

# Assessment of drug therapy problem and associated factors among adult hypertensive patients at Ayder comprehensive specialized hospital, Northern Ethiopia

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## Abstract

**Background:** Drug-therapy problems(DTPs) among hypertensive patients can result in patient's morbidity and mortality. The main aim of this study was to assess drug therapy problem and associated factors among hypertensive patients.

**Methods:** A hospital based cross sectional study was conducted. The data was collected from patients' medical charts and through interview. Drug therapy problem was categorized according to Cipolle methods of DTP classification. The data was analyzed using the Statistical Package for the Social Sciences (SPSS), version 21.

**Results:** A total of 241 patients were studied. The mean number of antihypertensive medications prescribed were  $1.41 \pm 0.53$ . A total of 357 drug therapy problems(DTPs) were identified. From the patients studied, 134(55.6%) had at least one evidence of drug therapy problem. Non adherence was the most commonly identified drug therapy problem occurred in (143(59.3%)) patients. Substance use (AOR=0.445, 95% CI= 0.227-0.870,  $p=0.018$ ) and comorbidity (AOR= 2.099, 95% CI= 1.192-3.694,  $p=0.010$ ) were the predictors of DTP.

**Conclusion:** More than half of the participants had evidence of onset drug therapy problem. Thus efforts that could boost antihypertensive compliance and minimize substance use should be adopted to reduce patients' drug therapy problems.

**Keywords:** assessment, drug, therapy, problem, Ethiopia.

**DOI:** <https://dx.doi.org/10.4314/ahs.v19i3.33>

**Cite as:** Weldegebreal AS, Tezeta F, Mehari AT, Gashaw W, Dessale KT, Legesse NY. Assessment of drug therapy problem and associated factors among adult hypertensive patients at Ayder comprehensive specialized hospital, Northern Ethiopia. *Afri Health Sci.* 2019;19(3): 2571-2579. <https://dx.doi.org/10.4314/ahs.v19i3.33>

## Background

Hypertension(HTN) is a silent killer disease in both developed and developing countries. It is among the leading risk factors for cardiovascular diseases and which is a major cause of death globally.<sup>1,2</sup> It is estimated that the

world wide prevalence of hypertension could increase from 26.4% in 2000 to 29.2% in 2025.<sup>3</sup> By 2025, 125.5 million people in sub-Saharan Africa will be expected to be affected by HTN.<sup>4</sup>

The prevalence of hypertension in Ethiopia is escalating because of increase in risk factors like smoking, obesity, harmful use of alcohol and lack of exercise. However, awareness about treatment and control of hypertension is extremely low in Ethiopia.<sup>5</sup> The intention of prescribing drugs to patients is treatment, prophylaxis or diagnosis of medical conditions; however, these drugs may have negative effects on patients if not used appropriately.<sup>6</sup> Inadequate treatment of hypertension can lead to congestive heart disease(CHD), acute myocardial infarction(A-MI), peripheral vascular disease(PVD), stroke, congestive heart failure(CHF) and renal failure. Because of these it is the leading cause of morbidity and mortality among

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non-communicable diseases, and accounts for 13% of all deaths globally.<sup>11,12,13,14</sup>

Analysis of the global burden of hypertension revealed that over 26% of the world's adult population had hypertension in 2000 and has shown a rapid increase in prevalence affecting significant numbers of individuals in sub-Saharan Africa. Although there is a shortage of extensive data, available data shows an overall prevalence of 5-20% in Oromo region.<sup>14,15</sup> Despite the availability of effective medical therapy, more than half of hypertensive patients on treatment has uncontrolled blood pressure. This is mostly because of drug therapy problems (DTPs).<sup>16,17,18,19</sup>

In Ethiopia the prevalence of DTP ranged from 73.5-80.7%.<sup>20,21</sup> The most frequently identified cause for drug therapy problems are drug choice problems, dosing problems and/or drug interactions.<sup>18</sup> On the other hand, patients usually had drug use problems caused by "drug use process, lack of information, and physiological or patient factor."<sup>19</sup>

The occurrence of 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, it resulted in poor health outcomes, lower quality of life, increased health care costs and erodes public confidence in health systems.<sup>12,14</sup>

Interventions to improve DTPs 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 problems and to identify those that are modifiable in hypertensive patients. The aim of the study was to assess DTPs and associated factors among adult hypertensive patients in Ayder Comprehensive Specialized Hospital(ACSH), Northern Ethiopia.

### **Research methods and participants**

A hospital-based cross-sectional study among adult hypertensive patients was conducted at the ambulatory hypertension clinic of ACSH from March to June 2016. ACSH is located in Mekelle City, the capital of Tigray Regional State, which is 783 km away from the capital

of Ethiopia, Addis Ababa. ACSH is the only teaching and referral hospital in the region. The hospital is having 400 beds to serve its patients. It provides general outpatient, inpatient and emergency services for about nine million people in the catchment area of Tigray, Afar and South-eastern parts of Amhara Regional States. ACSH provides general surgery and orthopedic, gynecology & obstetrics, pediatric and child health in addition to internal medicine, dermatology, psychiatric and dental services to the general public.

There were 2113 registered hypertensive patients at the ambulatory clinic of ACSH. Single proportion formula was used to calculate the minimum sample size needed. Considering 1.96 for the standard normal variable with 5% level of significance ( $\alpha$  - value), 0.8 prevalence of DTP in Adama, Ethiopia,<sup>9</sup> 95% confidence interval, 5% margin of error and 10% contingency, the sample size was calculated to be 241.

The study was approved by the Institutional Ethical Review Board of College of Health Sciences, Mekelle University. ACSH also give permission the study to be conducted on the hypertensive clinic. Informed written consent was obtained from all patients prior to face to face interview. Patients personal information like name were not recorded to maintain patient's confidentiality. A face-to-face interview using a pretested structured questionnaire was conducted to collect the socio-demographics, clinical characteristics and adherence status of patients to antihypertensive medication(s). Data on comorbidities, antihypertensive medications and a one-year blood pressure(BP) measurements were extracted from medical records of patients using a pretested data abstraction checklist.

All hypertensive patients aged 18 years and above, who had a regular follow-up for at least 12 months at ACSH hypertension clinic and whose medical records contained complete data and who were willing to participate were included in the study. Seriously ill patients who were not able to finish interview and patients with incomplete medical records were excluded from the study. The data were collected by trained clinical nurses working out of ACSH.

To maintain validity of the data collection tool, a structured questionnaire was developed and translated into

local languages (Amharic and Tigrigna) and back translated to English. The primary outcome of the study was presence of DTP.

### **Classification of drug therapy problem**

DTP was identified with reference to Joint National committee (JNC-8). Drug therapy problem was categorized according to a Cipollea method of DTP classification. There are seven basic categories of DTPs according to the book. These are: indication, effectiveness, safety and adherence.<sup>22</sup> The DTPs and their possible causes were identified from the patients' medical records and patients interview.

### *Variables*

The dependent variable was presence of DTP whereas the independent variables were age, sex, number of drugs, co-morbidity, socio-demographic characteristics, substance use, occupation, number of anti-hypertension medications, life style modification, mode of medication intake i.e. free or pay, duration of hypertension since diagnosis and family history of hypertension.

### *Operational definitions*

Hypertension was defined as sustained high blood pressure (SBP $\geq$ 140 or DBP  $\geq$ 90mmHg) or reported regular use of antihypertensive medication(s). Uncontrolled blood pressure was defined as systolic blood pressure of  $\geq$ 140 mmHg and/or diastolic blood pressure of  $\geq$ 90 mmHg.<sup>9</sup> Controlled blood pressure was defined as systolic blood pressure of  $<$ 140 mmHg and/or diastolic blood pressure of  $<$  90 mmHg.<sup>9</sup> A DTP is defined as any undesirable event experienced by a patient which involves, or is suspected to involve, drug therapy, and that interferes with achieving the desired goals of therapy, which can be identified using JNC-8 guidelines except compliance.<sup>23</sup> Any deviation from the JNC-8 guideline protocol was declared to have DTP.

### *Statistical analysis*

Data was analyzed using Statistical Package for Social

Sciences (SPSS® statistics) program version 21 (SPSS; Chicago, IL, U.S.A). Binary logistic regression analysis was employed to identify determinants of drug related problems. To identify determinants of DTP, variables with p-values  $<$  0.05 on a univariable logistic regression model were entered into a multivariable logistic regression model and variables with tailed p-value  $<$  0.05 were considered as statistically significant and were declared to be determinants of DTP.

## **Results**

### *Baseline characteristics of the participants*

A total of 241 adult hypertensive patients were enrolled and studied. The response rate was 100%. From the total patients studied, 142 (58.9%) participants were males. The average mean age of the participants was  $45.11\pm 11.79$  years with minimum peak age of 21 and maximum peak age of 73 years. Regarding age category of the patients, 69(28.6%) patients were in the ages of 45-54 years, 57(23.7%) less than 35 years, 56(23.2%) between 35-44 years and 13(5.4%) were 65 and above years. In addition, most, 197(81.7%) patients were married, 19(7.9%) widowed, 18(7.5%) single and 7(2.9%) divorced. Concerning level of education of the participants, most [137(56.8%)] of the patients had no formal education, 65(27%) were college and above, 24(10%) complete elementary (1-8) school and 15(6.2%) complete high school (9-12). Of all the participants, 126(52.3%) were private workers, 56(23.2%) government employee, 41(17%) jobless, 12(5%) students, and 6(2.5%) employed on non-governmental organizations.

### *Antihypertensive medications*

Patients were prescribed one or two or three antihypertensive medicines. The average mean number of antihypertensive medicines prescribed for patients was  $1.41\pm 0.53$  ranging from 1-3 medications per patient. From the total participants studied, enalapril was the most commonly prescribed medication in most of the patients. It was prescribed for 148(61.5%) patients and hydrochlorothiazide(HCT) was prescribed for 86(35.8%) patients (table 1).

**Table 1: Most frequently prescribed medications for HTN treatment at Ayder Comprehensive Specialized Hospital, March to June 2016**

Type of medication	Frequency	Percent
Enalapril	148	61.5
HCT	86	35.8
Nifedipine	63	26.1
Amilodipine	36	15.0
Atenolol	4	1.6
Propranolol	4	1.6
Methyldopa	1	0.4

HCT: Hydrochlorothiazide, HTN: Hypertension

*Drug therapy problem and associated factors*

A total of 357 DTPs were identified in 241 patients and the most common prevalent type of DTP identified was non adherence, which was identified in 143(40.1%) patients. Among the patients, 134(55.6%) had at least one identified DTP. From the patients having DTP, most (n=76, 56.7%) of the patients had one type of DTP and

53(39.6%) patients had identified with two DTPs. Patients having uncontrolled blood pressure were more likely to have DTP as compared to patients who had controlled BP (COR=0.567, 95 % CI=0.332-0.967, p=0.037). Therapeutic non-adherence was the most commonly identified DTP which was found to be identified in 143 (59.3%) patients (table 2).

**Table 2: DTP and types of DTPs identified at Ayder Comprehensive Specialized Hospital, March to June, 2016**

Variables		Number/patient	Percent(%)
<b>Presence of DTP</b>		<b>Patient</b>	
Yes		134	55.6
No		107	44.4
<b>Number of DTP</b>		<b>Number</b>	
One		76	56.7
Two		53	39.6
Three		4	3.0
Four		1	7.0
Total		134	100.0
<b>Type of DTP</b>		<b>Number</b>	
Adherence	Non-adherence	143	40.1
Indication	Needs additional drug therapy	61	17.1
	Unnecessary drug therapy	40	11.2
Safety	Adverse drug event	6	1.7
	Dose too high	3	0.8
Effectiveness	Dose too low	60	16.8
	Ineffective drug use	44	12.3
Total DTPs identified		357	100

DTP: Drug therapy problem, DTPs: Drug therapy problems

**The respondents' adherence was found to be affected by different factors**

We conducted bivariable logistic regression and Sub-

stance use (COR=0.449,95%CI:0.231-0.87, p=0.018) and comorbidity (COR=2.084, 95%CI:1.192-3.65, p=0.010) were significantly associated with DTP (table 3).

**Table 3: Bivariable logistic regression analysis of variables associated with presence of drug therapy problem among adult hypertensive patients in ACSH, March to June, 2016.**

Variable	Drug therapy problem		COR (95%CI), p-value
	No	Yes	
<b>Sex</b>			
Male	61(43%)	81(57%)	1
Female	42(42.4%)	57(57.6%)	0.978(0.582-1.64)p=0.934
<b>Age</b>			
≤35 year old	28(49.1%)	29(50.9%)	1
35-44	23(40.4%)	34(59.6%)	1.43(0.68-2.99)p=0.347
45-54	32(46.4%)	37(53.6)	1.12(0.553-2.25)p=0.759
55-64	17(37%)	29(63%)	1.65(0.75-3.64)p=0.217
≥65	3(27%)	9(75%)	2.897(0.710-11.87)p=0.138
<b>Marital status</b>			
Single	8(44.4%)	10(55.6%)	0.989(0.374-2.611)p=0.982
Married	87(44.2%)	110(55.8%)	1
Divorced	2(28.6%)	5(71.4%)	1.977(0.375-10.44)p=0.422
Widowed	6(31.6%)	13(68.4%)	1.71(0.63-4.69)p=0.295
<b>Residence</b>			
Urban	59(41.8%)	82(58.2%)	1
Rural	44(44%)	56(56%)	1.09(0.651-1.832)p=0.739
<b>Education level</b>			
No formal	56(40.9%)	81(59.1%)	1
Elementary (1-8)	12(50%)	12(50%)	0.691(0.29-1.65)p=0.405
High school (9-12)	7(46.7%)	8(53.3%)	0.79(0.271-2.304)p=0.666
College and above	28(43.1%)	37(56.9%)	0.914(0.503-1.66)p=0.767
<b>Occupation</b>			
Employed	27(43.5%)	35(56.5%)	1
Private worker	58(46%)	68(54%)	0.904(0.490-1.67)p=0.748
Jobless	18(34%)	35(66%)	1.5(0.703-3.207)p=0.295
<b>Family history of hypertension</b>			
No	72(42.9%)	96(57.1%)	1
Yes	31(42.5%)	42(57.5%)	0.984(0.565-1.72)p=0.955
<b>HTN duration in years</b>			
≤5	65(44.5%)	81(55.5%)	1
6-10	25(43.9%)	32(56.1%)	1.027(0.554-1.903)p=0.932
11-15	6(37.5%)	10(62.5%)	1.337(0.462-3.874)p=0.592
16-20	7(31.8%)	15(68.2%)	1.72(0.662-4.467)p=0.266
<b>Salt intake</b>			
No	45(45%)	55(55%)	1
Yes	58(41.1%)	83(58.9%)	0.854(0.509-1.433)p=0.550
<b>Physical activity</b>			
Physically inactive	101(43.7%)	130(56.3%)	1
Physically active	2(20%)	8(80%)	0.322(0.067-1.55)p=0.157
<b>Substance use</b>			
No	88(46%)	100(53.2%)	1
Yes	15(28.3%)	38(71.7%)	0.449(0.231-0.87)p=0.018*
<b>Mode of medication intake</b>			
Free	34(37.8%)	56(62.2%)	1
Paid	69(45.7%)	82(54.3%)	0.722(0.423-1.230)p=0.230
<b>Number antihypertensive medication</b>			
Monotherapy	57(38.8%)	90(61.2%)	1
≥ two medications	46(48.9%)	48(51.1%)	0.661(0.392-1.12)p=0.121
<b>Comorbidity</b>			
No	77(48.7%)	81(51.3%)	1
Yes	26(31.3%)	57(68.7%)	2.084(1.192-3.65)p=0.010*

\*: p value<0.05, 1: Reference, COR: Crude odds ratio, CI: Confidence interval

Multivariable logistic regression was employed to identify the predictors of drug therapy problem. The analysis model explains 52.3% ( $R^2=0.523$ ,  $p=0.002$ ) of the DTP variability of the response data confined around its mean. Two variables (substance use and comorbidity) were significantly associated with DTP in the bivariable logistic regression and after we conducted multivariable logistic regression, substance use (AOR=0.445, 95% CI=

0.227-0.870,  $p=0.018$ ) and comorbidity (AOR= 2.099, 95% CI= 1.192-3.694,  $p=0.010$ ) were found to be the predictors of DTP. Patients who reported substance use were less likely to have DTP than patients who did not use substance. Moreover, patients who had evidence of comorbidity were 2 times more likely to have DTP than patients who did not have evidence of comorbidity (table 4).

**Table 4: Multivariable logistic regression analysis of variables associated with presence of drug therapy problem among adult hypertensive patients in ACSH, March to June, 2016.**

Variable	Drug therapy problem		COR (95%CI)p-value	AOR(95%CI), p-value
	No	Yes		
<b>Substance use</b>				
No	88(46%)	100(53.2%)	1	1
Yes	15(28.3%)	38(71.7%)	0.449(0.231-0.87)p=0.018*	0.445(0.227-0.870)p=0.018*
<b>Comorbidity</b>				
No	77(48.7%)	81(51.3%)	1	1
Yes	26(31.3%)	57(68.7%)	2.084(1.192-3.65)p=0.010*	2.099(1.192-3.694)p=0.010*

\*:  $p$  value<0.05, 1: Reference, COR: crude odds ratio, AOR: Adjusted odds ratio, CI: Confidence interval

## Discussion

The prevalence of DTP identified in this study was accounted to be 55.6%. This is not consistent with the study done in Felege Hiwot Referral Hospital, South west Ethiopia. There were 357 numbers of DTPs, on the other hand, a less number of DTPs (105) was found in the study done in Felege Hiwot referral Hospital.<sup>24,25</sup> This might be due to the fact that the study in Felege Hiwot Referral Hospital enrolled and studied small number of medical patients. The mean number of DTP was  $1.48 \pm 0.597$  which is comparable with the findings reported in Jimma which was  $1.8 \pm 0.8$ .<sup>25</sup>

The most common DTP identified was non-adherence which was identified in 143(59.3%) of the patients. This result is consistent with the study conducted in Southern Kivu province of the Democratic Republic Congo and Ghana.<sup>26,27</sup> However, this was incongruent with the study done in Mexico which found a non-adherence prevalence of 42.8%.<sup>28</sup> A study conducted in Southern Kivu of DRC showed that 86.4% of hypertensive patients were non-adherence which is not in lined with this study.<sup>20</sup> This difference may be due to uncertainty or lack of knowledge about the aim or function of the drug, economic is-

sue and long duration of therapy. The result in this study found DTP which was dose too high (1.2%) which is not in line with the result of research done in China which was (19.1%).<sup>29</sup> This difference may be due to frequent administration of the antihypertensive medications.

Adverse drug events were occurred in 1.7% of the patients studied. This is not in line with research done in Sweden and in India which showed a prevalence of adverse drug event to be 25.7% and 10% respectively.<sup>30,31</sup> This may be because of difference in patient knowledge on which drug is the cause for adverse effect occurred, poor documentation and poor habit of adverse drug event report by patients.

Of the total type of DTPs, 11.2% was unnecessary drug therapy. This is not in line with findings from India which reported a prevalence of unnecessary drug therapy to be 16.7%. Moreover, dose related problems (25.9%) followed by need for additional drugs (25%) in this study are not in line with the study done in India which were 35.1% and 19.7% respectively.<sup>25,32</sup> A study conducted in South America, Brazil on the existence of DTPs showed that 44% was dosage too low which is not in line with this study which found dosage too low to be 16.8%.<sup>33</sup>

A study conducted in China regarding drug related problems found that, 24.1% were ineffective indication which is not in line with this study which described a prevalence of ineffective indication to be 12.3%.<sup>29</sup> This may be because of prescribing errors. In this study we also found that substance use and comorbidity were the predictors of DTP.

This study has some flaws and limitations. First because some data were collected through interview there might be recall bias especially during antihypertensive medication adherence status assessment. Second the effect of DTP on outcome of hypertension was not studied. Thirdly the identified DTPs were not intervened. Fourth some six seriously ill patients were excluded from the study thus this might affect the finding of the study.

### Conclusion

More than half of the patients studied had identified with at least one DTP. Non-adherence to antihypertensive medications was the most commonly identified DTP. Thus efforts that boost antihypertensive compliance should be adopted to solve drug related problem of hypertensive patients.

### List of abbreviations

ACSH: Ayder Comprehensive Specialized Hospital  
AMI: Acute Myocardial Infarction  
AOR: Adjusted Odds Ratio  
BP: Blood Pressure  
CHD: Congestive Heart Disease  
CHF: Congestive Heart Failure  
CI: Confidence Interval  
COR: Crude Odds Ratio  
DBP: Diastolic Blood Pressure  
DTP: Drug Therapy Problem  
DTPs: Drug Therapy Problems  
HCT: Hydrochlorothiazide  
HTN: Hypertension  
JNC-8: Eighth Joint National Committee  
PVD: Peripheral Vascular Disease  
SBP: Systolic Blood Pressure  
SPSS: Statistical Package for Social Science

### Declarations

#### Ethical approval and consent to participate

The study was approved by the Institutional Review Board of College of Health Sciences, Mekelle University.

Permission was also offered from ACSH to conduct the study. Informed oral consent was obtained from all patients.

### Consent to publish

Not applicable.

### Availability of data and materials

All relevant data are within the paper and its supporting information files.

### Disclosure statement

The authors declare that they have no competing interest to disclose.

### Funding

The authors received no specific funding for this work.

### Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agree to be accountable for all aspects of the work.

### Authors' information

SW, YL, TD and TM are a clinical pharmacists and lecturers at Mekelle University. TF is an assistant lecturer at Mekelle University. GW is a pharmacist.

### Acknowledgements

We would like to acknowledge the study participants and data collectors. We would also like to acknowledge Mekelle University for allowing us to conduct the study. Our deepest gratitude also goes to Ayder Comprehensive Specialized Hospital staff that helped us in collecting data.

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