

**EXPLORING DRUG THERAPY PROBLEMS AMONG HYPERTENSIVE PATIENTS
VISITING COMMUNITY PHARMACIES**Jeffrey S. Soni*¹ and Azuka C. Oparah¹¹Department of Clinical Pharmacy & Pharmacy Practice, Faculty of Pharmacy, University of Benin, Benin City Nigeria 300001.

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ABSTRACT

Drug therapy problems (DTPs) are a big burden on the healthcare system and there are numerous advantages in resolving them. Our study aimed to identify, determine the prevalence of drug therapy problems and their associated factors among hypertensive patients visiting community pharmacies for prescription refill. A prospective descriptive study was carried out in five randomly selected community pharmacies. Hypertensive patients' prescriptions were assessed for drug therapy problems during the patient's consultation. Data were collected using the pharmaceutical care sheet. The percentage and type of drug therapy problems identified calculated and analyzed using Students' t-test and one way ANOVA at 95% CI. Of 260 hypertensive patients interviewed, 136 (52.3%) were males, 204 (78.5%) married, 108 (41.5%) were below 5 years of hypertension treatment, 205 (33.4%) of the prescribed drugs were two combination anti-hypertensive drugs. A total of 202 (77.7%) DTPs were identified, 135 (65.8%) accounted for adverse drug reactions (ADRs) out of which 47 (35.9%) experienced headache, 32 (24.4%) experienced GIT disturbance and 18 (13.7%) experienced dry cough. 132 (65.3%) Patients had two types of DTPs. Among 202 (77.7%) DTPs encountered 41 (20.3%) and 49 (24.3%) were referred to hospital and community pharmacies respectively. Thirty-four (82.9%) were rejected from the hospital by physicians, while 38(77.6%) were accepted by community pharmacists. Demographic factors and some clinical characteristics number of drugs blood pressure class, number of comorbidity and number of antihypertensive drugs used (P=0.005) significantly affect DTPs. DTPs among hypertensive patients visiting community Pharmacies in Benin City were high and the most occurring DTPs identified resulted from ADRs problem. While the major associated factors were age, sex, number of drugs, blood pressure class, number of comorbidity and number of antihypertensive drugs used.

KEYWORDS: Drug therapy problems (DTPs), community pharmacies, hypertension, patients and associated factors.

INTRODUCTION

Drug Therapy Problems (DTPs) are a consequence of unmet drug-related needs (irrational drug use). Rational use of drugs requires that patients receive medicines appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community".^[1] A patient would be said to have DTP if he/she experienced any undesirable event which involves, or is suspected to involve drug therapy and that interferes with achieving the desired goals of therapy.^[2] The incidence of DTPs (and the related negative outcomes) encountered per patient is becoming higher and thus, a public health problem. Some years ago in the United States 12,000 deaths and 15,000 hospitalizations secondary to Adverse Drug Reactions (ADRs) were reported to FDA, many more of such went unreported.^[3] Also more than 1.5 million preventable medication-related adverse events occur each year.^[4]

There are several classifications for drug related problem, but in this study the classification of the Pharmaceutical Care Network Europe (PCNE) is used to clarify the concepts.^[5] Both physicians and pharmacists are responsible for the medication errors in irrational drug use, while patient adherence is also very important in terms of accurately maintaining treatment. One of the other major reasons for DTPs is the tendency of the patient to use OTC medicine without consulting a pharmacist.^[6]

A study in Brazil indicated that out of the 56.5% of uncontrolled health related problems encountered, 380 (73.6%) of them were DTPs (actual) and 81 (21.3%) were having risks for potential DTPs. Consequently, out of every two patients, one of them would have at least one form of DTP.^[7] An average of 2.6 DTPs was identified by Root *et al* (2012), in Minnesota.^[8] In

Yogyakarta Indonesia, 63% unnecessary drug therapies in geriatric hospitalized patients were reported.^[9]

Furthermore, 81% of 827 patients in 5 hospitals in Norway were observed to have DTPs at the rate of 2.1 DTP per patient.^[10] Another study revealed that 85% of patients had at least 1 DTP, and 29% of them had 5 or more DTPs, with an average of 3.7 DTPs encountered per patient.^[11]

In Nigeria however, there was a study on HIV infected patients that showed up to 89% of prescriptions with potential DTPs.^[12] Another study on diabetic patients reported that all the prescriptions had DTPs (potential or actual), with an average of 4 DTPs per patient.^[13]

DTPs of various forms affect various outcomes of drug treatment; one of such outcomes is the measurable and observable clinical outcomes.^[3,5,11] DTPs also lead to poor quality of life (QoL) of patients, thereby compromising the goal of drug therapy. The economic implication of DTPs is also very high, seen from both patients' and government's (health care budget) perspective.^[14]

It is well known that the incidence of polypharmacy has increased in patients with CVD because of the associated co-morbidities.^[15] Polypharmacy is one of the most important underlying causes of DRPs during therapy. In studies related to the determination of DRPs, the frequency of DRPs has been reported to be high in this patients.^[16,17]

DTPs are a big burden on the healthcare system and there are numerous advantages in resolving them.^[17] This aim of this study therefore was to evaluate the profile of drug therapy problems, their associated factors, interventions and outcome of interventions made in some selected community pharmacies in Edo state, using the Pharmaceutical care form and PCNE classification system.

METHODS

Study design/setting

A prospective, longitudinal, observational study was carried out to determine DTPs, causes of them, possible interventions and its outcome in community pharmacies between May and October 2019. This was carried out in five randomly selected community pharmacies in Benin City, Edo state Nigeria. The community Pharmacies selected, were those whose superintendent pharmacists were resident and familiar with the concept of Pharmaceutical care practice, in addition, two final year Pharm D students and a principal investigator pharmacists were also attached at intervals to these community pharmacies. Community pharmacy is the area of the profession that engages in distribution, some providing Pharmaceutical care services and retailing of ethical as well as proprietary medicines to their clients who constitute the end users of the products. As at the

time of this study, there were about 89 registered community pharmacies in Benin City, the Edo State capital, and about eighty others scattered across other parts of the State.

Study Population/data collection

Two hundred and sixty four adult hypertensive patients were conveniently selected for this study. Pharmaceutical care form and PCNE V6.2 form were used for the identification and classification of the DTPs were identified by evaluating treatment effectiveness, adverse reactions, patient drug therapy and patient's problem/complaint.

Data Collection Procedure

Data collection was collected by research pharmacist and two final year Pharm D students via oral interview, patient's complaint and prescription assessment, using a comprehensive pharmaceutical care documentation format, which is based on the pharmaceutical care (PC) steps.^[17]

Documentation of the following patient data was done at the first visit: patient's chief complaint and/or doctor's diagnosis, family history, social history, past medical history, past medication history, present medication history (based on doctor's prescription). Systolic and diastolic blood pressure readings were determined at every visit, using a digital sphygmomanometer; three measures were taken at five minutes interval and averaged.

Medication assessment was done to identify the ratio of anti-hypertensive drugs prescribed to the total number of medications indicated in the patient's prescription. Also, Potential and actual Drug Therapy Problems (DTPs) were identified based on prescription assessment and patients complaint.

DTPs were categorized as actual (presently occurring) or potential (would likely occur) after careful investigation. Patients were asked to freely describe any problem or challenges they were having with their current medications, in confidence they were able to clearly identify their drug therapy problems.

Ethical Clearance

The study was conducted after ethical approval was obtained from Ethics Review Committee of Faculty of Pharmacy, University of Benin. Prior to data collection, written consent was obtained from all patients. Record card number was used as patient identifier and name of the patients was excluded to keep and respect confidentiality of all information obtained. For data analysis, a code number that had been given to each patient's data collection instrument was used.

Data analysis

Data were expressed as a percentage of the total number of patients included in the study. Statistical analysis was

performed using SPSS (version 23.0). student t –test, ANOVA and Chi-square test was done with the aid of Graph pad instat, used to test for significant differences within the groups, which are categorized in the PCNE form such as the type and the cause of the problem, intervention and outcome. $P < 0.05$ was considered as statistically significant.

RESULTS

A total of 260 hypertensive patients interviewed. Out of which, 136 (52.3%) were males, 204 (78.5%) married, 152 (58.5%) had post basic education, 152 (58.5%) were self-employed. Table1.

Table 1: Demographics characteristics of patients visiting community Pharmacies.

Variables	Frequency N (%)
Age (years)	
30-40	24 (9.2)
41-50	56 (21.0)
51-60	76 (29.2)
Above 60	104 (40.0)
Sex	
Male	136 (52.3)
female	124 (47.7)
Marital status	
Married	204 (78.5)
Single	16 (6.2)
Widowed	40 (15.4)
Level of education	
No formal education	4 (1.5)
Primary	12 (4.6)
Secondary	92 (35.4)
Tertiary	152 (58.5)
Occupation	
Civil servants	40 (15.4)
Retiree	64 (24.6)
Self employed	152 (58.5)
Unemployed	4 (1.5)

Clinical characteristics of the patients

Of the 260 patients, 108 (41.5%) were below 5years of hypertension treatment, followed by 96 (38.4%) above 10years of hypertension management, 84 (32.3%) were stage I hypertensive, 182(70%) had their blood sugar level below 126mg/dl, 78 (30%) had at least two comorbid cases, 128 (49.2%) had arthritis as a comorbid case, 125 (48.1%) had family members living with

hypertension, while, 32 (12.3%) had family members living with diabetes mellitus. Twenty nine (11.2%) were allergic to different types of medications Table 2

Table 2: Clinical Characteristic of patients visiting community Pharmacies.

Variables	Frequency N (%)
Duration living with hypertension (year)	
1-5	108 (41.5)
6-10	52 (20.0)
Above 10	96 (38.4)
Blood pressure classification (JNC7)	
Normal	64 (24.6)
Prehypertension	72 (27.7)
Stage I	84 (32.3)
Stage II or severe	40 (15.4)
Fasting blood sugar (FBS) mg/dl	
Below 126	182 (70.0)
Above 126	78 (30.0)
BMI	
Underweight	3 (1.1)
Normal	72 (27.7)
Overweight	136 (52.3)

Obese I	55(21.2)
Obese II	4 (1.5)
Number of comorbidity	
none	101 (38.8)
One	56 (21.5)
Two	78 (30.0)
Three	25 (9.6)
Type of comorbidity	
Diabetes	52 (20.0)
Arthritis	128 (49.2)
Asthma	19 (7.3)
Others	61 (23.4)
Family history of hypertension	
Yes with relatives	125(48.1)
No with relatives	135 (51.9)
Family history of Diabetes	
Yes with relatives	32 (12.3)
No with relatives	228 (87.7)
Family history of Asthma	
Yes with relatives	16 (6.2)
No with relatives	244 (93.8)
Drug Allergy	29 (11.2)
Antihypertensive	
Methyldopa	4 (13.8)
Antimalarial	
Chloroquine	9 (31.0)
Fansidar	4 (13.8)
Lonart	4 (13.8)
Antibiotics	
Septin	8 (27.6)

From the study populations 139 (53.5%) had never exercise, 102 (39.2%) never restrict salt diets and 64 (24.6%) still engage in drinking

Table 3: Life style factors of patients.

Life style	Frequency N (%)
Smoking history	
Never smoked	204 (78.5)
Stopped smoking	40 (15.4)
Still smoking	16 (6.2)
Alcohol history	
Never drank	120 (46.2)
Stopped drinking	76 (29.2)
Still drinking	64 (24.6)
Caffeine consumption	
Nil	180 (69.2)
Low	52 (20.0)
Moderate	24 (9.2)
High	4 (1.5)
Salt diet restriction	
Never	102 (39.2)
Rarely	40 (15.4)
Frequently	118 (45.4)
Exercise	
Yes	60 (23.0)
Never	139 (53.5)
Rarely	61 (23.5)

Patterns of anti-hypertensive drugs used by the visiting patients

From the classes of drugs prescribed 228 (37.2%) were calcium channel blockers, followed by diuretics 92 (15.0%). Also, 205 (33.4%) of the prescribed drugs were two combination anti-hypertensive drugs, 170 (27.7%) of the prescribed drugs were mono therapy, and 82(13.4%) were from three combination therapy Table 4.

Table 4: Pattern of anti-hypertensive drugs used by patients.

Drug prescription	Frequency N (%)
Drug class	
Calcium channel blockers (CCB)	228 (37.2)
Amilodipine	163
Nifedipin	65
Angiotensin converting enzyme inhibitors (ACEIs)	76 (12.4)
Lisinopril	51
Ramipril	18
Enalapril	10
Angiotensin receptor blockers (ARBs)	68 (11.1)
Vasartan	38
Irbesitan	20
Candesartan	11
Diuretics	92 (15.0)
Amiloride+hydrochlorothiazide	72
Frusemide	15
Spironolactone	5
Beta blockers (BBs)	16(2.6)
Propanolol	5
carvediolol	11
Adrenergic	24 (3.9)
methyldopa	
Adjuvants	109 (17.8)
Vasoprin	80
copridogel	29
Total	613
Mono therapy	
Amilodipine	82 (48.2)
Nifedipin	24 (14.1)
Lisinopril	29 (17.1)
Ramipril	18 (10.6)
Enalapril	10 (5.9)
Vasartan	4 (2.4)
Frusemide	3 (1.8)
Total	170
Two combination	
Carvediolol+ lisinopril	11 (4.4)
Amilodipine + lisinopril	61 (24.4)
Nifedipin + lisinopril	41 (16.4)
Amilodipine + hydrochlorothiazide	72 (28.8)
Irbesartan +amlodipine	20 (8.0)
Total	205
Three combination	
Valsartan + amilodipine + hydrochlorothiazide	50 (60.9)
Lisinopril + amilodipine + hydrochlorothiazide	21 (25.6)
Lisinopril + amilodipine + HCTs +propranolol	6 (7.3)
Lisinopril + amilodipine + HCTs+ spironolactone	5 (6.1)
Total	82
Other drugs	
Glibenclamide	41 (13.9)

Metformin	53 (17.9)
Insulin	7 (2.3)
NSAIDs	75 (25.4)
Antacids	20 (6.7)
Salbutamol	12 (4.0)
Sameterol	3 (1.0)
Corticosteroid	14 (4.7)
Antimalarial	70 (23.7)
Total	295

Drug therapy problems (DTPs)

A total of 202 DTPs were identified in 260 visiting patients. In 132 (65.3%) Patients there was two type of DTPs, while it was one type in 49 (24.3%) and three types in 21(10.4%) patients. 135 (65.8%) accounted for adverse drug reactions (ADRs) out of which 47 (35.9%) experienced headache, 32 (24.4%) experienced GIT disturbance and 18 (13.7%) experienced dry cough. Other drug therapy problems DTPs include; 18 (18.9)

needed additional drugs, followed by 15 (17.4%) non adherence, and 11 (15.4%) unnecessary drugs.

Out of the 202 DTPs encountered 41 and 49 were referred to hospital and community pharmacies respectively. Thirty four (82.9%) were rejected from hospital, while 38(77.6%) was accepted by community pharmacists.

Table 5: Drug therapy problems (DTPs) encountered and it pattern, among visiting hypertensive patients in community pharmacies.

Drug therapy problems (DTPs)	Frequency n (%)
Number of patients experienced with DTPs	202 (77.7)
Number of DTPs	
One	49 (24.3)
Two	132 (65.3)
Three	21(10.4)
Pattern of DTPs	
(a) Adverse drug reactions (ADR)	133 (65.8)
Increase heart rate	8 (6.1)
Nausea	12 (9.1)
Dry cough	18 (13.7)
Swollen legs/feet	10 (7.6)
Dizziness	14 (10.7)
Headache	47 (35.9)
GIT disturbances	32 (24.4)
(b)Unnecessary drugs	21 (15.4)
(c)Non adherence	25 (17.4)
(d)Additional drugs	28 (18.9)
(e)Dosage too low	9 (4.5)
(e)Dosage too high	7 (3.4)
(f) Drug-drug interactions	9 (4.5)
Interventions made	
DTPs referred to the hospitals	41(20.3)
Accepted	7 (17.1)
Rejected	34 (82.9)
DTPs referred to other community Pharmacies	49(24.3)
Accepted	38 (77.6)
Rejected	11(22.4)
DTPs Resolved in within the Pharmacy	112(55.4)

The result shows that from demographic factors such as age, sex and level of education significantly affects DTPs ($p=0.001$) and from clinical characteristics number of drugs ($P=0.01$) and blood pressure class, number of comorbidity and number of antihypertensive drug used ($P=0.005$) significantly affect DTPs. Drug therapy problems increase as age increase. The study also,

patients with one or more comorbidity and those on two medications had more DTPs.

Table 6: Risk factors associated with DTPs in community Pharmacies.

Variables	DTPs present (n)	DTPs absent (n)	P-Values
Age (years)			
30-40	13	11	<0.0001 X ² Chi-square
41-50	50	6	
51-60	49	27	
Above 60	90	14	
Sex			< 0.0001
Male	90	46	t-test RR-0.7327
Female	112	12	CI= 0.6412-08371
Level of education			
No formal education	4	0	P=0.0004 X ² Chi-square
Basic	93	11	
Post basic	105	47	
Occupation			
Civil servants	30	10	P= 0.1332 X ² Chi-square
Retiree	44	20	
Self employed	124	28	
Unemployed	4	0	
Blood pressure classification (JNC7)			
Normal	21	43	<0.0001 X ² Chi-square
Prehypertension	64	8	
Stage I	82	2	
Stage II or severe	35	5	
Number of comorbidity			
none	55	46	P<0.0001 X ² Chi-square
One	54	2	
Two	71	7	
Three	22	3	
Number of antihypertensive drug used			
One	71	41	P<0.0001 X ² Chi-square
Two	89	9	
>Three	42	8	

DISCUSSION

Almost half of the patients on mono therapy were prescribed amlodipine and it was the most popular prescribed antihypertensive drug class followed by adjuvants and diuretic. Amlodipine has been proven to be an excellent first-line choice among the myriad options of antihypertensive agents and also is a superior option in the HTN armamentarium, not only for controlling BP but also for safely improving patient outcomes.^[18]

Almost sixty percent of the studied patients were found to have more than one or more comorbid conditions including diabetes, Asthma, and arthritis. This is also similar to the study conducted by Hussen and Daba 2017 were more than half of the study patients had more than one comorbid conditions.^[19] It is obvious that, in the presence of co morbidities, patients are exposed to large number of antihypertensive and concurrent medications that might increase the pill burden to the patient. This might in turn increase the likelihood of adverse drug effects that would enforce the patient not to take the medications as agreed upon. These, in addition to other factors, might contribute to the occurrence of DTPs.^[19]

The result also shows that female patients suffered more of DTPs than their male counterpart. This may be due to the fact that women access healthcare facilities and also believe in taking their medications than men. This study negate the study carried out among some diabetes and hypertensive patients in Nigeria that shown male patients suffered more of DTPs than females.^[13,21]

More so, majority of our patients with DTPs were above sixty year of age, this was statistically significant. this older population is associated with Polypharmacy, is one of the variables often associated with ageing, it was found to be the independent predictor of DTPs in the study by Holh *et al.* (2001).^[22] A study has also shown that, majority of patients above sixty years of age had increased DTPs.^[9]

Prevalence of DTPs in this study was less compared to the DTPs prevalence report from other study setting of Ethiopia, which was 80.7%,^[23] and a study from Malaysia also reported 90.5 %, ^[20] although more than the one found in a study conducted by Hussen and Daba.^[19] These findings indicate that management of patients with hypertension is more complicated and prone to different DTPs. The differences in prevalence might be related to different factors including differences in the size of the

study population, the study period, the study setting as well as professionals involved in the identification of DTPs. Clinical pharmacists are crucial in the identification of DTPs since they are trained with adequate pharmacotherapeutic knowledge and pharmaceutical care services. Therefore, pharmacists in the community and hospital setting are suitable in the identification and resolution of DTPs.^[24]

The most common DTP identified was adverse drug reactions (ADRs) in 65.8% of patients. This study is in line with the study done by Khan and Ahmed,^[25] where the most common DTP was also adverse drug reactions, even though there was a variation in the percentage of ADRs encountered in these two studies.

In addition, among the adverse drug reactions (ADRs) encountered, majority of them experienced headache, followed by GIT disturbance and least experienced dry cough. Other drug therapy problems DTPs encountered include need for additional drugs, non-adherence, and unnecessary drugs. This was not so prevalent in this study as compared to the studies done by Hussen and Daba.^[19] The need for additional drug therapy was the second most common DTP and it accounted for almost sixty three percent of the total DTPs encounter.

In our study, non-adherence to antihypertensive agents was also one common DTP category accounting for 7.4% of all DTPs, as measured by medication refill. According to the report of the majority of respondents, forgetting to take the medications at the right time and feeling worse while taking the medications were the major contributing factors. Studies from two settings of Ethiopia reported high rates of non-adherence (26% and 19%) than the current study.^[23, 26] Two other literature findings also reported higher rates of non-adherence.^[27-28] There are also other findings with comparable results of non-adherence rate.^[29-30] These commonly reported rates of non-adherence of patients to the prescribed medications in different study settings, indicate that there is a worldwide medication adherence problem to antihypertensive medications. Studies, particularly in Ethiopia have documented non-adherence as a major concern in the treatment of patients with hypertension. Presence of comorbid conditions and Polypharmacy might contribute, as in the case of this current study.

In this regard, community pharmacists, in cooperation with physicians and other health care professionals, should invest their time more on ensuring their patients' adherence to their treatments based on individualized approach.

Variations in the rates of non-adherence might be due to differences in the socio economic status and literacy level of the study patients. The precision of the method for measuring adherence, the way of employing the questionnaire whether face-to-face interview or self-reporting by the patient, as well as the subjective nature

of the self-reported questionnaire might also contribute to the differences in the rate of non-adherence among different study settings.

Our findings also revealed that, the number of antihypertensive medications and comorbidities significantly associated with the occurrence of DTPs. Different study findings also showed that use of higher number of medications significantly affected DTPs.^[23,24] Patients taking multiple medications with frequent daily administration often had a complex drug schedule and were at high risk of experiencing DTPs. This might be due to intolerance of additive toxic effects of concurrent medications, possibility of drug interactions that might bring about changes to the required dose range and its desired effects and other related factors. Patients with multiple disease conditions and patients taking large number of medications should be closely monitored for DTPs to avoid clinically significant harmful consequences. The association between the presence of comorbid conditions and the occurrence of DTPs was consistent with some literature results.^[19,27]

In addition, level of education also showed a significant association with the occurrence of DTPs. In this study, patients with higher educational background were most encountered and had more of the DTPs, probably due to the urban setting where the study was done.

The determination and resolution of DTPs by the pharmacists was possible as a result of accurate and timely intervention. The interventions offered to physicians by clinical pharmacists had the highest acceptance in terms of the resolution and the prevention of DTPs.^[31] Studies have shown that there was a 41-96% acceptance of interventions made by pharmacists in both community and hospital settings.^[32-34] In the current study, DTPs were discovered and recommendations/interventions were made; only seventeen percent of the recommendations were accepted by hospital physicians while a greater number referred to the community pharmacists were accepted. Although the community pharmacists are not exactly the same as hospital pharmacists, the interventions were performed directly on the patient. Ultimately, it was observed that the patient-pharmacist-physician network was not adequate; patient information was obtained through direct contact with the patient/patient relatives and its reliability was controversial. In two studies performed,^[31,34] the acceptance rate of the interventions was low. The reason for this was described as the pharmacist had difficulties in accessing the patient's specific information. Also, the interventions offered by pharmacists were in the form of written reactive disclosures.^[34]

Limitations of the study

The study had some limitations due to the fact that not all the necessary information was obtained from the patients such as laboratory investigations, patients non willingness to wait for detailed drug counseling, lack of

adequate knowledge of patients' treatment details, poor or no response by patients due to the low appreciation of pharmaceutical care counseling at the time of the study.

In some cases, prescriptions were sent to community pharmacy by proxy and collected by patient's care providers/relatives. There were also the limitations of the availability of an adequate drug information system database, deficiencies in the healthcare system and the difficulties in accessing physician.

CONCLUSIONS

Drug therapy problems (DTPs) among hypertensive patients visiting community Pharmacies in Benin City was high and the most occurring DTPs identified resulted from ADRs problem. While the major associated factors were age, sex, number of drugs, blood pressure class, number of comorbidity and number of antihypertensive drug used.

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