



**PRESCRIPTION PATTERN AND COST OF ANTI-HYPERTENSIVE AGENTS IN AN
OUTPATIENT CLINIC IN A NIGERIA TERTIARY HOSPITAL**

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ABSTRACT

Introduction: Hypertension, also known as high blood pressure or arterial hypertension is a chronic medical condition in which the blood pressure in the arteries is persistently elevated. There is an enormous financial burden associated with the disease which leads to cost-related non adherence. **Objective:** This study aimed to determine the prescribing pattern and cost of prescription for treatment of hypertension in an out-patient clinic of University of Port Harcourt Teaching Hospital (UPTH). **Method:** A retrospective study was carried out on 270 randomly selected patients who attended the Cardiology Clinic of UPTH between January 2021 and June 2021. Information extracted from the patients' folder include: demographic data (age, gender, social status); recorded blood pressure values; names of drugs prescribed (generic and brand products); mono-therapy, poly-therapy; or fixed dose combination; Costs of the drug products were further obtained from the Pharmacy Unit. The data obtained were analyzed using SPSS version 20 and significant value was taken at $p < 0.05$. **Result:** 270 prescriptions were randomly obtained. 112(41.5%) were for male patients and 158(58.5%) were female, with a total of 546 anti hypertensive drugs in the prescriptions. Most 94(34.8%) patients were within the ages of 56 - 65yrs. Majority 180(66.7%) were married, while most (26.7%) were house wives, with 49(18.2%) retired. Most, 192 (71.1%) prescription were multi therapy and 334(61.2%) were prescribed in generic names. The most prescribed class of anti hypertensive was the calcium channel blocker followed by angiotensin converting enzyme inhibitors (ACEI). The least prescribed was the vasodilators. The combination therapy was mainly angiotensin converting enzyme inhibitor plus calcium channel blocker. **Conclusion:** The study showed a close compliance with standard guidelines with respect to JNC-7 and International Society of Hypertension in Blacks. However, the cost per prescription is high relative to the Nation's per capital income and minimum wage. The use of triple combination was not very frequent.

KEYWORDS: Prescribing Pattern, Anti hypertensives, Costs, Tertiary Hospital.

INTRODUCTION

Hypertension also known as high blood pressure or arterial hypertension is a chronic medical condition in which the blood pressure in the arteries is persistently elevated. It can also be defined as blood pressure elevated enough to per-fuse tissues and organs, with the systolic blood pressure greater than 140mmHg (millimeter mercury) and diastolic pressure greater than 90mmHg. Blood pressure is expressed by two measurements, the systolic and diastolic pressure which are the maximum and minimum pressure, respectively, in the arterial system. Hypertension is a chronic medical condition and one of the most significant risk factor for cardiovascular morbidity and mortality.^[1] The systolic pressure occurs when the left ventricle is most contracted; the diastolic pressure occurs when the left ventricle is most relaxed prior to the next contraction cycle. Normal blood pressure at rest is within the range of 100 -140mmHg for systolic, and 60 -80mmHg for

diastolic.^[2,3] Classification of blood pressure for adults according to Joint National Committee (JNC- 8) guideline is given as follows: Pre-hypertension (120 - 139/80 - 89); Stage 1 hypertension (140-159/90- 99); Stage 2 hypertension 160 -179/100 - 109); Stage 3 hypertension ($\geq 180 - \geq 110$) (hypertensive emergency). There also exists isolated systolic hypertension ($>140/<90$).^[4,5]

Africa has the highest prevalence of hypertension in the world as 46% of adults aged 25years and above have raised blood pressure, and a study in Eastern Nigeria found a prevalence of 40.3% among the males.^[6] Uncontrolled hypertension can lead to severe long term consequences such as stroke, heart failure, and end stage kidney disease. It's also associated with diabetes mellitus. Hypertension is the most important preventable risk factor for premature death world wide.^[7] It increases the risk of Ischemic heart disease,^[8] stroke,^[9,10]

peripheral vascular disease, and other cardiovascular diseases including heart failure, aortic aneurysms, diffuse atherosclerosis, chronic kidney disease, and pulmonary embolism. Hypertension is also a risk factor for cognitive impairment and dementia. Other complications include hypertensive retinopathy and hypertensive nephropathy.^[9]

Hypertension related deaths constitute one third of global mortality and there is a scientific evidence to suggest that such adverse outcomes can be prevented by lowering blood pressure effectively.^[11] It is therefore important that once hypertension is diagnosed, a rational anti-hypertensive agent on a long term basis along with regular follow up is instituted. The primary goal of anti-hypertensive therapy is to prevent morbidity and mortality associated with hypertension. Many studies have demonstrated that life style modification and adherence to appropriate drug treatment are sufficient to maintain blood pressure at optimal levels.^[12] In Nigeria, there is a high incidence of hypertension and hypertension-related diseases with a consequent heavy burden on public health care system. In addition, there is an enormous financial burden associated with the disease.^[13] The cost of the prescription medication is thought to be a barrier for many patients to access the health care they need. This gives rise to cost-related non-adherence (CRN), which is defined as any form of medication under-use, due to cost, including unfilled prescription, delayed access to prescription, smaller doses, or less frequent doses.^[14] Developing countries like Nigeria struggle to maintain qualitative healthcare and usually find it difficult keeping up with international standard of medical care. Hypertension management is for life and anti-hypertensive medications are relatively expensive. A study conducted in rural community in Ibadan, South West, Nigeria found that economic burden of hypertension treatment was significant and that about half of the patients were spending a tenth or more of their income on health care related expenses.^[15] In addition to the direct cost in the form of amount paid for the prescribed drugs, there are other indirect costs related to loss of man-hour and savings due to high health expenditure. The situation in Nigeria is such that health care financing is mainly out of pocket payments and often the burden is borne entirely by the individual affected.^[16] Given the increase in health care expenditure and the limited resources for health care, there is clear need to explore prescription patterns and trends in chronic diseases such as hypertension.^[17] Thus, this study aimed to identify the prescribing pattern and cost of prescribed medication for the treatment of hypertension in outpatient Cardiology Unit of University of Port Harcourt Teaching Hospital, Rivers State.

METHOD

Study area

University of Port Harcourt Teaching Hospital (UPTH) is located at Choba in Port Harcourt in Rivers State, Nigeria within South-South Zone, in Niger Delta

Region. It is bound by four (4) neighbouring States (on the East by Imo and Abia States; on the South by Delta State and Akwa Ibom States). Patients from these neighboring States can also access medical care from UPTH, apart from Rivers State people.

Study population

The target population were hypertensive patients who attended Cardiology Unit of the Teaching Hospital between January 2021 and June 2021, to access treatment of hypertension.

Sample size/ Sampling method

The required sample size was determined using Leshie Kish^[18] formula

$$n = \frac{Z^2 pq}{d^2}$$

Where n = desired sample size in population > 10,000; z = standard deviation corresponding to 95% confidence interval level (1.96); p = proportion of target population estimated to have particular characteristics (50%) (0.5); d = degree of accuracy set at 0.5%

$$q = 1 - p$$

$$\frac{(1.96)^2 \times 0.5 \times 0.5}{0.05 \times 0.05}$$

$$n_1 = n/1 + \{n/N\}$$

Where n₁ = population < 10,000; N = population size = 826 (from Records Unit);

$$n_1 = 384 / [1 + (384/826)] = 384 / 1.46489104 = 262.14.$$

Approximated to 270

A total of 270 prescriptions were retrieved from patients folders (between January 2021 and June 2021)

Ethical approval

Ethical approval was obtained from the ethics Committee unit of the hospital. (UPTH/ADM/90/S.II/VOL.X/746)

Inclusion criteria: All patients diagnosed with hypertension who attended the Cardiology Unit to access medical care, both male and female. Patients whose age was 20 yrs and above. Patients who had hypertension with other comorbidity were also included.

Exclusion criteria: All patients who do not attend the Cardiology clinic in UPTH. Patients who were below 20 years. Patients who were not diagnosed of hypertension.

Study design

Random sampling method was used to select these prescriptions. The following data were extracted from the selected prescriptions: patients' demographic data (gender, age, social status); recorded blood pressure values, (systolic and diastolic); drug names (either brand

or generic); type of therapy (mono-therapy, poly-therapy, fixed dose combination; and costs of the drugs, (from the pharmacy Unit.

For brand named drugs and combination anti hypertensive agents, each generic name (active ingredient component) of the agent was counted separately. Subsequently each generic name was categorized into its major anti hypertensive drug class. The prices of these drugs were obtained from UPTH Pharmacy Department.

Poly therapy was defined as two or more drug combinations from different anti hypertensive drug class while mono-therapy was defined as the use of a single medication containing only one anti hypertensive agent; those taking two active ingredients in a combination pill were said to be receiving fixed dose combination (FDC) therapy. The pattern of drug combination was also examined, noted and recorded. Individuals with co - morbidity were also noted and recorded.

Costs of acquiring the drugs were calculated using the cost of the cheapest available drug and the most commonly prescribed dosage, for each drug on a weekly

and monthly basis. The annual drug expenditure (money spent on buying required doses of all anti hypertensive drugs prescribed in the study population for six (6) months was calculated. Drug expenditure due to a single drug was expressed as a percentage of total drug expenditure.

Data obtained were analyzed using Statistical package for Social Sciences (SPSS) version 20. Statistical significance was taken at $p < 0.05$.

RESULTS

A total of 270 prescriptions were collected, worked on and analyzed. The total prescriptions contained 546 drugs. The socio-demographic information of the patients were given in Table 1. Among these hypertensive patients male were 112(41.5%) and female 158(58.5%). Most 94(34.82%) of the patients were within 56 - 65 years of age and the least number 2(0.74%) were 20 -24 years of age, while 62(23%) were 65 years and above. The mean \pm SD age of the patients was 59.10 \pm 22.66. 180(66.7%) were married and 49(18.2%) were retired, as majority 72(26.7%) were house wives.

Table 1: Socio- Demographic data of studied population.

Variable	Frequency N = 270	Proportion
Gender		
Male	112	41.5%
Female	158	58.5%
Age (years)		
20 - 24	2	0.74%
25 - 35	20	7.41%
36 - 45	63	23.33%
46 - 55	29	10.74%
56 - 65	94	34.82%
> 65	62	22.96%
Mean \pm age = 59.10 \pm 22.66		
Marital status		
Married	180	66.66%
Single	29	10.74%
Widow	61	22.60%
Social Status		
Civil servant	61	22.60%
House wives	72	26.66%
Farmers	20	7.41%
Traders/Business	41	15.18%
Skilled workers	12	4.44%
Retired	49	18.15%
unknown	15	5.56%

The pattern of prescription of the anti hypertensives used are given in Table 2 and Fig 1.

The result showed that 78(23.78%) was mono-therapy and 61.17% of the prescribed drugs was based on generic names.

Table 2: Pattern of Anti hypertensive prescription among the patients for the study period.

Number of medication per therapy	Frequency N = 270	Proportion
Mono-therapy	78	28.89%
Multi -therapy	192	71.11%

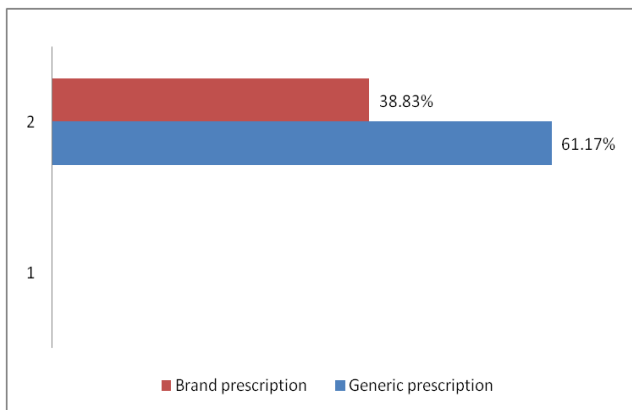


Fig. 1: Drug Prescription based on Generic or Brand name among the patients.

Most of the anti-hypertensives medications prescribed was based on generic name.

The distribution of various Classes of anti hypertensive as prescribed among these patients is shown in Fig. 2, the Calcium channel blockers (CCBs) being the most prescribed class.

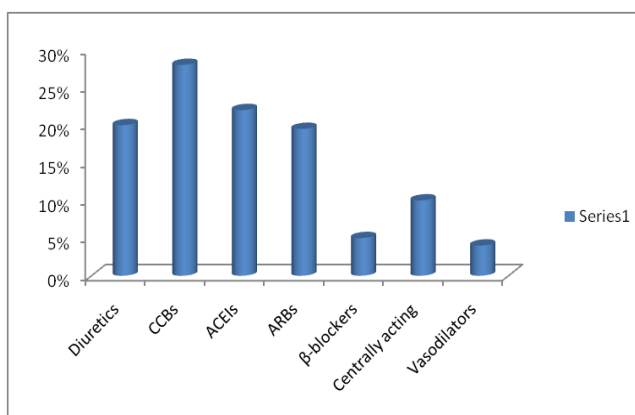


Fig. 2: Distribution of various Classes of Anti-hypertensive agents prescribed.

The systolic blood pressure values of the patients for the study period is given in Fig 3. and corresponding diastolic blood pressure values given in Fig. 4

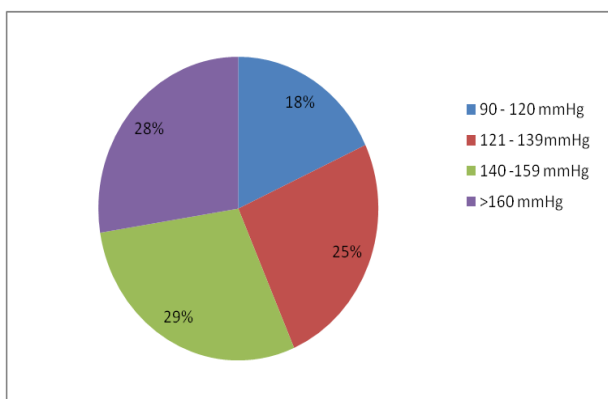


Fig. 3: Systolic blood pressure values distribution of patients for the study period.

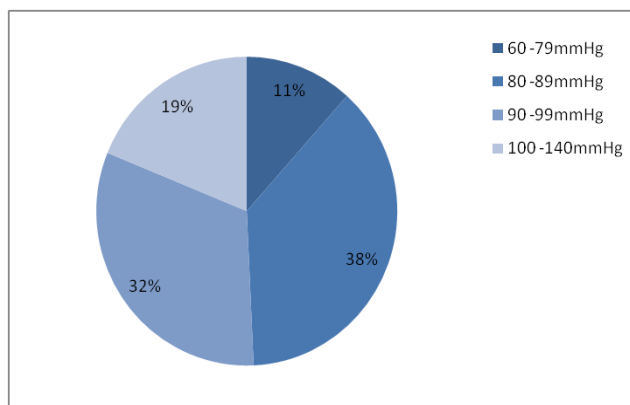


Fig. 4: Diastolic Blood Pressure values distribution of patients for the study period.

A good number of patients (19%)(32%) still had high diastolic blood pressure, and the systolic blood pressure values were equally high among the patients (28%)(29%).

Comorbidity were many among the patients which include: Diabetes mellitus; Heart disease; Asthma; Dyslipidemia; Stroke; other conditions like arthritis, ophthalmic conditions e.t.c. The distribution of these comorbidity among the patients are shown in Fig. 5.

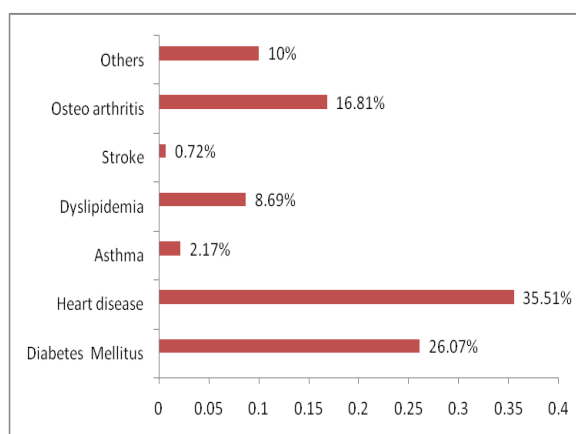


Fig. 5: Distribution of Comorbidity among the hypertensive patients.

Heart disease was the most common co-morbid condition among these hypertensive patients followed by diabetes.

Most often, drug Class combination therapy was prescribed for the management of these hypertensive patients. These drug Class combinations are given as follows:

ARB + CCB = (Angiotensin Receptor Blocker) + (Calcium Channel Blocker)

ACEI + CCB = (Angiotensin Converting Enzyme Inhibitor) + Calcium Channel Blocker)

ARB + CCB + D = Angiotensin Receptor Blocker + Calcium Channel Blocker + Diuretics

ARB + CCB + BB = Angiotensin Receptor Blocker + Calcium Channel Blocker + β -Blocker

ACEI + D = Angiotensin Converting Enzyme Inhibitor + Diuretics

CA + ARB = Centrally Acting Agent + Angiotensin Receptor Blocker

CA + ACEI + D = Centrally Acting Agent + Angiotensin Converting Enzyme Inhibitor + Diuretics

The frequency of use of these combination therapy is given in Fig 6.

The most frequent combination Classes as shown in the result was ACEI + CCB (Angiotensin Converting Enzyme Inhibitor + Calcium Channel Blocker). This is followed by ARB + CCB (Angiotensin Receptor Blocker + Calcium Channel Blocker).

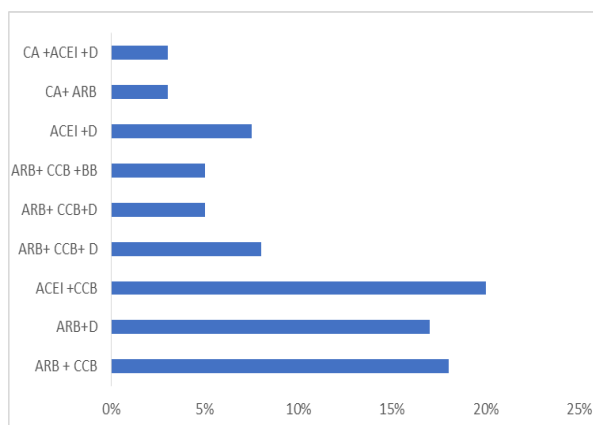


Fig. 6: Anti hypertensive class combination therapy prescription frequency.

The various Classes of Anti hypertensive drugs with the corresponding cost of each brand under the Class is given in Table 3.

Table 3: Various Classes of Anti hypertensives with corresponding costs of the brands under each Class.

S/No	Drug Class	Cost per Card (Naira) (N)
1	Diuretics	
	Hydrochlorothiazide (Esidrex)	600.00
	Furosemide (Lasix)	100.00
	Spironolactone (Adactone)	500.00
2	Calcium Channel Blocker	
	Amilodipine (Norvasc)	350.00
	Nifedipine (Adalat)	250.00
	Felodipine (Plendil)	1,600.00
3	Angiotensin Converting Enzyme Inhibitor	
	Lisinopril	350.00
	Ramipril	750.00
	Enalapril	700.00
	Captopril	400.00
	Thiapril	700.00
4	Angiotensin Receptor Blocker	
	Losartan	600.00
	Valsartan (Co-Diovan)	3,750.00
	Temisartan (Micardis)	1,000.00
5	β -Blocker	
	Atenolol	600.00
	Carvedilol	700.00
	Betaloc Zoc	600.00
6	Vasodilator Hydralazine	250.00
7	Central Acting Agent Methyl dopa	250.00

The average cost of medication under each class of anti hypertensive, and the frequency of prescribing of each class is given in Fig. 7. The result showed the least cost of the classes as the centrally acting anti hypertensive

agents, while the most prescribed was the Calcium Channel Blockers (CCBs). The costliest of the Class was the Angiotensin Receptor Blocker (ARB) which was the 4th most prescribed.

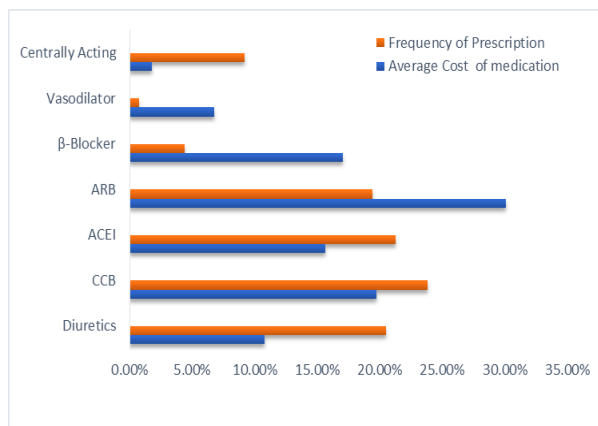


Fig. 7: Average cost of medication in each Class and Frequency of prescription.

Meanwhile, Fig 8 shows the Anti hypertensive drugs in WHO Essential Medicine List and their rate of prescription.

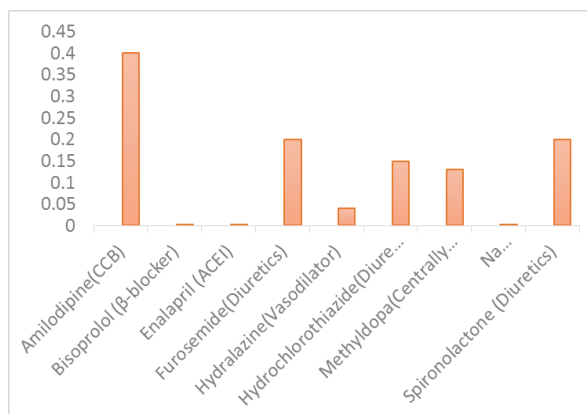


Fig. 8: Anti hypertensive drugs prescribed from WHO Essential Medicine List.

The result showed that Amilodipine (which is Calcium Channel Blocker) (CCB) is the most prescribed. Followed by Furosemide (Diuretics).

DISCUSSION

Hypertension is one of the public health problems that cut across the globe.^[19] It is a chronic medical condition with the most significant risk factor for cardiovascular morbidity and mortality. It has an economic burden and an indirect cost related to loss- man hour.^[15] The mean age of patients in this study was 59.10 ± 22.66 years. This is in line with previous studies that ascribed hypertension as disease of older people and disease that comes up with increase in age.^[20, 21]

This study encountered more female than male which is consistent with some previous works.^[22,23,24,25] It was opined that this may be because men are not regular in keeping medical appointments or that it's a reflection of poor awareness of blood pressure status among males. Patients in the age group 56 - 65 years have more incidence of hypertension than younger age group. This result is similar to some other study^[26] and further confirmed that hypertension is affected by age.

A good number 192 (71.11%) of patients were on multiple therapy and this may be attributed to possibility of many patients presenting with multiple disease conditions, as 207(76.81%) were found to have co-morbid conditions, with heart disease being the most common comorbidity, followed by diabetes. This agreed with other studies.^[27] The use of multiple therapy is encouraged by JNC- 7, WHO/ISH and ESH guidelines which states that “small doses of different classes of anti hypertensive drugs is more beneficial than a high dose of one”.^[23, 28] Calcium channel blocker (CCB) was the most prescribed anti hypertensive drug, followed by angiotensin converting enzyme inhibitor (ACEI); while diuretics was third in line. This is however in contrast to study in some other part of the country^[26,29] where diuretic was the most prescribed anti hypertensive drug. But the combination of CCB + ACEI is the most used. These drugs are indicated for patients in whom the use of diuretics or β-blocker is contraindicated, including patients with diabetes mellitus, heart failure, coronary artery disease, bronchial asthma, and gout. The use of ACEIs and CCB is in keeping with the trend of their use in developing and developed countries. ACEIs are recommended for their known kidney protective effect, known to enhance insulin sensitivity and slow down the

progression of diabetes.^[30,31,32] However, a look at the result of the blood pressure of these patients, within the period of this study, the systolic pressure was still high in 57% of the patients as (29%) had (140 - 159mmHg) while (28%) had >160mmHg). On the other hand 51% of the patients had high diastolic blood pressure as (32% had 90 -99mmHg; and 19% had 100 -140mmHg). These values do not reflect the advantage of the preferred choice of the anti hypertensive, as more proportion should be on the lower Blood pressure controlled range.

This study also showed that diuretics were among the most commonly prescribed anti hypertensives (third most prescribed). This finding reflects the usefulness of diuretics in patients in this environment. According to ESH guidelines, thiazide diuretics are useful in elderly patients of African origin, those with congestive heart failure (CHF), and hypertension. Angiotensin receptor blockers (ARB) accounted for 19.41% of anti hypertensives prescribed in this study which is lower than that reported in other similar study (25.6%).^[29] Similar to ACEIs, Angiotensin Receptor Blocker (ARBs) have advantageous effect in slowing down the progression of diabetes and cardiovascular benefits found with ACEIs.^[33] The top four combinations of anti hypertensives prescribed in this study indicate a very close adherence to the JNC -7, 2003 treatment guidelines. The physicians in this tertiary institution have adhered to these guidelines, and this may be a reflection of the quality of training received by the physicians.

The ranking in terms of cost from highest to the lowest was ARB > ACEI > CCB > Diuretics > β - blockers > Centrally acting agents > Vasodilators. The anti hypertensives cost analysis showed that ARB accounted for 54.77% of the total anti hypertensive drugs cost incurred, although the total amount prescribed only represented 19.41% of the overall anti hypertensive drugs. Again, the cost of ACEI and CCB were high (17.3% and 11.81% respectively) in relation to their prescribed percentages (21.25% and 20.51%). The cheapest anti hypertensive drug was the diuretics with respect to the total amount prescribed. This can offer some advantages over other drugs used to control blood pressure in terms of decreasing cardiovascular morbidity and mortality events. However, the use of thiazide as first choice therapy will result in substantial cost savings due to favourable price.³⁴ The mean cost of prescription was found to be N1,284.76 (equivalent to USD 8. 57). The minimum wage in Nigeria as at the time of this study was N18,000.00 (Eighteen thousand Naira, equivalent to \$120 then. These earnings were low, and if a good percentage of the monthly income is spent on medications for management of hypertension, it leaves little for other things. The implication is that patients may prioritize their spending and leave the purchase of medications in order to put food on the table for family among other essential needs.

It's also important to note that only 22.46% of the patients in this study were civil servants. The rest were either house wives, retired men and women who were farmers, or retired civil servants, or retired traders, business men and women. This therefore, poses a huge financial burden on these categories of patients. The cost of prescription medication is thought to be a barrier for many patients to access the health care they need. Cost-related non adherence which is defined as any form of medication under-use because of cost, including unfilled prescriptions, delayed prescriptions, smaller doses or less frequent doses.^[14] In addition to direct costs in form of amount paid for the prescribed drugs, there are also indirect costs related to loss of man-hour and savings due to high health care expenditures. The situation in Nigeria is such that health care financing is mainly out of pocket payment and often the burden is borne entirely by the individual affected.^[16]

The prevalence of co-morbidity was high among the study group, with 76.81% of prescription being for patients with co- morbidity. Again the association between co- morbidity and cost of prescription was found to be high. A study in a rural community in Ibadan, also found that the mean cost of treatment was significantly higher for those with co -morbidity.^[35] This implies that patients with co- morbidity spend significantly $p<0.05$ more per prescription compared to their counterparts without co-morbidity. It also makes a case for lifestyle modification for all patients and stricter monitoring of blood pressure control in such patients.

CONCLUSION

This study has shown that the pattern of anti hypertensive prescription at University of Port Harcourt Teaching Hospital (UPTH) out patient department is in close compliance with standard guidelines with respect to JNC- 7 and International Society of Hypertension I Blacks (ISHIB). There is a high prevalence of co-morbid conditions mostly diabetes mellitus, heart disease, and dyslipidemia.

While there is a close compliance to standard guidelines, the cost per prescription is high relative to the Nation's per Capital income and minimum wage levels.

An integrated primary approach should be adopted in the control of hypertension and also ingenious way of healthcare financing such as community based health care financing and other social health insurance schemes have to be promoted to enable people to pay for their health care costs.

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Conflict of interest

The authors declare no conflict of interest over this work

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