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## Original Research Article

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# Drug related problems and implications for pharmaceutical care interventions in hypertensive outpatients in a Nigerian hospital

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## Abstract

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**PURPOSE:** To study drug related problems (DRPs) among hypertensive patients, pattern of antihypertensive drugs used and percentage of patients that achieved JNC 8 target goal BP in a Nigerian hospital.

**METHODS:** This was a prospective cross-sectional study over a period of three months. A total of 109 eligible hypertensive patients were consecutively sampled. Data was collected from the patients' folders and direct interviews using a data collection form. Compliance to medication was assessed using the four (4) items patients' report Morisky compliance score indicator. .

**RESULTS:** A total of 171 DRPs were identified and effect of drug treatment not optimal was the highest (71.6%) DRP encountered. The mean systolic and

diastolic blood pressures (SBP and DBP) were found to be  $150 \pm 27.71$  and  $92 \pm 16.29$  mmHg respectively, and only 26.6% of the patients achieved JNC 8 target goal blood pressure (BP). Number of drug related problems and adherence score correlated positively and significantly with SBP at  $P \leq 0.01$ .

**CONCLUSION:** A total of 171 DRPs were identified which could partly be associated with majority of the patients not achieving their target goal BP. This has justified the introduction of pharmaceutical care interventions to hypertensive outpatients receiving care in the hospital.

**Keywords:** hypertension, drug treatment, target goal BP

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**Indexing:** Index Copernicus, African Index Medicus

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## Introduction

Despite several studies on hypertension and its management, hypertension still remains a major public health problem. It remains among the major causes of micro and macro-vascular complications such as coronary heart disease (CHD), acute myocardial infarction (AMI), peripheral vascular disease (PVD), stroke, congestive heart failure and renal failure [1]. It has been shown that, untreated hypertension shortens life expectancy by five years [2].

Pharmacotherapy remains the cardinal approach in management of hypertension worldwide and despite the availability of wide range of these agents, the World Health Organization (WHO) has estimated that about 62% of cerebrovascular disease and 49% of ischemic heart disease burden worldwide are attributable to sub optimal control of blood pressure levels [3]. Hypertension frequently resists treatment with monotherapy, in addition to being a chronic

disease, hypertension commonly co-exists with other chronic medical conditions such as diabetes, chronic kidney disease etc. Together, these require the chronic use of multiple drugs for optimal management which could lead to number of DRPs. This has buttressed the need for provision of pharmaceutical care (PC) intervention to optimize the drug therapy, succeed in achieving positive clinical outcomes within reasonable economic expenditures and improve patient's health related quality of life [4].

Identification of DRPs (events or circumstances involving drug therapy that actually or potentially interfere with desired health outcomes [5]), is the key in planning and implementation of PC interventions [1]. According to the Pharmaceutical Care Network Europe (PCNE) Classification Scheme for Drug-Related Problems V7.0, 2016, DRPs are classified into: 1. Treatment effectiveness (i. No effect of drug treatment/ therapy failure, ii. Effect of drug treatment not optimal, iii. Unnecessary drug-treatment, iv. Untreated indication; 2. Adverse drug event (Patient

suffers, or will possibly suffer, from an adverse drug event); 3. Others (i. Patient dissatisfied with therapy despite optimal clinical and economic treatment outcomes, ii. Unclear problem/complaint. Further clarification necessary). Studies have shown that, provision of PC to hypertensive patients helps in achieving and maintaining target goal BP, thereby decreasing the risk of the above mentioned complications, decreasing the cost of management, improving the patients' quality of life and satisfaction to therapy [6-7].

This study was conducted in Specialist Hospital Sokoto to study the drug related problems in hypertensive outpatients.

## Methods

### Study design

This study was prospective, cross-sectional design conducted over a period of three months (July to October 2017).

### Study area and setting

The study was conducted in Sokoto State, North-western Nigeria; one of the six (6) geopolitical zones in the country. The setting used for this study was Specialist Hospital Sokoto. This hospital is located at Sultan Abubakar Road Sokoto. Data were collected during cardiology clinics held on Tuesdays and Thursdays of every week at male and female Medical Outpatient Departments of the Hospital.

### Study population

Hypertensive patients attending outpatients' clinics at Specialist Hospital Sokoto made the population of the study.

### Inclusion and exclusion criteria

#### Inclusion criteria

Patients who were above 18 years old and diagnosed of essential hypertension. The patients must have been taking anti-hypertensive treatment for at least past one month and come to Out-Patients Department for refill and who were willing to respond to relevant interview questions.

#### Exclusion criteria

Patients who were diagnosed of secondary hypertension, pregnancy induced hypertension and those who had not started anti-hypertensive drug therapy. Patients who could not respond, such as unconscious and mentally unstable hypertensive patients.

### Sampling techniques

A sample of 109 eligible and consented patients were conveniently sampled during the clinic days.

### Instruments and data collection procedure

A preformed data collection form was used to collect relevant data from the patients' folders and through direct patient interviews. Data on DRPs, causes and level at which Pharmaceutical Care Interventions(PCIs) need to be made were collected using a preformed classification scheme adopted from the PCNE Classification Scheme for Drug-Related Problems V7.0, 2016. This version of PCNE classification has 3 primary domains for problems, 8 primary domains for causes and 5 primary domains for Interventions. The domain for problem has seven (7) sub domains, while causes and interventions have 35 and 16 sub domains respectively. Those sub-domains can be seen as explanatory for the principal domains. Appropriateness of doses were determined using doses in JNC 8 evidence based randomized controlled trials guidelines and eMartindale: The complete drug reference for drugs not listed in the above guideline.

Compliance to medication was assessed using the four (4) items patients' report Morisky compliance score indicator with Yes-1/No-0 responses. A total score of 4 indicates non-adherence, 3 poor adherence, 2 average adherence, 1 satisfactory and 0 adherent. Verbal consent of the patients was obtained and folders of those who were willing and agreed to respond were collected after physician consultation. Patients' height and weight were measured at the point of data collection. Other relevant data were collected from the patients' folders and information not available in the folders was retrieved during interviews.

### Data analysis

The data obtained were sorted, coded and entered into the Statistical Package for Social Sciences (SPSS), version 16.0 software and analyzed. Descriptive statistics including frequency and percentages as well as mean and standard deviation were conducted on demographic data and other appropriate variables. Chi-square was used to explore the significant association between variables while correlation was used to test for magnitude and direction of expected related variables.

### Ethical consideration

Ethical clearance (SHS/SUB/133/VOL 1) was obtained from Hospital Ethics and Research Committee of Specialist Hospital Sokoto. Strict ethical standards and procedures were followed during data collection and throughout the research. Participation in this study was voluntary.

## Results

Out of the total 109 patients, 51% were male. The mean age of the patients was 55±11.77 years, married was the highest marital status constituting 97.2% of the patients. Majority of the patients (86.2%) have informal level of education. Hausa/Fulani (97.2%) was the major tribe of the patients. Housewives (42%) was the major occupation of the patients followed by 26.6%, 13.8%, 8.3% farmers, business persons and civil servants respectively. Kolanut use accounted for

41% of the social history. Diabetes was the highest comorbidity encountered (11.9%). Majority of the patients were within normal (healthy) BMI, however, 36.7% and 4.6% were overweight and obese respectively. The mean SBP was  $150 \pm 27.71$  mmHg and DBP was  $92 \pm 16.29$  mmHg Only 26.6% of the patients achieved JNC 8 target BP goal. (Table 1).

**Table 1:** Patients' demographic and hypertension treatment related data

Variable	n(%)	Mean±SD
<b>N=109</b>		
<b>Gender</b>		
Male	55(50.5)	
Female	54(49.5)	
Age (yr)		55±11.77
<b>Marital status</b>		
Married	106(97.2)	
Widowed	3(2.8)	
<b>Level of education</b>		
<b>Informal</b>		
Primary	1(0.9)	
Secondary	4(3.7)	
Tertiary	10(9.2)	
<b>Tribe</b>		
Hausa/Fulani	106(97.2)	
Yoruba	2(1.8)	
Others	1(0.9)	
<b>Occupation</b>		
Business	15(13.8)	
Civil servant	9(8.3)	
Farmer	29(26.6)	
Student	2(1.8)	
Driver	4(3.7)	
Housewife	46(42.2)	
Teacher	2(1.8)	
Painter	1(0.9)	
Carpenter	1(0.9)	
<b>Social history</b>		
None	64(58.7)	
Kolanut	45(41.3)	
<b>Co-morbidities</b>		
None	88(80.7)	
Heart failure	8(7.3)	
Diabetes	13(11.9)	
<b>BMI</b>		
Underweight	7(6.4)	
Healthy	57(52.3)	24.2±4.64
Overweight	40(36.7)	
Obese	5(4.6)	
Duration of therapy (months)		28.83±42.68
<b>JNC 8 target goal BP</b>		
Achieved	29(26.6)	
Not achieved	80(73.4)	

*SD= standard deviation, BMI=Body mass index, SBP= Systolic blood pressure, DBP= Diastolic blood pressure.*

The mean number of antihypertensive drugs prescribed per patient was  $2.3 \pm 0.81$ . Monotherapy accounted for 12.8% out of which ACEI was the most common single drug prescribed. Combination therapy

with two or more drugs accounted for 87.2% out of which CCB + ARB (11.0%) two drug combinations were the most common pattern of combination therapy prescribed, followed by CCB+ ACEI (10.1%), CCB +CA (9.2%) (Table 2).

**Table 2:** Prescribing pattern of antihypertensive drugs used

Variables	n (%)	Mean ± SD
Number of antihypertensive per patient		2.30±0.81
<b>Monotherapy</b>		
ACEI	10(9.2)	
CCB	2(1.8)	
Diuretics	2(1.8)	
Total	<b>14(12.8)</b>	
<b>Combination</b>		
CCB +ARB	12(11.0)	
CCB + ACEI	11(10.1)	
CCB +CA	10(9.2)	
CCB +ACEI +TD	8(7.3)	
CCB + ARB + CA	8(7.3)	
CCB + TD	6(5.5)	
CCB +ACEI + CA	5(4.6)	
CCB + BB	4(3.7)	
CCB + ARB +TD	4(3.7)	
ACEI + CA	3(2.8)	
ACEI +ARB + CCB + TD	3(2.8)	
TD + K Sparing	2(1.8)	
Loop diuretic +ACEI	2(1.8)	
TD + CCB + CA	2(1.8)	
CCB + ARB +BB	2(1.8)	
TD + CCB + CA + K Sparing	2(1.8)	
ACEI + TD +CA	1(0.9)	
CCB +ACEI + BB	1(0.9)	
ARB +TD +CA	1(0.9)	
Loop diuretic + K sparing	1(0.9)	
+BB		
TD + K Sparing + CCB + ACEI +CA	1(0.9)	
TD +CCB +ACEI +K Sparing	1(0.9)	
Loop diuretic + K Sparing +CCB + ACEI	1(0.9)	
Loop diuretic + ACEI + CCB	1(0.9)	
Loop diuretic + ARB + CCB	1(0.9)	
Loop diuretic + K sparing + CCB	1(0.9)	
Loop diuretic + K sparing	1(0.9)	
Total	<b>95(87.2)</b>	

*SD= standard deviation, TD= thiazide diuretics, ARB= angiotensin receptor blockers, ACEI= angiotensin converting enzyme inhibitor, CCB= Calcium channel blockers, BB= Beta blockers, CA= centrally acting a agonist.*

A total of 171 DRPs were identified out of which effect of drug treatment not optimal (71.6%) accounted for the highest DRP as shown in Table 3. The average adherence score of the respondents was  $1.0 \pm 0.68$  indicating satisfactory adherence. However, only 21(19.3%) of the respondents were completely adherent. (Table 4). There was significant association between SBP and total number of drug related problems encountered and patient's adherence score  $P < 0.01$ .

However, there was no significant association between SBP and BMI, as shown in Table 5.

**Table 3:** Drug related problems identified

Problem	n (%)
No effect of drug treatment/therapy failure	
No	78(71.6)
Yes	31(28.4)
Effect of drug treatment not optimal	
No	31(28.4)
Yes	78(71.6)
Unnecessary drug treatment	
No	108(99.1)
Yes	1(0.9)
Untreated indication	
No	109(100)
Adverse drug event occurring	
No	65(59.6)
Yes	44(40.4)
Patient dissatisfied with therapy despite optimal clinical outcome	
No	92(84.4)
Yes	17(15.6)
Unclear problem/complaint. Further clarification necessary	
No	109(100)
Total number of problems	<b>171</b>

**Table 4:** Patients adherence

Adherence score indicator	n (%)
Adherent	21(19.3)
Satisfactory	73(67.0)
Average	12(11.0)
Poor	2(1.8)
Non-adherent	1(0.9)
Total	<b>109(100)</b>
Mean score	1.0±0.68

**Table 5:** Correlation between SBP and number of DRPs, adherence score and BMI

Associated variables	Correlation coefficient	P-value
SBP and Total No. of problems encountered	0.468	0.000*
SBP and Patient's Adherence score	0.356	0.000*
SBP and BMI	0.143	0.137

\*Correlation is significant at  $P < 0.01$ .

SBP= Systolic blood pressure, BMI= Body mass index

## Discussion

The mean age of the patients in this study was found to be similar to those in some similar studies [8-9]. This may further agree with studies that reported

hypertension as mostly a disease of middle aged an elderly people [10-11].

The percentage of obese and overweight respondents in this study corresponds with that of a study carried out in northern Nigeria by Chuckwonye, et al 2013 [12] but differs from the results of studies carried out for the entire Nigerian population by Yusuf, et al, 2013 [13]. Majority of the patients were Hausa/Fulani whose major occupation was farming and majority of females among them are housewives, this is not surprising because the Hausa/Fulani are the major ethnic groups in Sokoto State and 80% of the people have agriculture as their major occupation.

Majority of the patients did not achieve the JNC 8 recommended target goal BP despite a more than 2 years mean duration since initiation of antihypertensive drugs therapy. The percentage of target goal BP achieved is lower than that achieved in most studies [8, 11, 14-15]. This can also be seen in the mean SBP/DBP of the study subjects. This is partly associated with the number of DRPs identified in the study subjects. Other factors such as life-style modification, more objective assessment of patients' adherence, assessment of sources and quality of antihypertensive drugs that could also affect BP control may also contribute to majority of the patients not achieving target goal BP.

Diabetes mellitus was found to be the most common co-morbid disease in the study. This is in concordance with the previously conducted study in Nigeria [11], and another carried out in Malaysia [16]. Diabetes have been recognized as the most common comorbid disease in hypertension among black population. This is because there is a substantial overlap between diabetes and hypertension in aetiology and disease mechanism. They share common pathways such as Sympathetic Nervous System (SNS), Renin Angiotensin Aldosterone System (RAAS), oxidative stress, adipokines, insulin resistance, and Peroxisome Proliferator-activated receptor (PPARs)[17]. There is thus the need for aggressive treatment to achieve sustained control of blood pressure in these patients.

ACE inhibitors were the most commonly prescribed antihypertensive as monotherapy. This is not in compliance with the recommendation of the JNC 8 treatment guidelines which recommends the use of thiazide diuretics and calcium channel blockers as first line management for general black population. Although patients with co-morbidities such as diabetes and heart failure may benefit from ACEIs, their proportion in the study subjects did not justify ACEIs to be the commonly prescribed agents.

The use of drug combination therapy was the most common pattern of pharmacotherapy. Several studies have shown that the stage of hypertension, presence of comorbidities and end organ damage demand the use of multidrug antihypertensive therapy, which are used at lower doses to avoid the adverse effects that may occur with higher doses of a single drug [8-9].

CCB + ARB was the most commonly prescribed combination therapy. However, studies carried by

Nasution, et al, 2016 reported CCB and ACE inhibitors as the most commonly prescribed combination pattern. Though this disagrees with this study, it can be related by the fact that ARBs have superior tolerability over ACEIs, which inhibit degradation of bradykinin, leading to adverse effect, such as dry cough and angioedema [18]. A study conducted in Nigeria by Leslie and Adigun, 2000, reported that the incidence of cough in black Africans is somewhat higher than the rate reported in Caucasians. This however disagrees with studies conducted by Osibogun and Okwor, 2014 that had ARB and Diuretic as the most commonly prescribed pattern of combination therapy. The most commonly encountered drug related problems were “effect of drug treatment not optimal”, followed by “no effect of drug treatment” and “adverse drug event”. This is not in accordance with studies carried out by Hussein, 2014, which reported drug interaction as the most common drug related problem. There was significant association with patient adherence score and number of problems encountered with SBP. The more the number of drug related problems encountered, the more likelihood that the patient will not achieve target BP. By implication, pharmaceutical care interventions are needed at various levels including patient, drug and prescriber to resolve these problems and prevent the patients from morbidity and mortality associated with uncontrolled or poorly controlled hypertension. A meta-analysis of randomized control trials showed that pharmaceutical care interventions especially when led by a pharmacist in hypertensive outpatients result in greater reduction in systolic and diastolic BP [19].

## Limitations of the study

Interpretation of the results of this study should take into consideration the short duration of the study and small size of the sample. The data collection instruments used did not also take into account lifestyle modification which is crucial to the management of hypertension.

## Conclusion

Effect of drug treatment not optimal, adverse drug event, no effect of drug treatment/therapy failure were the major DRPs identified and majority of the patients did not achieve their target goal BP.

## Conflict of interest

There is no conflict of interest associated with this study

## Contribution of authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Aliyu Samaila, conceived and designed the study as well as analyzed the data, Hussaina Haruna Aliyu, collected the data, Nuruddeen

Usman, supervised data collection process and Aminu Ahmed Biambo designed and supervised data coding and entry. All authors contributed to the write up and approved the final manuscript.

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