Research Article

Assessment of Drug Therapy Problems and Contributing Factors among Adult Ambulatory Hypertensive Patients in Ayder Referral Hospital, Mekelle Northern Ethiopia

Werkya Mahammedsied[1], Mamo Feyissa[2]*, Workineh Shibeshi[2]

[1]Department of Pharmacy, Ayder Referral Hospital, Mekelle, Northern Ethiopia; [2]Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia

ABSTRACT

Background: Use of multiple medications to achieve target blood pressure among hypertensive patients makes them at high risk of drug therapy problems. This study is aimed to assess the magnitude of DTPs and contributing factors among adult ambulatory hypertensive patients in Ayder Referral Hospital.

Method: Institution based cross-sectional study was conducted to assess the DTPs among hypertensive patients on regular clinic follow-up. Data were collected by reviewing the patient medical records and patient interview using a structured data abstraction format. Descriptive statistics such as mean and percentage were used and data were presented as tables and figures. Logistic and multivariate regressions analysis was performed to identify factors related to DTPs using SPSS version 25.

Result: A total of 277 DTPs were identified from 203 (52.8%) study participants. The average DTPs per patient was 1.36 and at least one DTP was identified from 133 (65.5%) patients, 2 DTPs in 66 (32.5%) patients and 3 DTPs in 4 (1.97%) patients. Unnecessary drug therapy was the leading DTP 90 (32.5%) followed by needing additional drug therapy 69 (24.9%), dose too high 63 (22.7%) and ineffective drug therapy 33 (11.9%). Among antihypertensive medications, ACEIs were the most frequently associated with DTPs. The total number of medications taken by the patient was an important predictor of occurrence of DTP.

Conclusion: The prevalence of DTPs among ambulatory hypertensive patients was high in Ayder Referral Hospital. The most commonly identified DTPs were related to indication and safety of drug therapy.

Keywords: Drug therapy problems; Hypertension; Ambulatory; Mekelle; Ethiopia

Abbreviations: ACEI: Angiotensin Converting Enzyme Inhibitors; ADR: Adverse Drug Reaction; ARH: Ayder Referral Hospital; BP: Blood Pressure; CCB: Calcium Channel Blockers; DTP: Drug Therapy Problem; WHO: World Health Organization

INTRODUCTION

Hypertension is persistently elevated systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg [1-3]. It is a global health challenge because of its high prevalence and consequential risk of cardiovascular disease, stroke, kidney failure and premature mortality and disability [2]. It disproportionately affects populations in low- and middle-income countries where health systems are weak. According to world health organization (WHO) estimate 1.13 billion people worldwide have hypertension, two-thirds of them are living in low- and middle-income countries [4]. In Ethiopia, the overall prevalence of hypertension is estimated to be 19.6% in all adults greater 18 years old and 41.9% in elderly with age ≥ 50 [5,6].

For optimal BP control, use of combinations of antihypertensive medications is required. Furthermore, the presence of compelling indications and other comorbidities further complicate the management of hypertension [3,7]. This use of multiple medication therapy makes in hypertensive patients prone to drug therapy problems (DTPs). A DTP is an undesirable event, a patient experience that involves, or is suspected to involve drug therapy,

and that actually or potentially, interferes with a desired patient outcome [8].

DTPs are very common in patients with cardiovascular disease including hypertension as reported by studies in different countries. In Malaysia and Jordan, the studies revealed an average of 2.15 and 6.31 DTPs per patient respectively [9,10]. In Africa, the mean DTP per patient of 1.46 at the fourth month drug therapy was reported in Nigeria [11]. Similar studies in Ethiopia reported at least one DTP in 60.65%, 71% and 80.7% of hypertensive patients in Hiwot Fana, Dil-Chora and Adama General Hospitals respectively [12-14]. The average DTP per patient of 1.39 and 1.32 were also identified in Dil-Chora and Ambo General Hospitals respectively [13,15]. The most common types of DTPs revealed by several studies were need additional drug therapy, unnecessary drug therapy, non-adherence and drug interactions [10,13-16]. Presence of comorbidity, age of patients, polypharmacy, and uncontrolled blood pressure (BP) were factors associated with DTPs [13,17,18].

The DTPs significantly affect the patients' health outcomes and achievement of treatment goal. DTPs in hypertensive patients lead to poor control of BP [10], reduced hearth related quality of life [19], and increase the risk of morbidity and mortality [8,14,20]. In addition, DTPs are the dominant reason for hospital admission and emergency department visits [21]. However, majority of DRPs are preventable [22]. Hence, identifying and resolving DTPs is vital to help patients achieve treatment goals and ensure the best outcomes from drug therapy. The standard approach for identification, classification and resolution of identified DTPs are followed to make rational clinical decision. This is made by sequential assessment of an indication, effectiveness, dosing and safety profile of the product as well as adherence to medication [8]. Involvement of clinical pharmacists in direct patient care has significantly improved treatment outcomes through the identification and resolution of DTPs [23].

Considerable concern should be given for identification and resolution of DTPs in every health facilities since DTPs significantly affect the control of BP, morbidity and mortality, and health related quality of life among hypertensive patients. In addition, for planning interventional strategies to prevent and resolve DTPs, identification of contributing factors is paramount important. However, there is no studies that assessed the magnitude and contributing factors for DTPs in Ayder Referral hospital. Therefore, this study is aimed to assess the prevalence of DTPs and contributing factors among adult ambulatory hypertensive patients in Ayder Referral Hospital, Mekelle, Northern Ethiopia.

RESEARCH METHODOLOGY

Study setting

This study was conducted in Ayder Referral Hospital located in Mekelle, the capital city of Tigray region, northern Ethiopia with 500 inpatient beds and serving up to 8 million populations in its catchment area. Medical referral clinic is one of the specialty units of the hospital which provides medical services for hypertensive patients as ambulatory care and follow up. The clinic contains three nurses and two residents. Based on the appointment chart about 256 patients per month or about 64 per week were getting services in the clinic.

Study design

Institution based cross-sectional study design was conducted.

Study population

All ambulatory hypertensive patients on chronic follow up in in medical clinic of Ayder referral hospital were source population. Hypertensive patients receiving antihypertensive medications for at least 6 months, age ≥ 18 years, and who are willing and able to participate in the study were included. Patients seriously ill and unable to be interviewed and with incomplete date om medical records were excluded.

Sample size and sampling technique

Sample size was computed based on single population proportion formula by using the following Assumption of proportion (P) of 50% (P=0.5) to get possible large sample size, confidence level of 95% chosen, margin of error (d) = 5%. According a total of 384 samples of participants were needed in this study despite the large population. All hypertensive patients who came for regular visit during the study period and meet the eligibility criteria were included until the required sample size was reached.

Study variables

The dependent variable is occurrence of drug therapy problems. Independent variables for this study include socio demographic characteristics of patients (age, gender, level of education, residence and marital status, physical activities, smoking, alcohol use and use of traditional medicine) and clinical and treatment characteristics (duration of therapy, number of prescribed drugs, comorbid conditions, hospitalization, presence of complications).

Data collection procedure

The data were collected for the period of three months from July 15/ 2017 to October 15 /2017. The retrospective medication prescribing practice was assessed from patient's medical chart review. One-year data was reviewed starting from date of data collection. Data from medical record review included patient medical history, medication history, prescribed medications with their indication, dosage regimen, documented ADR and pertinent laboratory values.

In addition, face to face interview from participants was conducted to collect data on the medication adherence using structured and pretested questionnaire prepared in English, which was translated into Tigrigna (local language), then back translation to English to check the consistency. The interview questionnaire contained questions on the socio demographic characteristics, clinical characteristics and medication use behavior of patients.

Identification of drug therapy problems

After the data was collected, the principal investigators had evaluated ordered medications for appropriateness, effectiveness and safety to identify whether drug related problems were occurred. The standard references for treatment and the patient's characteristics were considered in evaluating of medications. The standard references that were used include JNC 8 Guidelines for the Management of Hypertension in Adults [3], National standard treatment guideline [1], Up-to-date version 21.2 and Micromedex with thorough consideration of patient and medicine related issues. Identified DTPs were classified using broadly accepted and standard DTPs classification system [8].

Data analysis

Descriptive statistics including mean and standard deviation for continuous variables and frequency and percentage for categorical data were used to summarize socio-demographic and relevant clinical characteristics of the study participants using SPSS version 25. A test of association was done using multiple linear regressions while P value < 0.05 was considered significant.

Ethical considerations

The ethical approval was secured from the ethical review board of school of pharmacy, Addis Ababa University tom conduct this study. Ayder Referral Hospital, department of internal medicine also provided letter of cooperation to start data collection. In addition, verbal informed consent from patients was obtained before engaging participants in the study for interview and review of the medical records. Dignity and autonomy of patients were kept safely throughout the study. All patient identifiers were excluded and all filled questionnaires were kept in privacy for access to authorized persons only.

RESULTS

Socio-demographic and clinical characteristics of study participants

A total of 384 participants were included in this study. Majority of the participants were females 227 (59.1%), married 253 (65.9%), orthodox followers 356 (92.7%), age group of 36 - 59 years 204 (53.1%), and average age being 56.7 years. Regarding health-related behaviors, 323 (84.1%) patients had coffee drinking habit, 186 (48.4%) were alcohol consumers, 375 (97.7%) were non-smokers, 266 (69.3%) do regular physical activity and 162 (42.2%) of participants use traditional medicine.

Clinically the participants mean duration on hypertension since diagnosis and antihypertensive treatment were 2 ± 0.885 years 1.9 ± 0.813 years respectively. About half of the study participants 185 (48.2%) had history of hospitalization, have at least one co-morbidity 165 (48.7%) and receiving two drugs daily 202 (52.6%). The comorbidities among the study participants were diabetes mellitus 37 (22.4%), hypertensive heart disease 34 (20.6%), asthma 33 (20%), dyslipidemia 28 (17%), chronic kidney disease 18 (10.9%), rheumatoid arthritis 10 (6.1%) and others (HIV, hepatitis and schizophrenia) 5 (3%). the detailed sociodemographic and clinical characteristics of study participants are described in Table 1.

Medication prescribing practice

The most frequently prescribed drugs were combinations of diuretics and ACEI 87 (22.7%) followed by diuretics alone 75 (19.6). The percentage of classes of drugs prescribed in the study participants is shown in the following Figure 1.

Types and causes of drug therapy problems identified

A total of 277 drug therapy problems were identified from 203 (52.9%) study participants with average of 1.36 DTPs per patient. Regarding the number of DTP in specific patient, one DTP was identified in 133 (65.5%) patients, whereas two and three DTPs were identified in 66 (32.5%) and 4 (1.97%) patients respectively.

Unnecessary drug therapy was the leading DTP 90 (32.5%) followed

Table 1: Socio-demographic and clinical characteristics of study participants ARH Mekelle, Northern Ethiopia (n=384).

Variables	Characteristics	Frequency n (%)	Mean ± SD
Gender	Male	157 (40.9)	
	Female	227 (59.1)	
Age group	≤ 35	16 (4.2)	
	36-59	204 (53.1)	
	≥ 60	164 (42.7)	
Marital status	Single	3 (0.8)	
	Married	253 (65.9)	
	Widowed	115 (29.9)	
	Divorced	13 (3.4)	
Educational status	Illiterate	175 (45.6)	
	Primary school	107 (27.9)	
	Secondary School	59 (15.4)	
	Graduates of College & above	43 (11.2)	
Religion	Orthodox	356 (92.7)	
	Muslim	22 (5.7)	
	Catholic	4 (1)	
	Protestant	2 (0.5)	
Residence	Urban	311 (81)	
	Rural	73 (19)	
Hospitalization	No	199 (51.8)	
	Once	113 (29.4)	
	Twice	49 (12.8)	1.52 ± 0.5
	Three times and above	23 (5.7)	
Co-morbidity	Yes	165 (43)	
	No	219 (57)	
Complication	Yes	66 (17.2)	
	No	318 (82.8)	
Duration of hypertension	1 – 5 years	310 (80.7)	
	6 - 10 years	54 (14.1)	
	11 - 15 years	8 (2.1)	2 ± 0.885
	>15 years	12 (3.1)	
Duration of therapy	1 - 5 years	206 (84.6)	
	6-10 years	46 (12)	
	11-15 years	5 (1.3)	1.9 ± 0.813
	>15 years	8 (2.1)	
Total number of medications	≤ 2	167 (43.5)	
	3-4	122 (31.8)	
	>4	95 (24.7)	

by needing additional drug therapy 69 (24.9%), dose too high 63 (22.7%) and ineffective drug therapy 33 (11.9%). Non- adherence to prescribed medication was identified in 125 (32.6%) of participants of which 72 (18.8%) had medium non-adherence and 53 (13.8%) had poor adherence. There mentioned major reasons for non-adherence were forgetfulness and none affordability of prescribed medications. Among the study participants, 64 (16.7%) had developed medication related side effects which are possible adverse drug reactions. Table 2 shows types and major causes of DTPs among ambulatory hypertensive patients in Ayder referral Hospital.

Drugs involved in drug therapy problems

A total of 67 drugs were involved in different types of DTPs, the most frequent drug classes involved being ACEI (27.1%) followed by CCB (16.96%) and diuretics (13.7%). Figure 2 detailed the classes of drugs associated with DTP.

Factors associated with the occurrence of drug therapy problems

All independent variables were analyzed in multiple regression analysis to identify the independent factors related with occurrence of DTPs. The average number of drugs taken by the patient was the only factor which was significantly associated with the occurrence of DTPs. Patients who take two medicines 2.223 (1.082,4.566 *P=0.03*) and four medicines 2.572 (1.062,6.229 *P=0.036*) daily are have significantly at higher risk of developing DTPs as compared to patients who take monotherapy. All other independent variables such as age, sex, chat chewing, smoking, use of traditional medicine hospitalization, duration of therapy and co-morbidities were not significantly associated with occurrence of DTP (Table 3).

DISCUSSION

Detecting and resolving as well as preventing drug-related problems is vital to ensure rational medication use which optimizes the therapeutic benefits and minimize the possible adverse effect from medications. In this study more than half 52.9% of the hypertensive patients treated at Ayder referral hospital. Our finding lower than the prevalence least one DTP in 80.7% hypertensive patients reported in Adama General Hospital and 82% in hypertensive patients with co-morbid diabetic patients in Jimma [14,17]. Our finding of mean number of 1.36 of DTPs per patient is consistent with the findings in Ethiopia which reported mean number of DTPs per patient of 1.32, 1.38, 1.39 in Ambo general hospital, Felege Hiwot Referral Hospital and Dil-Chora Referral Hospital respectively [13,15,24]. However, is lower than the mean number of DPTs 1.8 per patients reported in Hiwot Fana Comprehensive Hospital [16]. The variation seen on magnitude of DRPs across studies might be due to differences in classification of DRPs, the settings in which DRPs were assessed and the size of the study population and duration of study period. For instance, in our study the non-adherence was assessed separately and was not counted under DTP and only hypertensive patients were included.
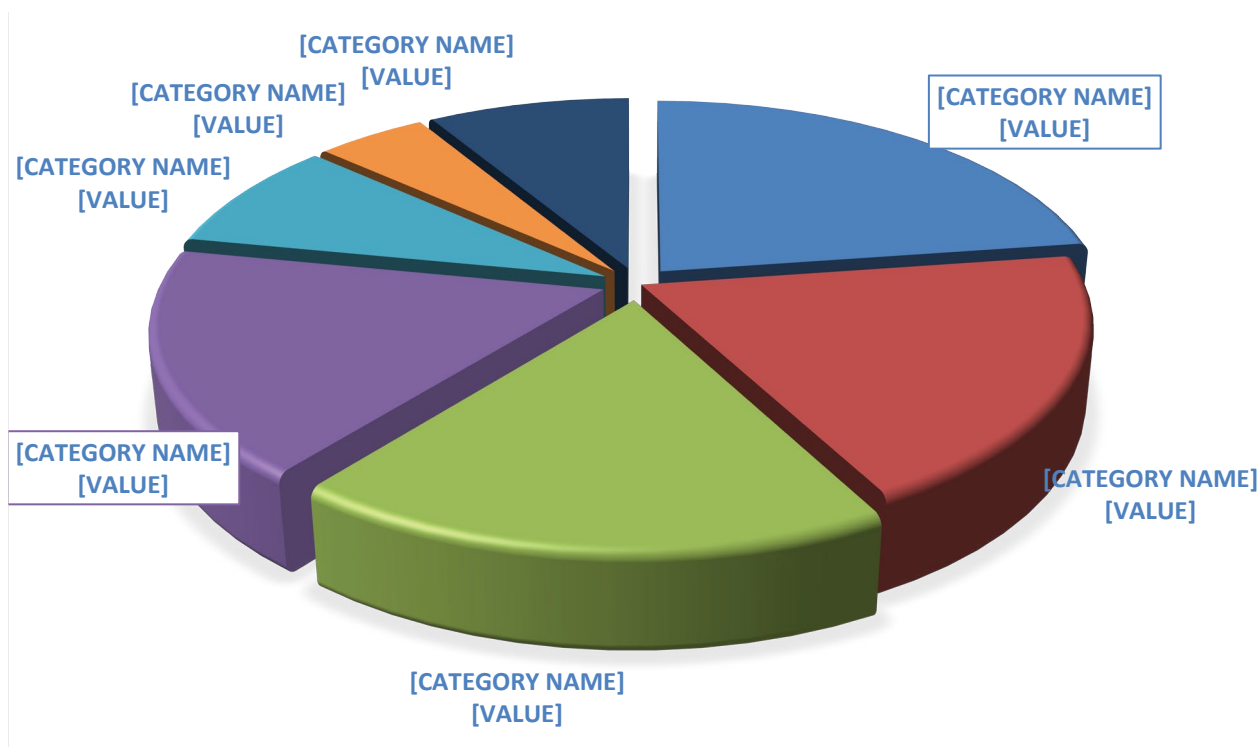

Figure 1: Percentage of classes of drugs prescribed for the study population ARH, Mekelle Northern Ethiopia.

Table 2: Types of drug therapy Problems identified and causes among ambulatory hypertensive patients ARH, Mekelle, Northern Ethiopia.

Class of DTPs	Cause of DTPs	Frequency n (%)	
		No. of DTPs	Total DTPs in the Category
Unnecessary drug therapy	No medical indication	32	90 (32.49)
	Duplicate therapy	40	
	Non drug therapy indicated	18	
Needs additional drug therapy	Untreated medical condition	69	69 (24.91)
Ineffective drug therapy	More effective alternative is available	33	33 (11.91)
Dose too low	Wrong dose	22	22 (7.94)
Dose too high	Wrong dose	47	63 (22.74)
	Frequency inappropriate	13	
	Drug interaction	3	
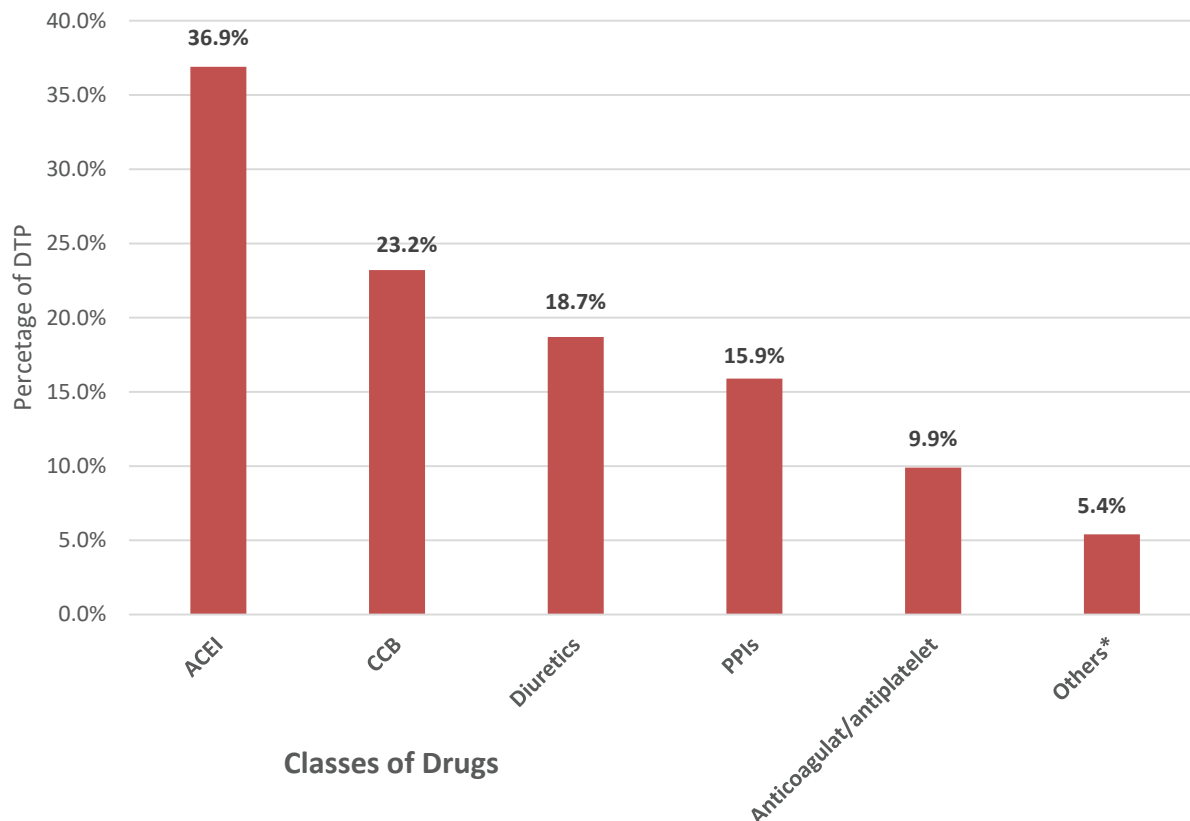
Abbreviations: ACEI: Angiotensin Converting Enzyme Inhibitors, CCB: Calcium Channel Blockers, PPIs: Proton Pump Inhibitors and Others* Antibiotics, analgesics, anticoagulants, minerals and vitamins.

Figure 2: Classes of drugs involved with DTPs among ambulatory hypertensive patients in ARH, Mekelle, Northern Ethiopia.

Table 3: Associations between socio demographic and Clinical characteristics with DTPs among ambulatory hypertensive patients in ARH, Mekelle, Northern Ethiopia.

Predictors		n (%)	COR (95%CI)	AOR (95%CI)	P value
Age category	<35	16 (4.2)	(1)	(1)	(1)
	36-59	204 (53.1)	0.429 (1.44,1.277,)	0.375 (0.119,1.176)	0.093
	>60	164 (42.7)	0.595 (1.98,1.791)	0.475 (0.1481.524)	0.211
Residence	Urban	311 (81)	(1)	(1)	(1)
	Rural	73 (19.0)	1.556 (0.924,2.622)	1.377 (0.800, 2.368)	0.248
Smoking	Yes	5 (1.3)	0.215 (0.45, 1.027)	0.248 (0.05, 1.236)	0.089
	No	379 (98.7)	(1)	(1)	(1)
No of Medications	One	71 (18.5)	(1)	(1)	(1)
	Two	123 (32)	2.598 (1.419, 4.756)	2.223 (1.082,4.566)	0.030*
	Three	95 (24.7)	2.225 (1.182, 4.189)	2.162 (0.962,4.858)	0.062
	Four	70 (18.2)	2.601 (1.317, 5.138)	2.572 (1.062,6.229)	0.036*
	>four	25 (6.5)	1.993 (0.972, 5.019)	2.029 (0.651,6.327)	0.223
Presence of comorbidity	Yes	187 (48.7)	0.887 (0.594, 1.325)	0.621 (0.377,1.023)	0.61
	No	197 (51.3)	(1)	(1)	(1)
No of anti-hypertensives	One	161 (41.9)	(1)	(1)	(1)
	Two	202 (52.6)	1.942	1.475 (0.887, 2.454)	0.134
	Three	21 (5.5)	1.733	1.336 (0.488, 3.659)	0.573

In our study the majority of DTPs were related to indication of therapy (unnecessary drug therapy 32.5% and needs additional drug therapy 24.9%) followed by safety (dose too high 22.7%). Similarly, in several studies the most common DTPs identified were related to indication of treatment [11,13,15-17,24]. However, the most common DTPs identified was drug interaction among hypertensive patients in Adama General Hospital, cardiovascular patients India tertiary Hospital and hypertensive patients in Malaysia [9,14,25]. This difference could be the variation in the underlying co-morbid conditions, study setting and number and type of prescribed medications.

In the present study number of medicines was the only factor significantly associated with occurrence of DTPs among hypertensive patients. Our finding is in line with the study by Gelchu and Abdella

in Hiwot Fana Hospital which reported multiple drug use as the only predictor of DTP [12]. Use of multiple drugs is also reported by other studies as independent predictor of DTP [13,18]. Unlike our study finding, other studies identified sex, age and the presence of comorbidity and uncontrolled BP as significantly associated with the occurrence of DTPs [13,17]. The variations among studies could be related with difference in participants sociodemographic and clinical conditions, clinical setting of study and number and type of medications used.

Among our study participants 32.6% reported non-adherence to their medications due to forgetfulness and unaffordability of medicines. This is consistent Hussen and Bekele study report of non-adherence to antihypertensive agents accounting 32.8% of all DTPs; forgetfulness being a major reason [13]. However, non-adherence is higher the finding of Belayneh et al., 19.5% and dosage too low [26]. This variation might be due to the difference in study design and study setting, where the study by, was prospective in design unlike our study which is retrospective and conducted on inpatient medical wards setting [26].

LIMITATIONS OF THE STUDY

Despite the fact that the study was conducted on relatively large sample size, and covers the outpatient settings, which is an area that has limited literature compared to inpatient settings the following limitations could be considered; being study conducted on single public hospital, use of retrospective study design and inability of make all the necessary intervention since the data was retrospective.

CONCLUSION AND RECOMMENDATIONS

The prevalence of DTPs among ambulatory hypertensive patients was found to be high in Ayder Referral Hospital. The most commonly identified DTPs were related to indication and safety of drug therapy. ACEIs were the most frequent drugs involved in DTPs. The number of drugs taken by the patient was an important predictor of DTPs. Therefore, the hospital management and health care providers should adhere to treatment protocols to improve the appropriate medication. In addition, optimal interventions should be taken to improve adherence of the patients. Involving of clinical pharmacists in direct patient care is the one highly recommended to reduce DTPs and optimize hypertensive patients' care.

AUTHORS' CONTRIBUTIONS

WM generated the idea, designed and conducted data collection; analyzed and interpreted the results. MF involved in supervision of the research and prepared the draft manuscript. WS involved in primary supervision of the study. All authors stated that they have complete access to study data that support the publication.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

ACKNOWLEDGEMENT

REFERENCES

1. FMHACA. Standard Treatment Guidelines For General Hospital. 2014.

2. WHO. Global Brief on Hypertension: Silent Killer, Global Public Health Crisis. Indian Journal of Physical Medicine and Rehabilitation. 2013.

3. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. Evidence-Based Guideline for the Management of High Blood Pressure in Adults Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014;311(5):507-520.

4. World Health Organization. WHO | Hypertension. 2019.

5. Kibret K, Mesfin YM. Prevalence of hypertension in Ethiopia: A systematic meta-analysis. Public Health Rev. 2015;36:14.

6. Shukuri A, Tewelde T, Shaweno T. Prevalence of old age hypertension and associated factors among older adults in rural Ethiopia. Integr Blood Press Control. 2019;12:23-31.

7. Williams B, Spiering W, Azizi M, Burnier M, Rosei EA, Coca A. ESC/ESH Guidelines for the Management of arterial Hypertension. Eur Heart J. 2018;39(33):3021-3104.

8. Cipolle RJ, Strand LM, Morley PC. Pharmaceutical Care Practice: The Patient?Centered Approach to Medication Management Services. 2012.

9. Redzuan A, Ramli A, Pheng M. Drug-Related Problems in Hypertensive Patients with Multiple Comorbidities. J Pharm Res. 2017;1(3):000113.

10. Farha RA, Basheti I, Al Ruz HA, Alsaleh A, AbuRuz S. Assessment of drug-related problems and their impact on blood pressure control in patients with hypertension. Eur J Hosp Pharm. 2016;23(3):126-130.

11. Ganiyu KA, Suleiman IA, Erah PO. Drug therapy problems in patients on antihypertensives and antidiabetic drugs in two tertiary Health Institutions in Niger Delta Region, Nigeria. J Pharm Allied Sci. 2014;11:1986-1995.

12. Gelchu T, Abdela J. Drug therapy problems among patients with cardiovascular disease admitted to the medical ward and had a follow-up at the ambulatory clinic of Hiwot Fana Specialized University Hospital: The case of a tertiary hospital in eastern Ethiopia. SAGE Open Med. 2019;7:205031211986040.

13. Hussen A, Bekele FD. Drug therapy problems and their predictors among hypertensive patients on follow up in Dil-Chora Referral Hospital, Dire-Dawa, Ethiopia. Int J Pharm Sci Res. 2017;8(6):2712-2719.

14. Hussein M, Lenjisa JL, Woldu MA, Tegegne GT, Umeta GT, Dins H, et al. Assessment of drug related problems among hypertensive patients on follow up in Adama Hospital Medical College, East Ethiopia. Clin Pharmacol Biopharm. 2014;3(2):2-7.

15. Tegegne GT, Gaddisa T, Kefale B, Tesfaye G, Likisa J, Albachew M, et al. Drug therapy problem and contributing factors among ambulatory hypertensive patients in Ambo General Hospital, West Shoa, Ethiopia. 2015;15(4).

16. Ayele Y, Melaku K, Dechasa M, Ayalew MB, Horsa BA. Assessment of drug related problems among type 2 diabetes mellitus patients with hypertension in Hiwot Fana Specialized University Hospital, Harar, Eastern Ethiopia. BMC Res Notes. 2018;11(1):1-5.

17. Yimama M, Jarso H, Desse TA. Determinants of drug-related problems among ambulatory type 2 diabetes patients with hypertension comorbidity in Southwest Ethiopia: A prospective cross sectional study 11 Medical and Health Sciences 1103 Clinical Sciences. BMC Res Notes. 2018;11(679):1-6.

18. Zazuli Z, Rohaya A, Adnyana IK. Drug-related problems in Type 2 diabetic patients with hypertension in Cimahi, West Java, Indonesia: A prospective study. Int J Green Pharm. 2017;11(2):S298-S304.

19. Farha Rab, Saleh Ua, Aburuz S. The impact of drug related problems on health-related quality of life among hypertensive patients in Jordan. 2017;15(3):995.

20. Fernández-Llimós F, Tuneu L, Baena MI, Faus MJ. Morbidity and mortality associated with pharmacotherapy: Evolution and current concept of drug-related problems. Curr Pharm Des. 2004;10:3947-3967.

21. Baena MI, Faus MJ, Fajardo PC, Luque FM, Sierra F, Andres JM, et al. Medicine-related problems resulting in emergency department visits. Eur J Clin Pharmacol. 2006;62:387-393.

22. Al-arifi M, Abu-hashem H, Al-meziny M, Said R, Aljadhey H. Emergency department visits and admissions due to drug related problems at Riyadh military hospital (RMH), Saudi Arabia. Saudi Pharm J. 2014;22(1):17-25.

23. Reis WCT, Scopel CT, Correr CJ, Andrzejevski VMS. Analysis of clinical pharmacist interventions in a tertiary teaching hospital in Brazil Análise das intervenções de farmacêuticos clínicos em um hospital de ensino terciário do Brasil. Einstein. 2013;11(2):190-196.

24. Tegegne GT, Yimam B, Yesuf EA, Gelaw BK, Defersha D. Drug therapy problem among patients with cardiovascular diseases in Felege Hiwot Hospital. Int J Pharm Teach Pract. 2014;5(3):989-996.

25. Shareef J, Sandeep B. Drug-Related Problems in Hypertensive Patients with Multiple Comorbidities. J Pharm Care. 2014;2(2):70-76.

26. Belayneh YM, Amberbir G, Agalu A. A prospective observational study of drug therapy problems in medical ward of a referral hospital in northeast Ethiopia. BMC Health Serv Res. 2018;18:808.