LIS	144(20.9)	138.2(13.4)	0.646	4	88.3(15)	85.7(12.2)	0.979	2.9
NIF+LIS	162.6(39.6)	160(25.5)	0.900	1.6	88.3(15)	86.7(12.2)	0.807	1.8
AML+LOS	141.9(24.2)	138.6(23.5)	0.727	1.7	84(12)	82.4(12.4)	0.741	1.9
TELM+HCT	140.3(22.8)	136.7(19.7)	0.453	2.6	88.3(16)	85(8.4)	0.664	3.7
LOS+HCT	140.3(18.8)	136.7(14.1)	0.849	7.1	80.1(0.2)	65(7.1)	0.095	18.8
AMIL+ TRIAM	144.3(28.3)	140(27.5)	0.534	2.9	85.1(14.1)	83.6(13.2)	0.657	1.8

**Key:** LIS= Lisinopril, AML = Amlodipine, LOS = Losartan, TELM = Telmisartan, HCT = Hydrochlorothiazide, AMIL = Amiloride, TRIAM = Triamterene

The results showed that 69 – 88% of enrolees achieved BP targets using monotherapies and dual therapies. There was no significant association between BP control and demographic variables except with BMI ( $P = 0.016$ ) and duration of antihypertensive therapy ( $P = 0.052$ ). The higher the BMI and longer the duration of therapy the lower the percentage of patients who achieved BP control (Table 5).

**Table 5:** Association between demographic variables and BP control

Variable	Controlled (%)	Uncontrolled (%)	Chi-square	P value
<b>Gender</b>				
Male ( $n=82$ )	74.5	25.5		
Female ( $n=43$ )	75.6	24.4	0.2712	0.869
<b>Morbidity</b>				
Hypertension ( $n=71$ )	69.7	30.3		

Hypertension/DM2 ( <i>n</i> =54)	74	26	0.3968	0.529
<b>Age (yrs.)</b>				
30 – 40 ( <i>n</i> =9)	72.2	27.8		
41 – 50 ( <i>n</i> =20)	79.1	20.9		
51 – 60 ( <i>n</i> =33)	73.6	26.4		
61 – 70 ( <i>n</i> =63)	74	26	1.527	0.676
<b>BMI (kg/M<sup>2</sup>)</b>				
≤ 25 ( <i>n</i> =39)	71.8	28.2		
26 – 29 ( <i>n</i> =46)	88	12		
30 – 35 ( <i>n</i> =22)	79.5	20.5		
≥ 36 ( <i>n</i> =18)	72.4	27.6	10.349	0.016
<b>Duration of therapy (yrs.)</b>				
≤ 5 ( <i>n</i> =47)	81.9	18.1		
6 – 10 ( <i>n</i> =45)	73.3	26.7		
≥ 11 ( <i>n</i> =33)	66.8	33.2	5.925	0.052
<b>Drug combination</b>				
Monotherapy ( <i>n</i> =80)	76	24		
Dural therapy ( <i>n</i> =45)	72	28	0.4158	0.519

**Key:** BMI = body mass index

## Discussion

The achievement of blood pressure control from antihypertensive therapy is fundamental to the long-term prevention of secondary complications of the disease. The demographic profiles of patients vary widely between studies, however in this study, there were more males compared to previous studies<sup>[49-51]</sup>. Several studies have reported prevalence of hypertension to be comparable between males and females, although the latter are known to have better health and treatment-seeking behaviour<sup>[11]</sup>. The higher number of male enrollees in this study may be due to more males consenting to participate, completed the study and had a lower attrition rate compared to females. The percentage of patients that achieved BP control target is higher than previously reported in studies in some low- and middle-income countries<sup>[23,52-55]</sup>. While the results of this study is comparable to a previous one in Sudan<sup>[56]</sup>, patients who achieved PB control target are considerably fewer than in similar studies<sup>[57,58]</sup>. One of the possible reasons for this variability may be related to the BP cut-off point of 140/90mm/Hg and 130/80 mm/Hg recommended by JNC 8 treatment guidelines used to benchmark this study.

The most frequently prescribed monotherapies were CCBs, ACEI/ARBs and Beta-blockers in contrast to some previous studies<sup>[59]</sup>. While some studies reported that ACEI/ARBs and thiazides were the most prescribed monotherapies<sup>[31,47,51]</sup>, contrasting findings have been reported partly because of the diversity of patient populations and study settings. The prescription of CCBs and/or ACEI/ARBs either alone or in combination therapy observed in this study is comparable to previous studies<sup>[60,61]</sup>. The presence of diabetes mellitus makes the use of thiazides and beta blockers inappropriate among patients with the disease which necessitate the use of ACEI/ARBs as first-line therapy.

More patients on monotherapies achieved BP control compared to those on combination therapies in a previous study<sup>[23]</sup>.

The highly variable fall in BP found in this study has also been reported<sup>[38,40,41]</sup> which has been attributed to multiple factors such as non-adherence, lack of affordability and side effects. Other factors affecting BP control have been reported to include inappropriate dose titration, wrong drug selection and cases refractory to therapy<sup>[32, 60]</sup>. For instance, the use of diuretics in older patients is known to be ineffective and therefore not recommended because their elevated BP is not volume dependent and also because of side effects related to provoking gout and glucose intolerance<sup>[24]</sup>.

The association between demographic variables on BP control have been widely reported in literature often with conflicting conclusions<sup>[47]</sup>. While this study found no significant association between gender, comorbidities, age, drug combination and BP control<sup>[47,62,63]</sup>, contrasting results have also been reported in similar studies. For instance, it was reported that diabetes mellitus<sup>[32,44]</sup> and advancing age<sup>[26,28]</sup> have a significant association with BP control, however this was insignificant in this study<sup>[31]</sup>. Patient BMI

has been found to have a significant influence on BP control which is consistent with previous studies [64,65]. It is known that obesity and high BMI are associated with chronic volume overload which have the effect of reducing the effectiveness of antihypertensive drugs [66]. Similarly, the effect of long-term antihypertensive therapy on BP control have also been reported [67,68] comparable to the findings of this study, although contrasting results have been reported [65]. One of the commonly reported challenges of long-term medication therapy is poor adherence, and increased incidence of side effects which often lead to intentional interruption of therapy and ultimately leads to poor BP control.

It is therefore not enough to prescribe antihypertensive medication(s), there is also the need to implement individualized pharmaceutical care and regular monitoring of BP if long-term benefits of therapy are to be realized among patients. This will not only sustain BP reduction, but will also guide clinical decisions of long-term therapies critical to prevention of secondary complications of hypertension.

### Limitations of the study

There were difficulties with recruiting more subjects into the study, hence the small sample size. While adherence was cross-checked during all clinical consultations, there was no independent verification that patients took medication(s) as prescribed which may affect BP values.

### Conclusion

Blood pressure control remains suboptimal among patients on long-term antihypertensive therapy, so there is a need to strengthen monitoring, adherence support and other patient-specific initiatives to achieve better BP control.

### Conflict of interest

The authors declare no conflict of interest.

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