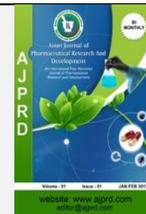


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Research Article

Antihypertensive Prescription Pattern and Associated Medication Costs: A Retrospective Review of Prescriptions in A Tertiary Hospital

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ABSTRACT

Background: Hypertension is the leading cardiovascular disease most associated with high risk of morbidity and mortality. Recent evidence indicate that in low and medium income countries hypertension is a growing healthcare challenge compounding already existing high burden of infectious diseases. The overall goal of treatment is to reduce the risk of associated secondary complications which increases the risk of mortality. The choice of antihypertensive medications vary widely between and within health facilities, however concerns remain whether prescribed drugs affordable as well as optimize treatment outcomes.

Aim: The aim of this study is to determine antihypertensive prescription pattern and its impact on affordability of drug treatment

Results/Discussions: The results showed that monotherapy with CCBs were the most prescribed drugs accounting for over half of all antihypertensive prescriptions. In addition CCB based combination therapies were found in more than three quarters of all prescriptions. The cost of one month supply of innovator brands was significantly higher than generic versions, which made them far less affordable to majority of patients. The prescription pattern did not significantly adhere to current treatment guidelines for the management of hypertension. This makes the case for improvement in prescription practices that emphasize rational drug therapy that take into cognizance costs, particularly among the poor.

Conclusion: Antihypertensive prescription pattern did not largely comply with guidelines and the widespread prescription of innovator drug brands makes medicines largely unaffordable to majority of patients. It is imperative that drug treatment of high blood pressure allow patients to benefit from reduced cost of low priced generic drugs.

Keywords- Hypertension, cardiovascular disease, Antihypertensive, antihypertensive prescription, morbidity

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INTRODUCTION

Hypertension is among the most common non-communicable disease of global public health concern. It is associated with increased rate of morbidity and mortality, its a major risk factor for chronic kidney disease, stroke and cardiovascular disease^{1,2} Recent

estimates showed that over a billion people are affected and projections indicate that it's likely to rise to 1.5 billion by 2025³. Epidemiological studies suggest that developing and low income countries have a greater burden of the disease, unfortunately healthcare systems are weak and access to effective treatment is limited. In Nigeria, hypertension

prevalence is reported to be between 12 – 36.6%^{4,5,6,7}. Prevalence vary widely with age, previous studies showed that those ≥ 65 have greater prevalence^{8,9} and prevalence in urban areas was reported to be higher than among rural dwellers¹⁰. Among the many factors adduced for the increasing prevalence of hypertension are ageing, excessive alcohol use, sedentary lifestyle, obesity, stress and environmental factors. Globally hypertension is estimated to cause 9.4 million deaths annually, half of mortality due to stroke and heart diseases is caused by hypertension^{11,12}. Clinical evidence clearly indicates that antihypertensive therapy significantly reduces overall risk of heart failure, myocardial infarct, stroke, cardiac revascularization and chronic kidney disease among hypertensive patients¹³.

Several guidelines for treatment of hypertension exist and are being constantly updated, so it is therefore expected that clinicians will adopt the recommendations in the management of hypertensive disorder. However evidence from several studies suggest poor adherence to treatment guidelines^{14,15,16,17,18,19}. Approach to the treatment of hypertension varies widely, however it is imperative that drug(s) selection should be based on rational principles²⁰. Rational prescribing is reported to have positive impact on clinical improvement and adherence to antihypertensive therapy²¹.

Treatment guidelines are generally intended to guide clinicians in selection of medication(s) that is appropriate for individual patients with due consideration to patient specific peculiarities. A number of studies reported that majority of patients do not achieve blood pressure target with monotherapies^{22, 23, 24}. Majority of patients therefore had to be placed on multiple drug regimens to achieve blood pressure control^{18,25,26,27,28,29,30}. A number of factors have been identified as having influence on antihypertensive drug prescription pattern and they include, age, comorbidities, adverse drug reactions, pregnancy, availability and cost of medications etc. So prescription pattern is a reflection of the influence of these and other factors on use of either monotherapy or multidrug therapies^{31,32,33,34,35}. In low income countries like Nigeria where patients pay out of pocket for medications and healthcare services, cost can be a significant barrier to financial access, availability and affordability to medications for hypertension. So adhering to treatment guidelines have been shown to improve cost effective drug therapy resulting in significant savings for patients^{36,37,38,39}. Prices of antihypertensives vary widely between drugs classes, brands, healthcare facility and market forces^{40, 41, 42}.

The level of adherence to treatment guidelines vary widely as the diversity of study settings^{43, 44,45,46,47}. The most frequently used antihypertensives were diuretics, CCBs, BBs, ACEI/ARBs and their various combinations⁴⁸. It is important that antihypertensive prescriptions should take cost effectiveness into consideration because treatment is chronic in nature⁴⁹.

METHODS

Setting: The study was carried out using prescription records of National health insurance scheme (NHIS) enrollees in the University of Maiduguri teaching hospital

Study design: This was a cross sectional descriptive retrospective study

Data collection: Prescription records between January 2017 and September 2018 of patients on NHIS at pharmacy department were used for the study. A total of 1602 prescriptions containing antihypertensive medications that met inclusion criteria were randomly selected. Exclusion criteria include incomplete prescriptions, NHIS numbers not indicated on prescription and those written on unofficial prescription forms. Data extracted from prescriptions included name(s) of drugs, demographic data, antihypertensive drugs, dosage, frequency of dosing and brand.

Data analysis: The data was entered into SPSS 21 for descriptive and inferential analysis. Student's test was used to find if differences in cost and affordability between innovator and generic brands of antihypertensive drugs and combination therapies. P values ≤ 0.05 was considered statistically significant.

Objectives: To determine antihypertensive drugs prescription pattern and their affordability

Ethical approval: The study received ethical approval from the human research ethics committee of the University of Maiduguri teaching hospital, Borno State, Nigeria

RESULTS

Demographic data

The average age of patients was 57.6 years and females accounted for more than two thirds of the population [Figure 1&2].

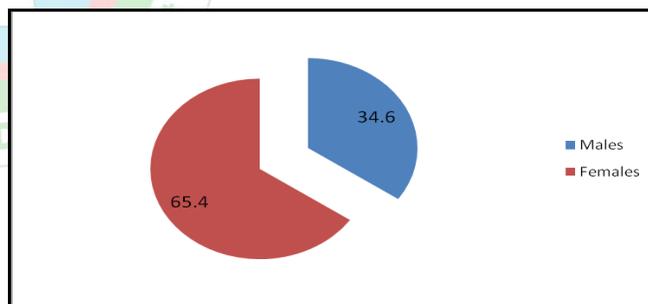


Figure 1: Gender distribution

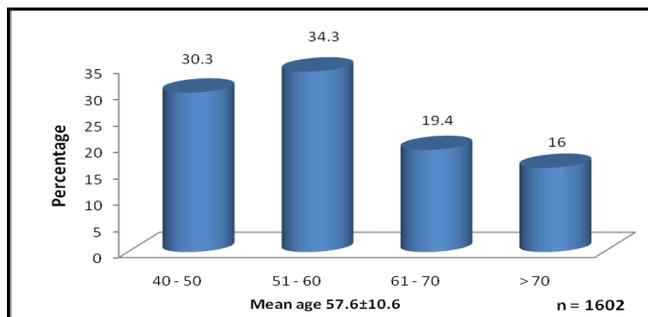


Figure 2: Age distribution

Antihypertensive monotherapies accounted for over two thirds of all prescriptions. Calcium channel blockers were prescribed for over half of all patients on monotherapies. The average price for one month supply of innovator brands was

2 – 15 times more expensive compared to that of their generic versions [P<0.05]. Diuretics prescription rate was less than ten percent, while ACEI/ARBs and B blockers

accounted for 23% and 5% of prescriptions respectively [Table 1].

Table 1: Comparison of median price ratios between monotherapies [n = 1170]

Drugs	Number [%]	IB [\$]	LPG [\$]	P- value
Amlodipine	560[47.9]	17.1	1.1	<0.001
Nifedipine	103[8.8]	2.1	0.8	<0.001
Losartan	73[6.2]	3.0	1.4	<0.001
Lisinopril	182[15.6]	2.1	0.9	<0.001
Captopril	15[1.3]	2.7	1.1	<0.001
Carvedilol	32[2.7]	1.9	1.4	<0.118
Atenolol	27[2.3]	1.7	0.9	<0.001
Bendrofluthiazide	107[9.1]	1.4	0.8	<0.001
Methyldopa	66[5.7]	3.8	2.4	<0.001

Calculation was based on exchange rate of N315 to 1 USD and one month supply of medicine

Combination therapies based on CCBs were the most prescribed; they accounted for about 78.8% of all dual therapies. The combination of diuretics with CCBs, B blockers and ACEIs together accounted for less than a

quarter of dual combination therapies. The cost of innovator brands in dual therapies were 2 – 9 times more expensive compared to their generic counterparts [P <0.001 [Table 2].

Table 2: Comparison of median price ratios of dual therapies [n = 338]

Drug combination	Number [%]	IB [\$]	LPG [\$]	P- value
Amlodipine + Atenolol	21 [6.2]	18.9	2.1	<0.001
Amlodipine + Losartan	45 [13.3]	20.2	2.5	<0.001
Amlodipine + Lisinopril	145 [42.9]	19.2	2.1	<0.001
Amlodipine + Captopril	36 [10.6]	19.8	2.2	<0.001
Amlodipine + Bendrofluthiazide	3 [0.9]	18.6	1.9	<0.001
Nifedipine + Losartan	7 [2.1]	5.1	2.2	<0.118
Nifedipine + Lisinopril	6 [1.8]	3.0	1.7	<0.001
Nifedipine + Atenolol	6 [1.8]	3.8	1.7	<0.001
Nifedipine + Bendrofluthiazide	3 [0.9]	3.5	1.7	<0.001
Lisinopril + Bendrofluthiazide	17 [5.0]	3.5	1.7	0.001
Lisinopril + Carvedilol	5 [1.5]	3.9	2.4	0.202
Losartan + Atenolol	3 [0.9]	4.8	2.4	0.131
Atenolol + Bendrofluthiazide	11 [3.3]	3.2	1.7	0.208
Methyldopa + Bendrofluthiazide	7 [2.1]	2.7	1.7	0.044
Methyldopa + Lisinopril	2 [0.6]	5.2	3.3	0.044

Calculation was based on exchange rate of N315 to 1 USD and one month supply of medicine

Among triple combination therapies, CCBs in combination with ACEI/ARBs were found in about 79% of all triple

combination therapies. In addition B blockers were co-prescribed in about 69% of patients [Table 3]

Table 3: Comparison of median price ratios of triple combination therapies [n = 94]

Drug combination	Number [%]	IB [\$]	LPG [\$]	P- value
Amlodipine + Atenolol + Bendrofluthiazide	560[47.9]	17.1	1.1	<0.001
Amlodipine + Atenolol + Lisinopril	103[8.8]	2.1	0.8	<0.001
Amlodipine + Lisinopril + Carvedilol	73[6.2]	3.0	1.4	<0.001
Amlodipine + Atenolol + Losartan	182[15.6]	2.1	0.9	<0.001
Amlodipine + Losartan + Bendrofluthiazide	15[1.3]	2.7	1.1	<0.001
Lisinopril + Atenolol + Bendrofluthiazide	32[2.7]	1.9	1.4	<0.118
Nifedipine + Atenolol + Lisinopril	27[2.3]	1.7	0.9	<0.001
Methyldopa + Atenolol + Losartan	107[9.1]	1.4	0.8	<0.001

Calculation is based on N315 to 1 USD and 1 month supply of medicine

Antihypertensive drugs prescribed as innovator brands are generally 2 – 15 times more expensive compared to generic versions. Affordability is generally lower for innovator brands and they become progressively less affordable as

combination of drugs increased. It would take 2 – 11 days of daily wages to afford one month supply of antihypertensive drugs prescribed in branded form compared to generics which were generally affordable.

Table 4: Comparison of affordability between innovator and generic versions

Drugs/ combination	IB [Days]	LPG [Days]
Amlodipine	9.0	0.6
Nifedipine	1.1	0.4
Losartan	1.6	0.7
Lisinopril	1.2	0.5
Captopril	1.4	0.6
Carvedilol	1.0	0.7
Atenolol	0.9	0.5
Bendrofluthiazide	0.7	0.4
Methyldopa	2.0	1.3
Dual therapies [n = 338]	IB [Days]	LPG [Days]
Amlodipine + Atenolol	9.9	1.1
Amlodipine + Losartan	10.6	1.3
Amlodipine + Lisinopril	10.1	1.1
Amlodipine + Captopril	10.4	1.2
Amlodipine + Bendrofluthiazide	9.8	1.0
Nifedipine + Losartan	2.7	1.1
Nifedipine + Lisinopril	1.6	0.9
Nifedipine + Atenolol	2.0	0.9
Nifedipine + Bendrofluthiazide	1.8	0.9
Lisinopril + Bendrofluthiazide	1.8	0.8
Lisinopril + Carvedilol	2.1	1.3
Losartan + Atenolol	2.5	1.3
Atenolol + Bendrofluthiazide	1.7	0.9
Methyldopa + Bendrofluthiazide	1.4	0.8

Methyl dopa + Lisinopril	2.7	1.7
Triple combination therapies [n = 94]	IB [Days]	LPG [Days]
Amlodipine + Atenolol + Bendrofluthiazide	10.6	1.5
Amlodipine + Atenolol + Lisinopril	11.0	1.6
Amlodipine + Lisinopril + Carvedilol	10.9	1.8
Amlodipine + Atenolol + Losartan	11.5	1.8
Amlodipine + Losartan + Bendrofluthiazide	11.3	1.7
Lisinopril + Atenolol + Bendrofluthiazide	2.7	1.4
Nifedipine + Atenolol + Lisinopril	3.2	1.4
Methyl dopa + Atenolol + Losartan	4.5	2.5

Affordability was based on a 30 day supply of medicines

DISCUSSION:

Demographic information indicated that the mean age of patients was comparable to other studies where adults over 40 years of age were more frequently diagnosed with hypertension^{18,49}. Ageing is a known risk factor for the development of hypertension, however there are conflicting conclusions as to gender based risk of the disease. While some studies reported higher diagnosis of hypertension in females as observed in this study^{50,51}, others suggest there is no significant difference between males and females⁵². Antihypertensive medications are critical to long term blood pressure control and prevention of secondary complications. The drugs and their various combinations are usually tailored to meet blood pressure control target of individual patients. Prescription pattern of blood pressure lowering medications varies widely in spite of evidence based clinical guidelines. The results of this study showed that monotherapy with Calcium channel blockers were the most commonly prescribed antihypertensive medications. This is in contrast with many previous studies which reported that diuretics were the most prescribed class of antihypertensive medications^{49,51,53,54}. Current treatment guidelines recommend diuretics as first line medication and other drugs may be added if there is inadequate clinical response, however this appears not to be practice as shown in the results of this study.

The result also showed that Amlodipine was the most prescribed in contrast to several previous studies^{55,56,57}, though other studies reported similar results to that of this study^{42,45,50,58,59,60}. The prescription rate of ACEI/ARBs and other classes of antihypertensive medications have been

widely reported in literature^{61, 62,63,64,65} with varying levels of prescription prevalence. Antihypertensive drug prescription practices in this study were not in tandem with the current treatment guidelines. While combination therapies are indicated in the presence of complications and/or comorbidities, drug combinations observed in this

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study are not reflective of the principle of incremental addition until blood pressure control target is achieved^{66,67}. The age of patients in this study suggest that many will benefit from diuretic based combination therapies while the elderly may be given CCBs as first line monotherapy. The prescription of CCBs, ACEI/ARBs and B blockers as first line monotherapies have little evidence supporting their superiority over diuretics and diuretic based combination therapies in achieving blood pressure control and reduction of morbidity and mortality⁶⁸.

The availability and cost of medications is a problem of global concern particularly in low and medium income countries. In Nigeria cost of treating hypertension is mostly borne entirely by patients and in many cases in amounts that may be regarded as catastrophic expenditure⁶⁹. The results of this study showed that cost of treating hypertension with monotherapies range from 1.4 – 17.1 USD and 0.8 – 2.4 USD for innovator and low priced generic versions respectively. The cost rises significantly with combination therapies, so affordability tend to reduce with increasing prescription of combination therapies. A comparison of one month cost of antihypertensive medication and income of least paid public sector employees revealed that monotherapies cost about 6.8% of monthly salary, while dual and triple therapies accounted for 16.1 and 27.4% of monthly salary respectively. The result of this study is much higher than previously reported^{49,70}. The low affordability of antihypertensive drugs observed in this study has been previously reported in literature^{71, 72, 73}. High cost of medicines can be a significant hindrance to achieving blood pressure target, so the use of cheaper generic drugs should be emphasized.

CONCLUSION: There is need to emphasize adherence to current treatment guidelines and also prescribe generic brands to lower cost of treatment. Antihypertensive combination therapies should adopt step wise approach using the most current clinical evidence.

Conflict of interests: The authors declare no conflict of interest

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