

Clinical Pharmacology & Biopharmaceutics

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# Assessment of Drug Related Problems Among Hypertensive Patients on Follow up in Adama Hospital Medical College, East Ethiopia

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## Abstract

Hypertension is an important worldwide public-health challenge because of its high frequency and risk factor for cerebrovascular, cardiovascular and kidney disease. Drug therapy problems are a significant challenge to health care providers. It severely compromises the effectiveness of treatment making this a critical issue in population health both from the perspective of quality of life and of health economics. Therefore, the objective of this study is to determine the pattern and magnitude of drug therapy problems in the study hospital and to find out risk factors for these problems. The study was questionnaire-based Cross sectional design which was conducted from April to May 2014 at Adama Hospital Medical College. A convenient sampling method was used and a total of 192 hypertensive patients were included in the study. Data were analyzed using SPSS software program. In this study 155 (80.7%) patients have at least one drug therapy problem and a total of 452 drug therapy problems were identified in them. The most common drug therapy problem interaction constituting 19.5% and 18.6% respectively. Under dose accounts only 0.9% of all drug therapy identified. Marial status, number of drugs and number of comorbidities significantly affect drug therapy problems. The study showed that 80.7% of the patients in the study have drug therapy problems. Number of complications and number of drugs significantly affect drug therapy problems. Therefore, patients with multiple diagnosis and patients using multiple drugs should be closely monitored for drug therapy problem, to avoid clinically significant harmful consequences.

**Keywords:** Drug therapy problem; Hypertension patient; Adama; Ethiopia; Adverse drug reaction

## Abbreviations and Acronyms

ACE: Angeotensin Converting Enzyme; ADRs: Adverse Drug Reactions; AHMC: Adama Hospital Medical Collage; DTP: Drug Therapy Problem; FDA: Food and Drug Administration; HTN: Hypertension; JNC7: Seventh Report of Joint National Committee; OPD: Outpatient Department

# Introduction

#### Background

Hypertension is a silent killer disease in both developed and developing nations of the world [1]. It is an important worldwide public-health challenge because of its high frequency and risks factor for cerebrovascular, cardiovascular and kidney disease [2-4]. 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 [3-6]. High blood pressure is estimated to cause 7.1 million deaths annually, accounting for 13% of all deaths globally [2,3,5,7].

It is estimated that the world wide prevalence of hypertension would increase from 26.4% in 2000 to 29.2% in 2025 [8-10]. Most of this rise can be attributed to an expected increase in the number of people with hypertension in economically developing regions [3].

In Ethiopia little is known about the magnitude and determinants of hypertension. However, recent evidences indicate that hypertension is increasing partly because of the increase in risk factors including smoking, obesity, and harmful use of alcohol and lack of exercise [2].

Awareness about treatment and control of hypertension is extremely low among developing nations including Ethiopia. So the prevention and control of hypertension has not received due attention by these countries. This is mostly because in these countries health care resources are overwhelmed by other priorities including HIV/AIDS, tuberculosis, and malaria [2].

Drug therapy problems severely compromise the effectiveness of treatment making this critical issue in population health both from the perspective of quality of life and of health economics. Interventions aimed at improving drug therapy problems would provide a significant positive return on investment through primary prevention of risk factors and secondary prevention of adverse health outcomes [1,3,8].

#### Statement of the problem

Hypertension is considered a disease of high prevalence and low control, and its inadequate treatment can lead to coronary heart disease (CHD), acute myocardial infarction (AMI), peripheral vascular disease (PVD), stroke, congestive heart failure and renal failure [2,7]. Because of these consequences it is the leading cause of morbidity and mortality among non-communicable diseases, and accounts for 13% of all deaths globally [2,3,5,7].

Analysis of the global burden of hypertension revealed that over 26% of the world's adult population had hypertension in 2000 [7,10], and has shown a rapid increase in prevalence affecting significant numbers of individuals in Sub-Saharan Africa. Although there is

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Received August 22, 2014; Accepted September 19, 2014; Published September 23, 2014

**Citation:** Hussein M, Lenjisa JL, Woldu MA, Tegegne GT, Umeta GT, et al. (2014) Assessment of Drug Related Problems Among Hypertensive Patients on Follow up in Adama Hospital Medical College, East Ethiopia. Clinic Pharmacol Biopharmaceut 3: 122. doi:10.4172/2167-065X.1000122

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shortage of extensive data, 10.5% of the Ethiopian population has been estimated to have HTN. Available data shows an overall prevalence of 5-20% in Oromia region [7].

Studies worldwide indicate that despite the availability of effective medical therapy, more than half of hypertensive patients on treatment have blood pressures over 140/90 mm Hg threshold [7,11]. This is mostly because of drug therapy problems which include but not limited to non-compliance, ADRs, improper drug selection and drug interactions [12].

The occurrence of a DTP among hypertensive patients could prevent or delay patients from achieving desired therapeutic goals. It has been attributed to unnecessary over-prescription of drugs, substantial worsening of diseases, avoidable increases in hospital admission rates, and longer hospital stays leading to a significant medical burden. As a result, substantial numbers of patients do not get the maximum benefit of medical treatment, resulting in poor health outcomes, lower quality of life, increased health care costs and erodes public confidence in health systems [3,7].

Clearly interventions to improve drug therapy problems are needed to overcome the harms imposed by the problem. If such interventions are to be successfully designed, targeted, and cost effective, it is critical to understand the complex reasons for drug therapy problem and to identify those that are modifiable in hypertensive patients. Therefore, this study was conducted to assess the prevalence, pattern, and factors contributing to DTPs among hypertensive patients at Adama Referral Hospital, East Shoa, Ethiopia.

#### Significance of the study

This study is significant in several perspectives. Firstly, in Ethiopia, particularly in the study area, little is known about the DTP status and associated factors among the target population as studies are scarce in this regard. Therefore, this study generated essential data that could fill this gap.

Secondly, having data regarding the burden of DTP among hypertensive patients will help policy makers to effectively plan in preventing risks caused by these problems. Thirdly, identifying risk factors of DTP is important in that it creates opportunities for designing effective intervention to mitigate problems related to drug therapy there by maximizing patient care. Lastly, the findings from this study are used as a baseline for future researchers who want to undertake similar study in the country.

## **Operational definition**

**Hypertensive patient** is patient with high blood pressure and has already started anti-hypertensive medication.

**DTP:** In this study it include ADR, non-adherence, inappropriate dose, drug interaction and drug interaction

**Non adherence:** intentionally missing of drug and unintentionally missing more than four times a month was considered as non-adherence.

**Potential drug interaction:** The extent to which interaction may occurs between drugs.

# Objective

## **General objective**

• The general objective of this study is to identify drug therapy problems and their risk factors among hypertensive patients on follow up at Adama Hospital Medical Collage.

#### Specific objective

- To determine prevalence of drug therapy problem among hypertensive patients in AHMC.
- To determine pattern of drug therapy problem, among hypertensive patients in AHMC.
- To identify risk factors of drug therapy problem among hypertensive patients in AHMC.

## **Methods and Materials**

## **Study Design**

Hospital based cross-sectional study design was employed.

#### Study area and period

This study was conducted from April to May 2014 in Adama referral hospital. This hospital is found in Adama town, Oromia regional state which is located at 99 km away from the capital city of Ethiopia, Addis Ababa, to the east.

Based on figures from the Central Statistical Agency in 2007, this town has a total population of 220,212, an increase of 72.25% over the population recorded in 1994 census [7]. In the town there are different health facilities including health centers, clinics and hospitals. There are four hospitals from which three are privates and one is governmental. Adama referral Hospital is a teaching as well as regional referral Hospital under ministry of education of Ethiopia. The referral Hospital is meant to serve 5 million people as per the three tier system of the National Ministry of Health. Services provided at this hospital include: emergency, admissions, laboratory, minor and major surgeries, ultrasound scanning, pharmaceutical service, ambulance and the like. Chronic illness care is one of the services provided in outpatient clinic in the hospital to the population both within and outside of Adama town.

#### Source of population

All hypertensive patients who attend Adama referral hospital were source of study population.

## **Study population**

All the hypertensive patients found at Adama referral hospital during data collection and those fulfill the criteria were included.

## Inclusion and exclusion criteria

## Inclusion criteria

- 1. Hypertensive patients who were willing to respond.
- 2. Patient above 18 years old.
- 3. Participants who have been taking anti hypertensive treatment for at least past one month and come to OPD for refill.

## **Exclusion criteria**

- 1. Pregnancy induced hypertension.
- 2. Patients who had not started anti hypertensive.
- 3. Patients who could not respond. E.g. too sick to be interviewed and unconscious patients.
- 4. Mentally unsTable hypertensive patients.

#### Sample size determination

All patients fulfill the criteria and present to OPD of AHMC during data collection period (from April to May 2014) were included.

# Sampling techniques

Convenience sampling method was used to collect data. Patients found during the study period at the study area who fulfill the criteria were sampled.

## Data collection procedure and instruments

A questionnaire consisting of both closed ended and open ended questions was used during the interviews. For each patient, a form was completed with regard to patients age, gender, marital status, level of education, duration of treatment, life style modification, drugs patient was using, indications for each drugs, adherence questions, adverse drug reaction occurs and drug causes DTP. Data was collected by fifth year pharmacy students. With exception of DDI data which was later identified using Micromedix online software, all DTPs were identified first by ward clinical pharmacist and then presented to ward physician for his comment. Finally, only DTPs on which ward clinical pharmacist and physician had consensus were included in this study. Then data was collected upon the supervision of principal investigator.

## Study variables

## Dependant (Outcome) variable

Dependant (Outcome) variable includes adherence to anti-hypertensive drugs, unnecessary drug therapy, ADR, drug interaction and inappropriate dosing (over and under dose).

#### Independent (Exposure) variable

Socio demographic characteristics (i.e. age, sex, marital status, level of education and occupation), and clinical characteristics (i.e. number of co-morbidity, number of medication and duration of treatment and life style factors).

#### Data analysis

All data collected were feed into the computer and analyzed using the Statistical Package for the Social Sciences (SPSS), version 16.0 software. Descriptive statistics like frequency and percentage were generated. Chi-square ( $x^2$ ) was used to test association between variables and a p value of < 0.05 was considered as statistically significant. The results were presented in the form of tables.

#### Data quality assurance

Pretest was done on ten patients one week before data collection was started. Based on the result, the questioner was rearranged and modified.

#### Ethical consideration

Before data collection to conduct this study, ethical clearance was obtained from Ambo University College of Medicine and health sciences, pharmacy department, and the letter was submitted to Adama referral hospital medical director office and research office of the college prior to the beginning of undertaking the study in the area. All the study participants were informed about the purpose of the study; their right to refuse is maintained. Ethical conduct is maintained during data collection and throughout the research process.

## Result

#### **Demographic characteristics**

A total of 192 hypertensive patients were interviewed. The

demographic characteristics of patients are included in Table 1. The study was conducted on 93 (48.4%) males and 99 (51.6%) females. The average age of patients was  $58.39 \pm 11.57$  which vary from 30-83. More than half of patients 102 (53.1%) were with age range of 56-70 years, 7 (3.6%) were single, 65 (33.9%) had primary school and as many as 122 (63.5%) were unemployed (Table 1).

Page 3 of 6

#### Clinical characteristics of the patients

Many patients 67 (34.9%) were in the stage of therapy of greater than five years, followed by 54 (28.1%) for 1-3 years. It was also found that approximately 77% of the patients suffered from two or more diseases. The most common hypertension co morbid disease was Diabetes mellitus followed by Heart disease (Table 2).

Most of the patients in the study reported that they had modified their life to control the disease. From the study populations only 18.8% were never engage in physical activity. Number of social drug users was

Characteristics	Frequency	Percentage (%)	
Age(year)			
18-35	9	4.7	
36-55	67	34.9	
56-75	102	53.1	
>75	14	7.3	
Sex			
Male	93	48.4	
Female	99	51.6	
Marital status			
Ever Married	185	96.4	
Single	7	3.6	
Level of education			
No formal education	48	25.0	
Primary	65	33.9	
Secondary	38	19.8	
Tertiary	41	21.4	
Occupation			
Government employee	23	12.0	
Self employee	42	21.9	
Non government employee	5	2.6	
Un employee	122	63.5	

 Table 1: Demographic characteristics of patients, Adama Referral Hospital, Ethiopia,

 April to May 2014.

Duration(year)	Frequency	Percent (%)	
<1	35	18.2	
1-3	54	28.1	
4-5	36	18.1	
>5	67	34.9	
Number of co-morbid	·		
One	45	23.4	
Two	125	65.1	
Three	17	8.9	
Four	5	2.6	
Types of co-morbidity	·		
Diabetic	139	74.3	
Chronic heart failure	14	7.5	
Chronic kidney disease	15	8.0	
Hyperlipidemia	3	1.6	
Others *	16	8.6	

\*peptic ulcer disease (4), hypothyroidism (1) and pneumonia (11)

 Table 2: Clinical characteristics of the patients, Adama Referral Hospital, April to May 2014.

#### Page 4 of 6

higher for alcohol users than others which include chat and cigarette. The total drug users were 87 (Table 3).

#### Patterns of anti-hypertensive drugs used by the patient

In this study the average number of anti-hypertension medications prescribed was  $1.58 \pm 0.69$  with minimum of one and maximum of four, while the average number of total drug was  $2.96 \pm 1.065$  which range from 1 to 6. From patients on follow-up 99 (51.6%) patients were on mono therapy and the rest 93 (48.4%) received a combination of anti-hypertensive drugs (Table 4).

In mono therapy, ACE inhibitor (Enalapril) was most commonly prescribed (n=72; 72.7% of mono therapy) while in combination therapy, a two drug combination consisting of calcium channel blockers (Nifedipine) and ACE inhibitors (Enalapril) were given to the majority of patients (n=50; 53.8% of combination therapy) (Table 4).

## Drug therapy problems (DTP): Tables 5 and 6

A total of 452 DTPs were identified in 155 patients. In 93 (57.4%) patients there was only one type DTP, while it was two types in 57 (36.1%) and three types in 5 (6.5) patients.

In this study most of the drugs prescribed to the patients contains appropriately adjusted dosage. Only nifedipin under dose was prescribed for 4 (0.9%) persons, but there was no prescription which contain anti-hypertensive drug over dose.

In 10 (2.2%) cases there was no indication (heart failure and edema) for such therapeutic scheme: a combination of three drugs including Calcium channel blocker, ACE-inhibitor and Thiazide diuretics (6 patients), a combination of three drugs including Calcium channel blocker, Beta blocker and Thiazide diuretics (1 person) and a combination of four drugs including beta-blocker, ACE-inhibitor, calcium channel blocker, and Thiazide diuretics (3 patients).

Anti-hypertensive was prescribed concomitantly with other drugs with known potential drug interaction risk in 127 patients (66.1% of the study sample). The most frequently prescribed combination of this kind was an ACE inhibitor (Enalapril) with oral hypoglycemia in 72 patients. Most common drug interaction type identified in these patients was moderate drug interaction which account 88.4% followed by minor (8.9%) and major type of drug interaction which was only 2.7%.

Duration(year)	Frequency	Percent (%)	
Alcohol			
Rarely	36	18.8	
Never	156	81.2	
Chat			
Frequently	9	4.7	
Rarely	14	7.3	
Never	169	88.0	
Exercise			
Yes	90	46.4	
Rarely	66	34.4	
Never	36	18.8	
Salt diet restriction			
Frequently	19	9.8	
Rarely	89	46.4	
Never	84	43.8	

Table 3: Life style factors , Adama Referral Hospital, April to May 2014.

Drug prescription	Frequency	Percent
Individual drugs	,	
Enalapril	155	43.4
Nifedipin	85	23.8
HCT	30	8.4
Furosamide	61	17.1
Atenolol	19	5.3
Total drugs	357	100
Mono therapy		
Enalapril	72	72.7
Nifedipine	24	24.2
Atenolol	3	3.1
Total	99	100
Two Combined drugs		
Enalapril + HCT	13	16.3
Enalapril + Atenolol	6	7.5
Enalapril—Nifedipine	50	62.5
Others*	11	13.7
Total	80	100
Malty combination drugs		
Enalapril + Nifedipin + HCT	6	46.2
Nifedipin + HCT + Atenolol	3	23.1
Enalapril + Nifedipine + HCT + Atenolol	4	30.8
Total	13	100
Other drugs		
Glibenclamide	33	10.75
Combination	102	33.2
Insulin	104	33.9
NSIADS : Aspirin, Indomethacin , Diclofenac	30	9.8
Anti acid	11	3.6
Others**	27	3.3

\*HCT+Atenolol=4, enalapril+spironolactone =2, enalapril+furosamide=5, \*\*Amoxicillin(4), Digoxin(3), Proton pump inhibitor(6), Cimetidin(2), Metfoemin(2), Tramadol 2, vitamin B complex (1), Cough syrup (2), Hydrocortisone(3) and Cephalexin (1)

 Table 4: Most frequently prescribed medications for HTN treatment, Adama Referral Hospital, April to May 2014.

The total number of ADRs was 93 in 192 patients which account 48.6% of total DTP. The most commonly identified ADRs were gastrointestinal disturbance, dry cough, peripheral edema, dizziness, increased heart rate, headache and paresthesis (Table 5).

Therapeutic non-adherence was recorded in 86 patients (44.8%). Only in 14 of them, it was due to the occurrence of an ADR. The respondents' adherence was affected by different factors. The major factors include patient memory (forget), feel better, feel worse, patient believe on drug efficacy, fear of side effect or drug caused side effect, use of traditional medicines (healer) or religious belief and cost of the medication.

The result shows that from demographic factors marital status significantly affects DTP (p=0.001) and from clinical characteristics number of drugs (P=0.01) and number of complication (P=0.005) significantly affect DTP. Drug therapy problems increase as age increase, but it is not statistically significantly (p=0.214). The study also shows that female patients have higher ratio of drug therapy problem when compared with male. The result is not statistically significant again (p=0.425).

#### Discussion

In this study DTP was identified in 155 patients in which it accounts 80.7% of total patient. The most common DTP identified was drug interaction in 64.4% of patients. This result is not consistent

	Number	Percent	
Number of patients with DTP	155	80.7	
Number of DTP			
One	93	60	
Тwo	57	36.8	
Three	5	3.2	
Total	155	100	
Pattern of DTP			
1.	ADR	93	20.6
Gastro intestinal disturbance	24	25.8	
Dry cough	14	15.1	
Peripheral edema	13	14.0	
Headache	10	10.8	
Dizziness	8	8.6	
Paresthesia	8	8.6	
Increased heart rate	7	7.5	
Others*	9	9.7	
2.	Unnecessary	10	2.2
3.	Under dose	4	0.9
4.	Non adherence	86	19.0
5.	Drug-drug interactions (DDIs)	259	57.3
Minor DDIs	23	8.9	
Moderate DDIs	229	88.4	
Major DDIs	7	2.7	
Total DTP identified	452	100	

\*allergy (2), Impotence (2), Fatigue (3), and Gout (2)

 Table 5: DTP and its pattern, Adama Referral Hospital, April to May 2014.

with the result of research done in Nabulus district in North Palestine which was 40% [13] and in Mexico which was 42.5% [9]. These may be due to difference in health worker accessibility and absence of drug interaction checker. ACE Inhibitor (Enalapril) caused drug interaction more likely according to this study. The result of research done in Palestine which states ACE inhibitor and Beta blockers were the cause of drug interactions supports this result [13]. But the difference is that, in Palestine beta blocker was the main cause of DDI (31.5%) followed by ACE inhibitor (23.4%) and this difference may be due to the variation in commonly prescribed medications in two countries.

The most frequently prescribed combination of inappropriate drug was an ACE inhibitor with oral hypoglycemic agents (in 72 patients). This is mostly because most patients were co morbid with diabetic mellitus and was taking both anti-hypertensive agent and anti-hypoglycemic agent. This study shows that 5.2% of all patients were prescribed unnecessary drugs. This result is comparable with the result of research done in Mexico by Mino-León D, et al. which was 5.48%.

The data obtained through self- reporting questionnaires revealed the proportion of treatment non-compliance was 44.8% which accounts 19.5% of all DTP. This result agreed with the result of research done in Mexico 2007 which was 42.8% [9] and in Malaysia which was 46.6% non-compliant [3]. But the study done in Dessie, Ethiopia showed that 68.03% of hypertensive patients were not complaints to anti-hypertensive drugs and the rest were compliant [14]. Non adherence due to ADR was 7.3% which is consistent with the result of research done by Belayneh et al. [14] which was (7%). But the result is very low when compared with the result of research done in Dessie, Ethiopia which was 58.21% and in Ghana which was 21%. This may be because of difference in attitude between the people as some people believe side effect of the drug is an indication for drug efficacy, and so they did not stop medication even if ADR occurred. The other factors which may bring this difference may be the difference in knowledge between people.

Adverse drug interactions were occur in 42.7% of total samples in this study. The result is not in line with research done in Sweden and in India which was 25.7% and 10% respectively [4,15]. This may be because many patients in our study have co morbid condition which is significantly associated with DTP. In this study gastrointestinal disturbance was the main ADR identified followed by dry cough and peripheral edema while in research done in India the main ADR identified was dry cough and peripheral edema caused by anti-hypertensive drugs [15]. The difference may be due to difference in patient knowledge on which drug is the cause for adverse effect occurred.

Marital status, number of medications and number of complications significantly affect DTP. Single patients have high DTP than ever married patients. This is mostly because these single patients were in lower age than ever married and also because they have less number of co morbid conditions and so using less number of drugs, Drug therapy problem increase with increase in number of co morbidity. This may be because as co morbidity increase number of drugs patients using increase. This increase drug intersection which is the main DTP identified in our case, Drug therapy problem increase with age. But the result was not statistically significant.

Variables	DTP present	DTP absent	Ratio of DTP present	p-value
Age range				
18-35	7	2	77.8	
36-55	58	9	86.6	
56-75	86	16	84.3	0.214
>75	14	0	100	
Sex				
Male	78	15	83.9	0.425
female	87	12	87.9	
Marital status				
Ever married	159	26	85.9	0.000
Single	6	1	85.7	
Education				
No formal education	40	8	83.3	
Primary	57	8	87.7	0.505
Secondary	33	5	86.8	
tertiary	35	6	85.4	
Occupation				
Government employee	20	3	87	
Self employee	32	10	76.2	
Nongovernmental employee	5	0	100	0.099
Un employee	108	14	88.5	
Number of complication				
1	33	12	73.3	
2	112	13	89.6	0.005
3	15	2	88.2	
4	5	0	100	
Number of hypertension d	rugs			
1	80	19	80.8	
2	71	8	89.9	0.010
3	10	0	100	
4	4	0	100	

 Table 6: Risk factors of DTP Adama Referral Hospital, April to May 2014.

Page 6 of 6

# Conclusion

The study showed that 80.7% 0f the patients have DTP which is too high. Drug interaction, adverse drug interaction, non-adherence, drug without indication and inappropriate dosage was the DTP identified. Adverse drug reaction was the main DTP identified while under dose was the least cause of DTP. Number of complication, number of drugs and marital status significantly affect DTP.

## Recommendations

The results of our study indicate that patients with multiple diagnosis and patients using multiple drugs should be closely monitored for DTPs, to avoid clinically significant harmful consequences.

To detect and solve the problem of drug interaction, both the private and governmental pharmacy units need to appoint skilled pharmacist and to be supplied with drug interaction software if possible.

Forgetting is one of the major reasons for non-adherence. So patients should be encouraged to adopt systems and methods for remembering to take their medication such as use of mobile alarm and alarm clock. Financial access has been deemed as one of the important barrier to adherence. Doctors should consider the financial status of their patients in prescribing anti-hypertensive medications to enable affordability, e.g. generic prescribing should be encouraged.

#### Acknowledgements

We are very grateful to our college staff members for unreserved guidance and constructive suggestions and comments from the stage of proposal development to this end. We would like to thank Ambo University for supporting the budget which required for this research. Finally our deepest gratitude goes to Adama referral hospital staff workers who helped and allowed us in collecting and gathering data from the hospital.

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