

Assessment of Drug Therapy Problems and Cardiovascular Disease Risk among Adult Hypertensive Patients at All Africa Leprosy and Tuberculosis Rehabilitation and Training Centre, Addis Ababa, Ethiopia

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This is to certify that the thesis prepared by Miftah Shafi, entitled “*Assessment of Drug Therapy Problems and Cardiovascular Disease Risk among Adult Hypertensive Patients at All Africa Leprosy and Tuberculosis Rehabilitation and Training Centre, Addis Ababa, Ethiopia*” and submitted in partial fulfillment of the requirements for the Degree of Master of Sciences in Pharmacy Practice complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

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Abstract

Assessment of drug therapy problems and cardiovascular disease risk among adult hypertensive patients at All Africa Leprosy and Tuberculosis Rehabilitation and Training Centre, Addis Ababa, Ethiopia

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Hypertensive patients are at high risk of developing drug therapy problems (DTPs) and poor adherence due to different factors like: presence of comorbidities, polypharmacy and complexity of drug regimens. Occurrences of DTPs in hypertensive patients are associated with harmful health outcomes and unnecessary costs. Identifying types of DTPs and associated factors are very essential in DTPs prevention and reducing unnecessary health expenditures. Rise in each systolic blood pressure 20 millimeters of mercury and 10 mmHg diastolic blood pressure is associated with increasing risk of death from stroke and heart disease. This study was aimed to assess DTPs and cardiovascular disease risk among hypertensive patients on follow up at All Africa Leprosy and Tuberculosis Rehabilitation and Training Centre. A hospital based cross sectional study was conducted among 305 hypertensive patients. Data was collected through patient interview and medical charts review. DTPs were assessed based on Cipolle DTPs classification systems and cardiovascular disease risk was calculated by using American Heart Association pooled cohort Cardiovascular Risk Calculator. Descriptive statistics, binary logistic regressions were utilized and $P < 0.05$ was used to declare statistical significance. Out of 305 study participants, 223(73.1%) had at least one DTP. The commonest identified DTP was needs additional drug therapy (32.1%) followed by drug interaction (25.8%) and dosage too low (12.3%). Nonadherence was identified in 51.5% of study participants. The atherosclerotic cardiovascular disease (ASCVD) risk among 144 patients who had lipid profile was calculated and 40.3% of them had 20% or higher risk. Based on multivariate analysis alcohol use, number of medications and blood pressure (BP) control had association with DTPs occurrence whereas physical activity, salt restriction and duration of treatment had significant association with adherence. Occupation, alcohol use and BP control were statistically significant to ASCVD risk of 20% or higher.

Key word: Hypertension, Drug therapy problems, Cardiovascular disease risk, Ethiopia

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List of Abbreviations and Acronyms

ACEIs	Angiotensin Converting Enzyme Inhibitors
ADRs	Adverse Drug Reactions
AHA	American Heart Association
ALERT	All Africa Leprosy and Tuberculosis Rehabilitation and Training Centre
AOR	Adjusted Odds Ratio
ASCVD	Atherosclerotic Cardiovascular Disease
BP	Blood Pressure
CCB	Calcium Channel Blockers
COR	Crude Odds Ratio
CVD	Cardio -Vascular Disease
DBP	Diastolic Blood Pressure
DI	Drug Interaction
DM	Diabetes Mellitus
DRPs	Drug Related Problems
DTPs	Drug Therapy Problems
ESC	European Society of Cardiology
HCT	Hydrochlorothiazide
mmHg	millimeters of mercury
MMAS	Morisky Medication Adherence Scale
SBP	Systolic Blood Pressure
SPSS	Statistical Package for Social Science
WHO	World Health Organization

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1. Introduction

1.1. Background

Hypertension is a cardiovascular disease, which causes disability and premature death throughout the world. Hypertension is defined as office systolic blood pressure (SBP) values ≥ 140 millimeters of mercury (mmHg) and/or diastolic blood pressure (DBP) values ≥ 90 mmHg (Williams et al., 2018). Common cardiovascular disease (CVD) risk factors in patients with hypertension are cigarette smoking, diabetes mellitus (DM), dyslipidemia, obesity, physical inactivity, unhealthy diet, low socioeconomic status, chronic kidney disease, family history and advanced age (Whelton et al., 2017).

The global prevalence of hypertension is increased in 2000 to 972 million in both economically developed and developing nations. By 2025 the estimated number is expected to be increased to a total of 1.56 billion (60%) (Kearney et al., 2005). In Africa, hypertension had risen from 55 million in 1990 to 130 million in 2010 and by 2030 expected to be 217 million (Adeloye and Basquill, 2014). The prevalence of hypertension among Ethiopian population was estimated to be 19.6% (Kibret and Mesfin, 2015).

Blood pressure (BP) is classified as optimal, normal, high-normal, or grades 1–3 hypertension, according to office BP. Patients with high-normal BP and low–moderate cardio-vascular (CV) risk should be provided lifestyle interventions and patients with grade 2 or 3 hypertension, antihypertensive drugs should be initiated in addition to lifestyle interventions (Williams et al., 2018). Adults with stage 1 hypertension who have an estimated 10-year atherosclerotic cardiovascular disease (ASCVD) risk of 10% or higher should be managed initially with a combination of nonpharmacological and antihypertensive drug therapy (Whelton et al., 2017). If hypertension is left uncontrolled it leads to end stage renal disease, heart failure, myocardial infarction, stroke and is the number one attributable risk factor for death throughout the world (Chobanian et al., 2003).

Drug therapy problem (DTP) is any undesirable event or circumstance experienced by a patient that involves or is suspected to involve drug therapy and that interferes with achieving the desired goals of therapy (Cipolle et al., 2012).

DTPs with no resolution can contribute to repeated hospital admissions, prolonged hospitalizations and increased healthcare expenditures. The reason could be improper drug or the dosage, drug-drug interactions or the patient factors such as drug –disease interaction or adherence problems or any other drug related problems (Misita, 2013). DTPs might occur at any stage of the medication process from prescription to follow up of treatment (Cipolle et al., 2004). DTPs involving medications can be categorized in to one of the seven types (Figure1). These include unnecessary drug therapy, need for additional drug therapy, ineffective drug, dosage too low, adverse drug reaction, dosage too high and nonadherence (Cipolle et al., 2012).

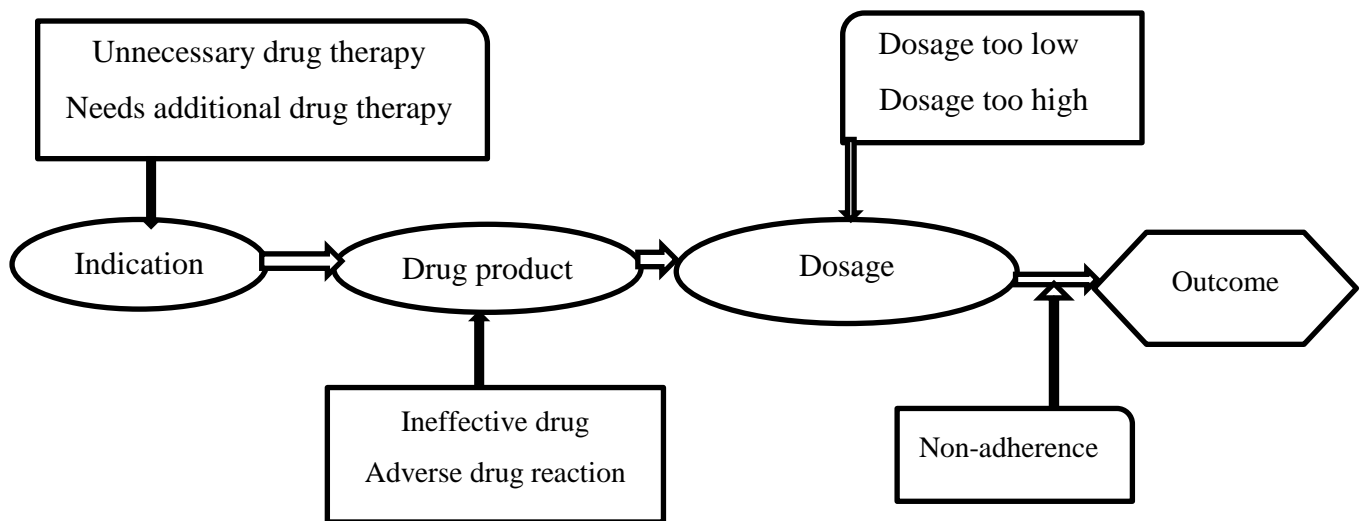


Figure 1: Drug Therapy Problem categories (Cipolle et al., 2004)

Poor adherence is especially common when a patient has poor knowledge, understanding and perception of hypertension or when a complex antihypertensive drug regimen is prescribed (Mohammad et al., 2016). Although the efficacy of antihypertensive agents has been confirmed, the BP control within the desirable range remains unsatisfactory. Poor adherence is one of the most important causes of uncontrolled BP. It also increases the risk of ischemic heart disease 3–4 fold and the overall cardiovascular risk by 2–3 fold (Cutler et al., 2008). Poor adherence to antihypertensive medications leads to the development of hypertensive complications and increase risk of cardiovascular events which in turn reduces the ultimate clinical outcomes (Asgedom et al., 2018).

1.2. Statement of the problem

Hypertension is becoming widely prevalent in both economically developed and developing nations (Kearney et al., 2005). It's prevalence in Ethiopia is also increasing due to change in life styles (Kibret & Mesfin, 2015; Belayneh, 2015). Hypertension rarely occurs in isolation, it is often clusters with dyslipidemia, DM and other CVDs. These comorbidities might predispose patients for taking number of drugs for long time and cause complexity of drug regimens. The relationship between increasing number of drugs used and number of DTPs is strong (Viktil et al., 2006). DTPs are high in patients with increased number of prescribed and over the counter drugs use (Singh et al., 2011). In addition to these availability of new drug products potentially increase the risks of patient for DTPs. DTPs severely minimize the effectiveness of treatment making this critical issue in population health both from the perspectives of quality of life and health economics (Hussein et al., 2014).

DTPs are major concern in health care system because of increased cost, morbidity and mortality. DTP is associated with prolonged length of hospital stay, increased economic burden, and an almost 2-fold increased risk of death (Stafford et al., 2009). The costs associated with DTPs have more than doubled to an estimated annual average of \$177.4 billion (Ernst and Grizzle, 2001). The decrease in healthy life-years is partly attributable to the institution of polypharmacy to treat various comorbidities (Periquito et al., 2016). One third of all emergency department visits were medication-related, including adverse events of which 70%-90% were preventable (Farha et al., 2017).

Adherence to antihypertensive medications is vital because hypertensive patients usually presented with comorbidities, multiple drugs for life long and these might adversely affect the adherence level. Poor medication adherence is associated with poor treatment outcomes, wastes healthcare costs and contributes to reduced BP control (Mohammad et al., 2016).

Hypertension increases risk for heart disease in a long-term fashion. Adults with hypertension develop ASCVD five years earlier than their normotensive peers whose life expectancy is 5 years longer. Each SBP rise of 20 mm Hg, and 10 mm Hg rise in DBP, is associated with a doubling in the risk of death from stroke, heart disease or other vascular disease (Dixon et al., 2018). During hypertension management, it is important to consider CVD risk in addition to BP measurement. Clinicians should consider a management paradigm based on CVD risk in addition to blood pressure measurements (Navar et al., 2017). Almost 70% of adults between

the ages of 60 and 79 years have evidence of cardiovascular disease as indicated by either coronary heart disease, heart failure, stroke or hypertension (Dixon et al., 2018).

Even though different studies (Hussein et al., 2014 ; Tegegne et al., 2015; Hussen and Daba, 2017; Gizaw and Dubale, 2017; Ayele et al., 2018) were done on DTPs in different settings, there is no study regarding DTPs and CVD risk among hypertensive patients at All Africa Leprosy and Tuberculosis Rehabilitation and Training (ALERT) Centre. Therefore, the aim of this study was to assess DTPs and cardiovascular disease risk among hypertensive patients on follow up at ALERT Centre, Addis Ababa, Ethiopia.

This study might provide additional information regarding DTPs and CVD risk and used as a reference material to other researchers when they conduct further studies on related topics. Identification of DTPs are important components of pharmaceutical care and may contribute in reducing drug related morbidity and mortality. In addition, identification of predictors for the occurrence of DTPs and CVD risk might be helpful in looking for patients at risk. The findings of this study also might be important in designing appropriate policies, plans and resolution strategies for the prevention and management of DTPs, CVD risk and their predictors.

1.3. Literature review

1.3.1. Drug therapy problems and associated factors

DTPs are major concern for patients with CVD that influence the desired outcome. A prospective interventional study carried out in India for a period of 7 months among 112 hospitalized cardiovascular patients 53 drug related problems (DRPs) were identified from 44 patients. The most common DRP was found to be drug interactions (DI) (49.05%) followed by adverse drug reaction (ADR) (18.86%), and failure to receive drugs (9.43%)(Shareef et al., 2014).

A cross sectional study done in Jordan from five hospitals included 3,112 outpatients with chronic disease and 74% of them were hypertensive patients. This study identified 32,348 DRPs with an average of 11.2 DRPs per patient. The most common DRPs were a need for additional or more frequent monitoring, a problem in patients' adherence to self-care activities or non-pharmacological therapy and patient was not given instruction in or did not understand non-pharmacological therapy or self-care advice. The numbers of DRPs were associated with older age, being unmarried, having an education level of high school or less, not having health insurance, and presence of certain clinical conditions, including hypertension, DM, dyslipidemia, ischemic heart disease, cardiac catheterization, heart failure and gout (Al-azzam et al., 2016).

A study done in Indonesian four primary health centers among 49 hypertensive patients showed 66 DTPs. Thirty seven (75.5%) of the study participants experienced one DTP, 9(18.3%) of the participants experienced 2 DTPs, 1(2.1%) of them had 3 DTPs and 2(4.1%) of them had 4 DTPs (Nasution and Tanjung, 2016). Similarly, in Indonesian type 2 diabetic patients with hypertension a total of 261 DRPs were identified. Drug choice problem was the most frequent problems and number of medications significantly associated to number of DRPs (Zazuli et al., 2017).

A cross sectional study done in Malaysia included 200 type 2 DM patients with hypertension identified 287 DRPs. The most common type of DRPs encountered were drug choice problems, dosing problems and DI (Huri and Wee, 2013). Similarly, a prospective study conducted in Malaysia among 207 hypertensive patients revealed a total number of 172 DRPs with an average of 2.15 ± 1.5 DRPs per patient. The most frequent category of DRP was drug interactions (33.7%), followed by ADRs (23.9%), drug choice problems (14.5%), dosing problems (13.4%), and others (8.1%) (Redzuan et al., 2017).

A retrospective cohort study done in Saudi Arabia and United Kingdom indicated DTPs are the major health issues that lead to hospitalization. DTPs were present in more than 50% of the total study cohort (58.7% in the United Kingdom and 52.6% in Saudi Arabia. Out of these 70.9% and 41.5% led to hospitalization in the United Kingdom and Saudi Arabia respectively. Polypharmacy was the main risk factor in both these studies (Hamid et al., 2016).

A prospective observational study done at Dessie referral hospital which included 147 patients found a total of 159 DTPs and need additional drug therapy (35.85%) was the most common followed by unnecessary drug therapy (30.19%) and dosage too low (13.2%) (Belayneh et al., 2018).

A prospective cross sectional study carried out among 300 type 2 diabetes patients with hypertension at Jimma university specialized hospital found a total of 494 DRPs. The most common DTPs were need for additional drug therapy (29.35%), ineffective drug (27.94%) and dose too low (15.8%). Independent predictors of DRPs were age 41–60 years, age > 60 years and presence of comorbidity (Yimama et al., 2018). Similarly a cross sectional study conducted at Jimma which included 150 hypertensive patients showed majority of the study participants experienced side-effects like fatigue(100%), headache (95%), peripheral neuropathy (70%), gastrointestinal side effects (65%), cough (50%) and 53% of respondents miss their medication by different reasons (Yenesew et al., 2015). Another finding from Jimma and Felege Hiwot referral hospital showed a total number of 164 DTPs identified. Needs additional drug therapy was the most commonly identified DTP. Number of comorbidity was statistically associated with number of DTPs (Tegegne et al., 2015).

A prospective cross sectional study conducted at Bonga, Ethiopia included 130 adult patients with cardiovascular disease showed 163 DRPs with the mean number of 1.5 ± 0.8 . Drug indication related problems constituted the highest part 64(39.26%) and followed by non-compliance to drugs 46(28.22 %), drug safety 32(19.63%) and drug effectiveness 21(12.89%) related issues (Gizaw and Dubale, 2017).

A cross sectional study carried out among 271 hypertensive patients on follow up of dil-chora referral hospital at Dire Dawa in Ethiopia found that, more than 71% of study participants had at least one DTP. Needs additional drug therapy (62.4%) and nonadherence (32.8%) were the two most common DTPs. Presence of comorbidity, taking ≥ 3 medications per day and uncontrolled BP were factors associated with presence of DTPs (Hussen and Daba, 2017).

A retrospective cross sectional study done in Harar at Hiwot Fana specialized university hospital among type 2 diabetes patients with hypertension identified 364 DRPs. The effect of drug treatment being not optimal 179 (49.2%), untreated indication and symptoms 77 (21.1%), unnecessary drug treatment 39 (10.7%) and ADRs 69 (19%) were the most frequent categories of DRPs identified (Ayele et al., 2018).

A cross sectional study conducted at Ambo general hospital among 151 ambulatory hypertensive patients, 200 DTPs were found. The most common DTP was indication type problems. None of the independent variables were associated with both presence and number of DTPs (Albachew et al., 2015).

A hospital based cross sectional study done at Adama referral hospital, which included 192 hypertensive patients showed 155 (80.7%) patients had at least one DTP and a total of 452 DTPs were identified from these study participants. The most commonly identified DTP was DI 259(58.7%), followed by nonadherence (19.5%) and ADR (18.6%). Marital status, number of drugs and number of comorbidities significantly affect occurrence of DTPs (Hussein et al., 2014).

1.3.2. Adherence and associated factors

A cross sectional study done in China among 2445 hypertensive patients visiting four general outpatient clinics of Hong Kong showed more than half of the study participants were adherent to their medications. Advanced age and unemployment were predictors associated to good adherence (Kang et al., 2015).

A cross sectional study carried out in Saudi Arabia among 308 hypertensive patients showed 27.9% were classified as perfect adherents and 72.1% as non-perfect adherents to antihypertensive medications. Non-formal education, reporting a poor relationship with physicians and having no comorbidities were predictors of non-perfect adherents (Alsolami et al., 2015). Similarly, in Saudi Arabia among 204 hypertensive patients attending primary care clinics showed more than half of the patients were nonadherent to their medications. Female gender, controlled BP, age >65 years and being diabetic were found to be independent predictors of medication adherence (Khayyat et al., 2017). Another finding from Saudi Arabia reported a high level of compliance with antihypertensive medications which was observed among 6.2% of patients whereas medium and low levels were observed among 67.4% and 26.4% of them respectively. Age > 50 years, females, widowed and those haven't history of chronic diseases were predictors of adherence (Alotayfi et al., 2018).

A cross sectional, multicenter study done in Malaysia among 653 hypertensive patients of primary health clinics revealed that good adherence was observed in 53.4% of the study participants. Gender, ethnic group and medicine knowledge positively affect adherence. On the other hand, number of drugs patients were taking, BP control and frequencies of the medications were found to negatively affect adherence (Ramli et al., 2012).

A cross sectional retrospective study carried out in Romania among 525 adult hypertensive patients showed that 69.8% of the patients had high adherence, 20.3% had medium adherence and 9.9% had low adherence. Gender, total cardiovascular risk, BP control, chronic kidney disease and antihypertensive regimens was found to affect level of adherence (Varga et al., 2018).

A descriptive cross sectional study done in Nigeria among 342 hypertensive patients showed (30.0%) of study participants had low medication adherence. Age, employment status and comorbidity were associated to adherence (Ajayi et al., 2018).

A cross sectional study conducted at Debre Tabor general hospital among hypertensive patients that included 337 hypertensive patients showed three-quarters (75.1%) of the participants were found to be adherent to their medication. Urban residence, age >60 years, taking less than two drugs per day and having knowledge about hypertension and its treatment were significantly associated with medication adherence (Teshome et al., 2017).

An institution based cross sectional study done at university of Gondar hospital among 384 hypertensive patients showed more than half of study subjects were adherent. Factors like gender, distance from the hospital and number of comorbidities were associated with medication adherence (Ambaw et al., 2012).

A cross sectional study conducted in Jimma which included 150 hypertensive patients showed that 79 (52.9%) were adherent, 31 (20.7%) were moderately adherent, while 40 (26.4%) were nonadherent to their antihypertensive therapy (Yenesew et al., 2015). Similarly study done in Jimma involved 280 hypertensive patients showed 61.8% of the study participants were found to be adherent. Comorbidity, alcohol intake, getting medications freely and combination of antihypertensive medications were inversely associated with antihypertensive medication adherence (Asgedom et al., 2018).

A cross sectional study done at Adama referral hospital among adults hypertensive patients on follow up revealed more than half (59.5 %) of the study participants were found to be adherent to their treatment. Age group (46-55years), lack of information and presence of comorbidities have shown as predictors for adherence (Hareri et al., 2014).

A study done at Tikur Anbessa Specialized Hospital among 286 hypertensive patients revealed that 69.2% of respondents were adherent to their medications. Marital status, work status, health care facilities and duration of hypertension were associated with medication adherence (Hareri et al., 2013).

1.3.3. Cardiovascular disease risk and associated factors

Quantification of total CV risk is an important part of the risk stratification process for patients with hypertension. A unique and important aspect of CV risk estimation in hypertensive patients is needed to consider the impact of hypertension mediated organ damage (Williams et al., 2018). Screening for and management of other modifiable CVD risk factors are recommended in adults with hypertension (Whelton et al., 2017). If hypertension treatment is delayed to adults with a SBP between 120 and 139 mm Hg, as well as prior CVD or CVD risk of 15% or higher, then 5.8 million untreated adults would be reclassified as treatment eligible; furthermore, 8.5 million treated patients would require medication intensification (Navar et al., 2017).

The 10-year Framingham global risk in 1,509 American persons aged ≥ 30 years showed 24% of subjects had low risk, 21% intermediate risk, 23% high risk, and 32% had CVD (Wong et al., 2009). Millions of Americans have CVD risk factors that place them at increased risk for having a CV event, despite the existence of proven strategies for preventing or managing CVD risk factors (Wall et al., 2018).

The sedentary lifestyle represents an important cause of obesity which increase the CVD risk levels (Paula et al., 2013). Ten year risk of CVD in Canadian adults were $8.10\% \pm 8.89\%$ and the risk was increased by increase in age, decrease in education, and decrease in physical activity and in smokers (Setayeshgar et al., 2013).

Estimation of 10 year CVD risk among 53,122 Malaysian population based on lipid profile formula in the cohort study showed 12.7% risk in males and 4.2% in females. A high 10-year CVD risk is reported among males, Malay ethnic group, those with lower education level, and those with low physical activity level (Borhanuddin et al., 2018).

Across the world, there are different study findings regarding DTPs and CVD risk among hypertensive patients and their predictors that are suggested to increase the occurrence. These studies report different results due to their variation in study design, setting, patient related factors and the likes. The current study was aimed to assess DTPs and CVD risk among hypertensive patients who were on follow up at ALERT Centre.

2. Objective

2.1. General objective

- To assess drug therapy problems and cardiovascular disease risk among hypertensive patients who were on follow up at ALERT Centre

2.2. Specific objectives

- To determine prevalence of drug therapy problems among hypertensive patients
- To identify predictors of occurrence of drug therapy problems of hypertensive patients
- To determine level of adherence of antihypertensive drugs among hypertensive patients
- To identify predictors of adherence
- To determine ten year cardiovascular disease risk among hypertensive patients
- To identify predictors of cardiovascular disease risk

3. Methods

3.1. Study setting

The study was conducted in one of the referral public hospitals in Addis Ababa called ALERT Centre. This hospital has a capacity of 240 beds with dermatology, ophthalmology, and surgery departments, also an orthopedic workshop, a rehabilitation program, DM and hypertension follow up services. Currently hypertensive patients are visiting the clinic every Monday afternoon.

3.2. Study design and study period

A hospital based cross sectional study design was conducted from October 8, 2018 to February 5, 2019 at follow up clinic of ALERT Centre.

3.3. Source population

All adult patients who were on follow up for hypertension management at ALERT Centre.

3.4. Study population

All adult hypertensive patients who presented to ALERT Centre during data collection period and fulfilled the inclusion criteria.

3.5. Inclusion and exclusion criteria

3.5.1. Inclusion criteria

- Patients who were taking anti-hypertensive treatment for at least 1 year

3.5.2. Exclusion criteria

- Incomplete patient medical record
- Patients who were not willing to participate in the study
- Critically ill patients (unable to respond)

3.6. Sample size determination and sampling technique

Sample size was computed based on single population proportion formula by using the following assumption. The proportion (P) population with hypertension having DTPs is taken as 50% to get possible minimum large sample size.

$$n = \frac{z^2 \alpha / 2 p(1-p)}{d^2}$$
$$= \frac{(1.96)^2 (0.5)(0.5)}{(0.05)^2} = 384$$

Where: Proportion of DTPs (p) = 50 % Confidence level of 95 % chosen with z-value of 1.96
Margin of error (d) = 5% n = 384 (sample size without adjustment and with p = 50%). Total population of patients in 4 months (N) were 1000.

$$\text{Corrected sample size} = \frac{n \times N}{n + N}$$

By using the correction formula and 10 % contingency 305 patients were included in the study. Systematic random sampling technique was used to recruit the samples. Sampling interval (kth) was obtained by dividing the total number of hypertensive patients that visited the clinic within the study period by the allocated sample size. Hence, sampling interval was calculated as follows:

$$K = \frac{1000}{305} = 3$$

The first patient was recruited randomly then every 3rd patient- selection continued from the patient registration list until the intended sample size was achieved.

3.7. Study variables

3.7.1. Dependent variables

- DTP
- Patient adherence to their medication
- CVD risk

3.7.2. Independent variables

- Sociodemographic variables (age, gender, educational status, marital status, residency, salt restriction, physical activity and alcohol use)
- Clinical characteristics (comorbidity, number of medication, duration of treatment and level of BP control)

3.8. Data collection and management

3.8.1. Data Collection Instrument

The relevant information about each patient including demographic data (age, sex, residence, etc.) and patients' clinical characteristics (BP control, current medication, comorbidity, etc.) were collected through patient interview by using the prepared questionnaire (Annex II). Physical examination, laboratory results, current medications, comorbidities, relevant previous medical and medication histories were obtained from the medical records (Annex III).

3.8.2. Recruitment of data collectors and training

One clinical pharmacist and two nurses were recruited for data collection and one day training was provided to familiarize them how to retrieve pertinent data from medical record and how to conduct patient interview.

Identification of drug therapy problems

The DTP evaluation tool was prepared based on Cipolle DTP categories with slight modification (Cipolle et al . 2012). DTPs were identified by using most updated guidelines like 2016 Ethiopian Non-Communicable Disease, 2018 European Society of Cardiology (ESC). Drug-drug interaction was evaluated by using Micromedex® health care series software. Major drug-drug interactions were recorded and taken as one type of DTP.

Adherence assessment

Medication adherence is very important for hypertensive patients to achieve BP control. Therefore, adherence was taken as a major objective and conducted separately by using Morisky medication adherence Scale (MMAS-8). The patients were administered interview questionnaire on Morisky medication adherence scale. MMAS-8 an eight-item self-reported adherence measure was used to measure patient adherence to their medications. It consists of eight questions with closed dichotomous (yes / no) answers. The last question has a five point Likert scale: “never”, “once in a while”, “sometimes”, “usually”, and “always.” The degree of adherence was determined according to the score resulting from the sum of all the correct answers: high adherence (eight points), medium adherence (6 to < 8 points) and poor adherence (< 6 point). For purpose of analysis high adherence were taken as adherent and medium and poor adherence were taken as nonadherent.

Cardiovascular disease risk assessment

The ten-year ASCVD risk was assessed by using AHA pooled cohort CV Risk Calculator (ACC/AHA, 2013) and 2013 AHA Guideline on the Assessment of Cardiovascular Risk (Bennett et al., 2014). The risk calculator uses parameters like age, gender, race, total cholesterol, high-density lipoprotein, low density lipoprotein, BP (systolic and diastolic), checking the patient is on (antihypertensive, statin and aspirin) smoking status and history of DM.

3.8.3. Data quality assurance

Before the actual data collection begun pretest was employed on 5% of study participants to check the appropriateness of the data collection instruments and based on the pre-test finding the necessary correction was made. Training was provided to data collectors before starting the data collection and they were adequately informed about the aim of the study and data collection methods. Continuous supervision of the data collection process by principal investigator was maintained. Finally, the principal investigator identified the DTPs.

3.9. Data analysis

The raw data collected from all patients was checked for its' completeness before data entry. The data was entered and analyzed by using Statistical package for social sciences (SPSS) version 23. Descriptive statistics such as frequency, percentage, mean and standard deviation (SD) was used to summarize patients' characteristics. Tables and charts were used to present the results. Binary logistic regression was performed to relate each independent variable to DTPs, level of adherence and ASCVD risk. Among the univariate analysis, those variables with $p < 0.20$ were selected for multivariate analysis. Multivariate analysis was used to assess predictability of the independent variables to DTPs, level of medication adherence and ASCVD risk. P value < 0.05 was considered statistically significant.

3.10. Ethical consideration

Letter of ethical clearance was obtained from the Ethical Review Committee of School of Pharmacy, College of Health Sciences, Addis Ababa University (Annex VI). So the letter was submitted to medical director of ALERT Center and allowed to conduct the research. Verbal consent from each patient was requested to participate in the interview and to extract data from their medical charts. Patients were informed about the objective of the study and their full right to refuse from participation at any point of time and also they assured by no means of the service they get from the institution is affected. Privacy and confidentiality was ensured during patient interview and review of patient medical charts. Thus, name and address of the patient was not recorded in the data abstraction formats.

3.11. Operational definitions

- **Alcohol use** : a regular consumption of any alcoholic beverage greater than 2 drinks per day for men and greater than 1 drink per day for women (1 drink = 355 ml for beer and 148 ml for wine) (Whelton et al., 2017).

Adverse drug reaction: Any undesirable experience that has happened to the patient while receiving a drug at normal doses used clinically is suspected to be caused by the drug (WHO, 1972).

- **Controlled BP:** BP < 140/90 mmHg in all patients (Williams et al., 2018).
- **Drug-therapy problem** : any undesirable event experienced by a patient that involves, or is suspected to involve, drug therapy, and interferes with achieving desired goals of therapy(Cipolle et al., 2012).
- **Non-adherent** : who score <8 based on Morisky Medication Adherence Scale-8
- **Physical activity:** Patients engaged in exercise or walking of a 30 minutes per day at least for 5 days or cumulative of 150 minutes/week (Whelton et al., 2017).
- **Salt restricted:** Patients add little amount of salt in their meal

4. Results

4.1. Sociodemographic characteristics of study participants

In this study, a total of 305 study participants were included. Majority 188(61.6%) of them were females. Mean age of the study participants was 61.7 ± 11.66 years and more than half of 187 (61.3%) of them were below 65 years. Majority 181(59.3%) of them were married. Of these 274(89.8%) participants are Addis Ababa residents. Regarding their education status, 49.5% had no formal education. Among the study participants, 53.4% were unemployed and 15.1% were retired. Concerning social habits, 20% use alcohol, 66.9% restricted to salt use, 58.7 % drink coffee and 43% engaged in physical activity. Majority 264(86.6%) of the study participants got their medication for free (Table 1).

Table 1: Sociodemographic characteristics of hypertensive patients attending follow up clinic of ALERT Centre, Addis Ababa, Ethiopia, October 2018 -February 2019

Variables	Category	Numbers (%)
Sex	Male	117(38.4)
	Female	188(61.6)
Age	< 65	187(61.3)
	≥65	118(38.7)
Marital status	Single	11(3.6)
	Married	181(59.3)
	Divorced	35(11.5)
	Widowed	78(25.6)
Residential area	Addis Ababa	274(89.8)
	Out of Addis Ababa	31(10.2)
Educational status	No formal education	151(49.5)
	Primary	105(34.4)
	Secondary	22(7.2)
	Diploma and above	27(8.9)
Occupation	Unemployed	163(53.4)
	Employed	25(8.2)
	Merchant	29(9.5)
	Daily laborer	22(7.2)
	Retired	46(15.1)
	Other*	20(6.6)
Social habits	Alcohol use	67(22)
	Cigarette smoking	7(2.3)
	Coffee use	179(58.7)
	Physical activity	131(43)
	Salt restricted	204(66.9)
	Khat use	28(9.2)
Source of medication	Free	264(86.6)
	Paid	41(13.4)

*farmer, driver

4.2. Clinical characteristics of study participants

About 46.2 % of study participants were on treatment for 5-10 years and had comorbidity 138(45.2%). More than three fourths (78%) of study participants took less than three drugs. Hypertensive heart disease was the most common hypertensive complication 65(13.1%). The average systolic BP range from 140-159 in 35.7% of study participants and diastolic BP <80 in 41% of study participants. The mean systolic and diastolic BP of the total 305 study participants were 135.65±13.97 and 80.77±8.10 mmHg respectively. Based on the three consecutive follow up average BP measurements of the study participants 170(55.7%) of them had controlled BP according to ESC 2018 guideline (Table 2).

Table 2: Clinical characteristics of hypertensive patients attending follow up clinic of ALERT Centre, Addis Ababa, Ethiopia, October 2018 -February 2019

Variables	Category	Number	Percent (%)
Duration of treatment	<5 years	83	27.2
	5-10 years	141	46.2
	≥10 years	81	26.6
Comorbidity (n=138)	Heart failure	16	5.2
	DM	13	4.3
	Arthritis	21	6.9
	Asthma	20	6.6
	Stroke	22	7.2
	Dyslipidemia	21	6.9
	Others*	25	8.2
Number of drugs	<3 drugs	240	78.7
	≥3drugs	65	21.3
Complications (n=65)	Hypertensive heart disease	40	13.1
	Peripheral neuropathy	20	6.6
	Nephropathy	5	1.6
Average systolic BP	<120	28	9.2
	120-129	69	22.6
	130-139	79	26
	140-159	109	35.7
	160-179	20	6.6
Average diastolic BP	<80	125	41
	80-84	76	24.9
	85-89	48	15.7
	90-99	49	16.1
	100-109	7	2.3
BP control	Controlled	170	55.7
	Uncontrolled	135	44.3

*Retroviral infection, Valvular heart disease, Ischemic heart disease

4.3. Patterns of Anti-hypertensive drugs

From the study participants 143(46.9%) of them were taking dual therapy followed by monotherapy 130(42.6%) and triple therapy 32(10.5%). Hydrochlorothiazide (HCT) + Enalapril 51(16.7%) was most frequently prescribed antihypertensive drugs followed by Nifedipine + HCT 29(9.5%) and Nifedipine + Enalapril 29(9.5%). Among patients taking mono therapy Enalapril 56(18.4%) was most frequently prescribed antihypertensive drugs followed by HCT 43(14.1%) and Nifedipine 26(8.5%) (Table 3).

Table 3: Antihypertensive medications among hypertensive patients attending follow up clinic of ALERT Centre, Addis Ababa, Ethiopia, October 2018 -February 2019

Variables	Category	Numbers	Percent (%)
Numbers of antihypertensive	One	130	42.6
	Two	143	46.9
	Three	32	10.5
Monotherapy	Enalapril	56	18.4
	HCT	43	14.1
	Nifedipine	26	8.5
	Others*	5	1.6
Dual therapy	HCT +Enalapril	51	16.7
	HCT +Nifedipine	29	9.5
	Nifedipine +Enalapril	29	9.5
	Amlodipine + HCT	8	2.62
	Amlodipine +Enalapril	5	1.6
	Enalapril +metoprolol	3	1
	Nifedipine +Atenolol	5	1.64
	Others **	13	4.3
Triple therapy	HCT +Enalapril+Nifedipine	9	3
	HCT +Enalapril+Amlodipine	1	0.3
	HCT+Enalapril+Spironolactone	1	0.3
	HCT +Enalapril+Metoprolol	7	2.3
	Enalapril+Nifedipine +Metoprolol	1	0.3
	Furosemide+Spironolactone+Metoprolol	4	1.3
	Others***	9	3
	Other than antihypertensive medications	Non-steroidal anti-inflammatory drugs	66
Antiplatelet		64	21
Statins		60	19.7
Protein pump inhibitors		30	9.8
Anti-asthmatic		26	8.5
Antidiabetic		19	6.2
Others ****		41	13.4

*methyl dopa, amlodipine ** enalapril+furosemide, metoprolol+furosemide, HCT+metoprolol

***HCT+enalapril+furosemide, enalapril+atenolol+HCT,

spironolactone+furosemide+nifedipine****allopurinol, highly active antiretroviral therapy, amitriptyline, tramadol, Propylthiouracil, antibiotics

4.4. Prevalence and types of drug therapy problems

A total of 446 DTPs were identified from 223(73.1%) of study participants. Among these participants 1 DTP was identified in 95(31.1%), 2 DTPs in 70(23%) and ≥ 3 DTPs in 58(19%) (Figure 2).The average number of DTPs per patient was 1.5.

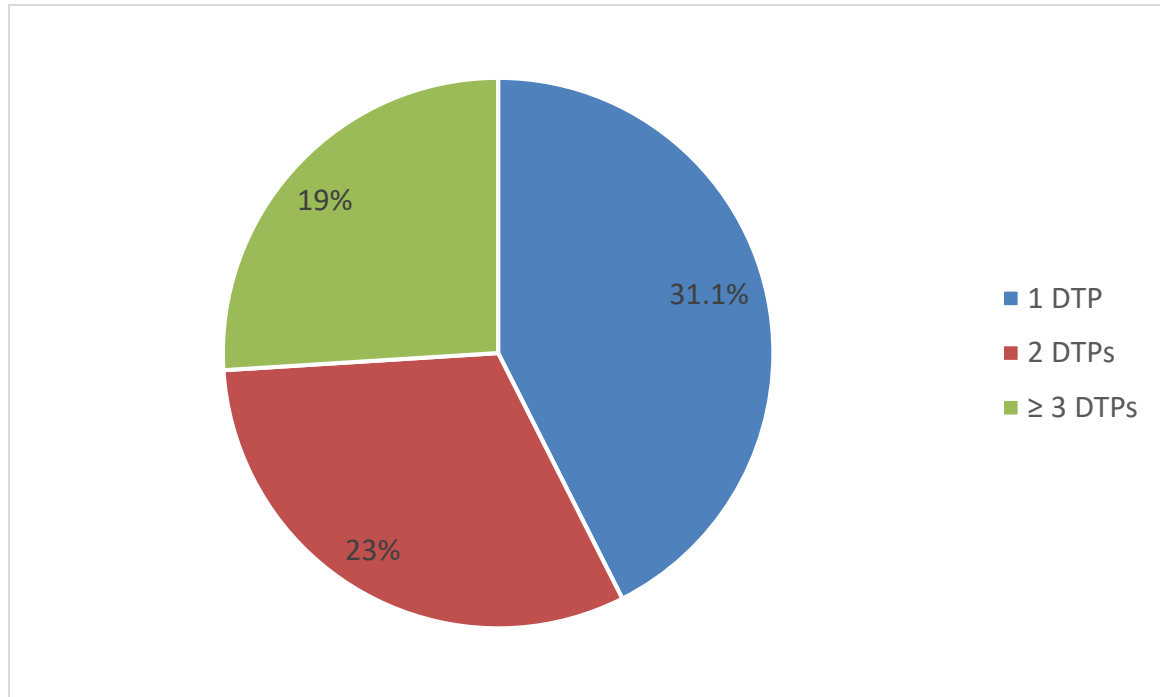


Figure 2: Number of drug therapy problems among hypertensive patients attending follow up clinic of ALERT Centre, Addis Ababa, Ethiopia, October 2018 -February 2019

The most common type of identified DTP was needs additional drug therapy 143(32.1%) followed by DI 115(25.8%), dosage too low 55(12.3%), ADR 51(11.4%), unnecessary drug therapy 38(8.6%), ineffective drug 31(6.9 %) and dose too high 13(2.9%) (Table 4). As illustrated in Table 5, there were 115 major DIs identified in 92 (30.2%) of study participants. From these HCT + Aspirin had the highest number.

Table 4: Types of DTPs identified among hypertensive patients attending follow up clinic of ALERT Centre, Addis Ababa, Ethiopia, October 2018 -February 2019

DTP category	Causes of DTP	No. of DTP	Percent (%)
Drug interaction		115	25.8
Unnecessary drug therapy	Duplicate therapy	2	8.6
	No medical indication at this time	36	
Needs additional drug therapy	Preventive therapy	110	32.1
	Synergistic therapy	33	
Ineffective therapy	More effective therapy available	22	6.9
	Condition refractory to drug	4	
	Drug not indicated for condition	5	
Dosage too low	Ineffective dose	55	12.3
Adverse drug reaction	Undesirable effect	51	11.4
Dosage too high	Dose too high	10	2.9
	Needs additional monitoring	3	
Total		446	100

Table 5: Types of drugs involved in drug interaction among hypertensive patients attending follow up clinic of ALERT Centre, Addis Ababa, Ethiopia, October 2018 -February 2019

Drugs involved in drug interaction	Numbers	Percent (%)
HCT +Aspirin	32	27.8
Aspirin + Glibenclamide	5	4.3
Metformin +Aspirin	11	9.6
Allopurinol +Enalapril	1	0.9
Spirolactone +Aspirin	8	7
HCT + Indomethacin	18	15.7
Amitriptyline +Indomethacin	2	1.7
Aspirin +Indomethacin	1	0.9
Furosemide +Aspirin	22	19.1
Enalapril+Digoxin	1	0.9
Enalapril +Spirolactone	13	11.3
Aspirin +Clopidogrol	1	0.9
Total	115	100

About 11.4 % of study participants experienced ADRs that were confirmed by treating physicians most probably associated to the drug they took. Headache was the major encountered ADRs followed by peripheral edema and dry cough (Table 6).

Table 6: Types and prevalence of ADRs among hypertensive patients attending follow up clinic of ALERT Centre, Addis Ababa, Ethiopia, October 2018 -February 2019

Drug(s)	Types of ADR	Numbers	Percent (%)
Atorvastatin	Myopathy	3	5.9
Enalapril	Dry cough	9	17.6
Nifedipine	Ankle edema	10	19.6
Spironolactone	Gynecomastia	1	2
Nifedipine	Constipation	8	15.7
Enalapril, Nifedipine	Headache	12	23.5
Hydrochlorothiazide	Hyperuricemia	6	11.8
Ciprofloxacin	Allergy	1	2
Aspirin+clopidogrol	UGIB*	1	2
Total		51	100

* Upper gastrointestinal bleeding

4.5. Predictors of drug therapy problems

The variables included in the univariate analysis were age, gender, alcohol use, physical activity, comorbidity, aspirin use, statin use, non-steroidal anti-inflammatory drug use, BP control, number of medication, duration of treatment, complication and salt consumption. As illustrated in Table 7, in univariate analysis, factors that were associated with DTPs were gender, alcohol use, presence of comorbidity, BP control and number of drugs ($p < 0.2$). According to multivariate analysis (Table 7) three variables were statistically significant with the occurrence of DTPs. Patients who took more than 3 medications were 4.8 times more likely to develop DTPs as compared to patients took less than 3 medications (adjusted odds ratio (AOR)=4.751, 95% confidence interval (CI): 1.776-12.714, $P=0.02$). The odds of DTPs were 1.6 times higher among patient who had uncontrolled BP as compared to patients who had controlled BP (AOR=1.567, 95% CI: 1.001-3.230, $P=0.012$). Patient who did not use alcohol had lower risk by 58 % of developing DTPs as compared with patients who use alcohol (AOR=0.418, 95% CI: 0.181-0.963, $P=0.040$) (Table 7).

Table 7: Multivariate analysis of factors associated with DTPs among hypertensive patients attending follow up clinic of ALERT Centre , Addis Ababa, Ethiopia, October 2018 -February 2019

Variables	Category	DTPs (%)		Crude odds ratio (COR)	AOR	P-value
		Yes	No			
Gender	Female	131(58.7%)	57(69.5%)	1	1	0.202
	Male	92(41.3%)	25(30.5%)	1.6(0.933-2.749)	1.507 (0.802-2.832)	
Alcohol use	Yes	56(25.1%)	11(13.4%)	1	1	0.040*
	No	167(74.9%)	71(86.6%)	0.462(0.229-0.934)	0.418 (0.181-0.963)	
Comorbidities	No	137(60.6%)	30(38%)	1	1	0.121
	Yes	89(39.4%)	49(62%)	0.562(0.335-0.943)	0.622(0.341-1.134)	
Number of Medications	<3	171(74%)	69(93.2%)	1	1	0.002*
	≥3	60(26%)	5(6.8%)	5.18(1.995-13.449)	4.751 (1.776-12.714)	
BP control	Controlled	117(52.5%)	53(64.6%)	1	1	0.012*
	Uncontrolled	106(47.5%)	29(35.4%)	1.656(0.981-2.795)	1.567 (1.001-3.230)	

4.6. Adherence status and reasons for nonadherence

Based on Morisky medication adherence scale 111(36.4%) of study participants had poor adherence, while 148(48.5%) and 46(15.1%) of them had high and medium adherence respectively. For the purpose of data analysis, the initial three categories of adherence were re-categorized in to two categories. High adherence with score equal to eight were taken as adherent and medium and low adherence was taken as non-adherent with score of less than eight (Figure 3).

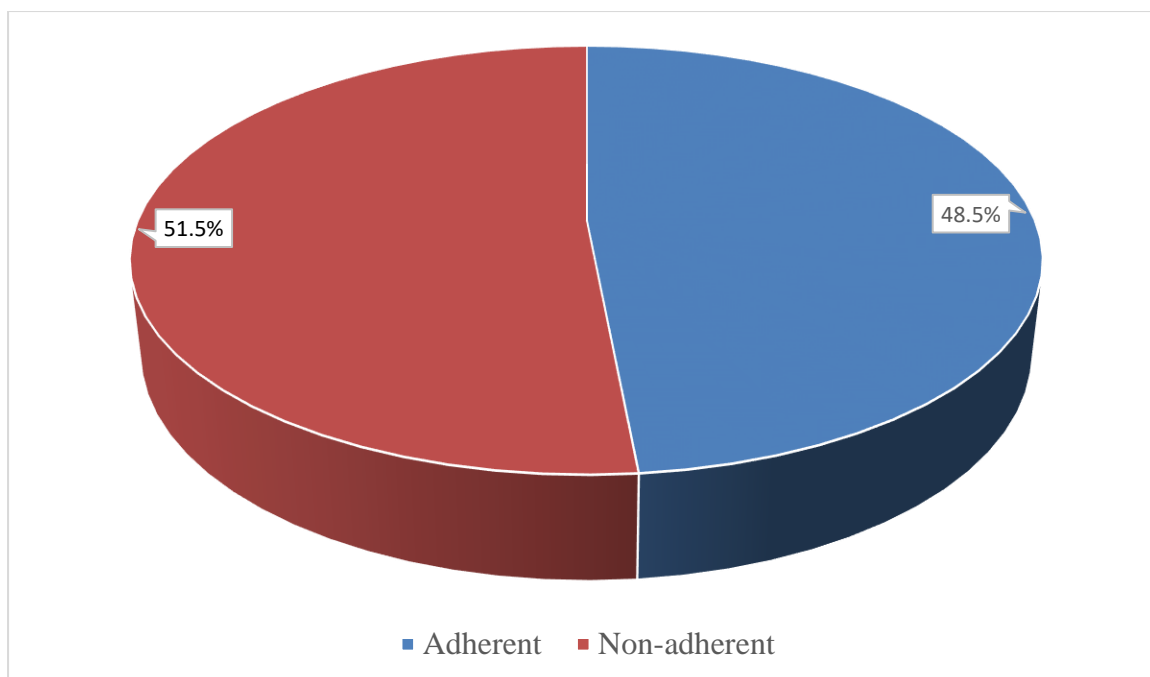


Figure 3: Adherence status of hypertensive patients attending follow up clinic of ALERT Centre, Addis Ababa, Ethiopia, October 2018 -February 2019

According to patients' response, the main reasons for non-adherence were forgetfulness followed by disbelief in drug effectiveness, fear of side effect, unavailability of drug product and patients' feeling as better (Table 8).

Table 8: Possible reasons for nonadherence reported by hypertensive patients attending follow up clinic of ALERT Centre, Addis Ababa, Ethiopia, October 2018 -February 2019

Reasons for non-adherence	Number	Percent (%)
Forgetfulness	105	66.9
Fear of adverse effect	17	10.8
Drug product is not available	13	8.3
Disbelief in drug effectiveness	10	6.4
Patient felt better	8	5
Drug product too expensive	4	2.5
Total	157	100

4.7. Predictors of adherence

The variables included in the univariate analysis were age, gender, alcohol use, physical activity, comorbidity, aspirin use, statin use, non-steroidal anti-inflammatory drug use, BP control, number of medication, duration of treatment, residence, ADR, marital status, source of medication, complication and salt restriction. As illustrated in Table 9, in univariate analysis, factors that were associated with nonadherence were marital status, alcohol use, salt restriction, exercise, BP control and duration of treatment ($p < 0.2$). Physical activity, salt restriction and duration of treatment were statistically significant with nonadherence ($p < 0.05$). Physical activity (AOR=0.490, 95% CI: 0.287-0.836, $P=0.009$) was protective factor against occurrences of nonadherence to antihypertensive medications. Salt restriction (AOR=0.554, 95% CI: 0.308-0.995, $P=0.048$) also had a protective effect against occurrences of nonadherence and taking treatment for ≥ 10 years (AOR=0.460, 95% CI, 0.251-0.844, $P=0.012$) had a protective effect on nonadherence (Table 9).

Table 9: Multivariate analysis of factors associated with adherence among hypertensive patients attending follow up clinic of ALERT Centre , Addis Ababa, Ethiopia, October 2018 -February 2019

Variables	Category	Adherence N (%)		COR	AOR	P-value
		Nonadherent	Adherent			
Marital status	Single	7(4.5%)	4(2.7%)	1		
	Married	99(63%)	82(55.4%)	2.15(0.582-7.944)	2.077(0.535-8.057)	0.291
	Divorced	16(10.2%)	19(12.8%)	1.483(0.870-2.529)	1.22(0.677-2.198)	0.507
	Widowed	35(22.3%)	43(29.1%)	1.035(0.464-2.304)	0.836(0.345-2.024)	0.691
Alcohol use	No	116(73.9%)	122(82.4%)	1	1	
	Yes	41(26.1%)	26(17.6%)	1.658(0.954-2.884)	1.724(0.949-3.132)	0.074
Salt restricted	No	64(40.8%)	37(25%)	1	1	
	Yes	93(59.2%)	111(75%)	0.484(0.297-0.790)	0.554 (0.308-0.995)	0.048*
Physical activity	No	107(68.2%)	67(49%)	1	1	
	Yes	50(31.8%)	81(51%)	0.387(0.242-0.616)	0.490 (0.287-0.836)	0.009*
BP control	Controlled	75(47.8%)	95(64.2)	1	1	
	Uncontrolled	82(52.2%)	53(35.8%)	0.510(0.322-0.808)	0.845(0.470-1.520)	0.736
Duration of treatment	<5 years	43(27.4%)	40(27%)	1	1	
	5-10 years	62(39.5%)	79(53.4%)	0.600(0.321-1.121)	0.641(0.303-1.151)	0.122
	≥ 10 years	52(33.1%)	29(19.6%)	0.438(0.249-0.769)	0.460(0.251-0.844)	0.012*

4.8. Cardiovascular disease risk assessment

From total of 305 study participants 144 had lipid profile. The ten-year ASCVD risk was calculated for only those participants with lipid profile and categorized to low risk (< 5%), borderline (5-7.4%), intermediate (7.4-19.9%) and high risk ($\geq 20\%$). Majority 58(40.3%) of them had 20% or higher risk (Figure 6). For identifying predictors for cardiovascular disease risk, it was dichotomized to <20% and $\geq 20\%$. More than half (59.7%) of the study participants had risk of <20% and 40.3% of them had 20% or higher cardiovascular disease risk.

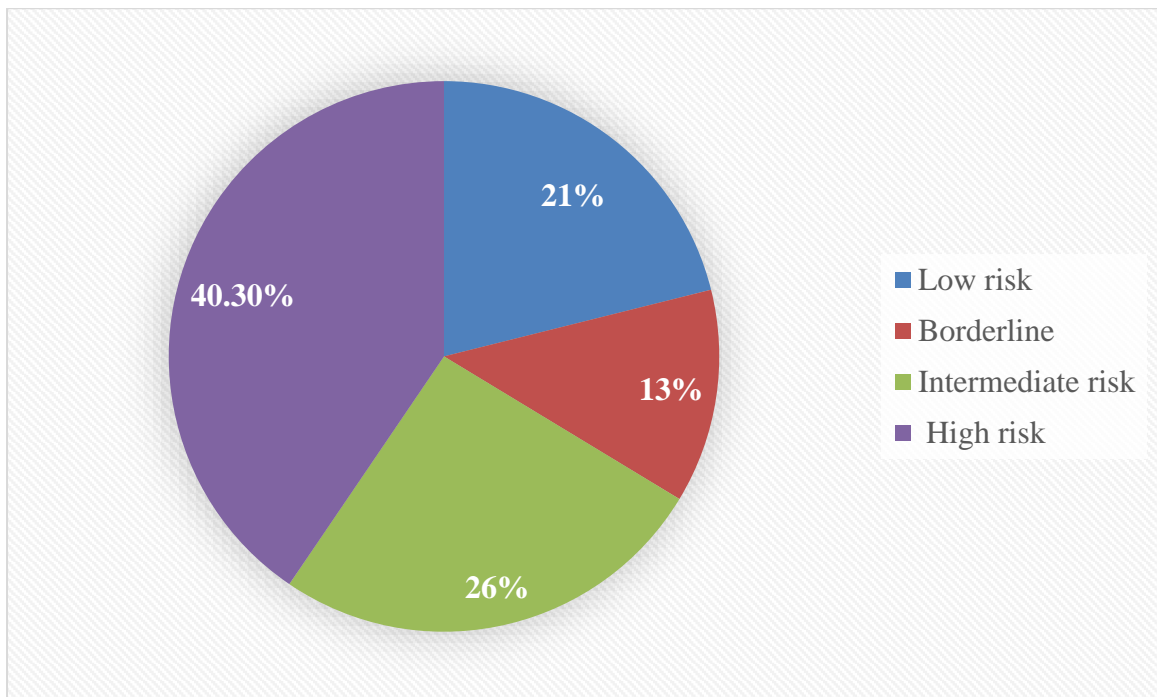


Figure 4: Atherosclerotic cardiovascular disease risk assessment among hypertensive patients attending follow up clinic of ALERT Centre, Addis Ababa, Ethiopia, October 2018 -February 2019(n=144)

4.9. Predictors for cardiovascular disease risk

As illustrated in Table 10, in univariate analysis, factors that were associated with DTPs were physical activity, alcohol use, occupation, residence, salt restriction, presence of complication, BP control, and number drugs ($p < 0.2$). From these variables occupation, alcohol use and BP control were statistically significant to ASCVD risk of 20% or higher. Study participants who did not use alcohol had lower risk by 75% of having ASCVD risk of 20% or higher as compared to participants who use alcohol (AOR=0.253, 95% CI: 0.092-0.695, $P=0.008$). Retired study participants were 5.56 times more likely to have 20% or higher ASCVD risk as compared to study participants who were employed (AOR=5.562, 95% CI: 1.391-22.230, $P=0.015$). Study participants who achieved controlled BP had lower risk by 68% of having ASCVD risk of 20% or higher risk as compared to study participants who did not achieved BP control (AOR=0.323, 95% CI: 0.105-0.996, $P=0.049$)(Table 10).

Table 10: Multivariate analysis of factors associated with cardiovascular disease risk among hypertensive patients attending follow up clinic of ALERT Centre , Addis Ababa, Ethiopia, October 2018 -February 2019(n=144)

variables	category	ASCVD risk (%)		COR	AOR	P-value
		≥20%	<20%			
Physical activity	No	36(62.1%)	44(51.2%)	1 0.640(0.325-1.262)	0.619(0.260-1.472)	0.278
	Yes	22(37.9%)	42 (48.8%)			
Alcohol use	Yes	9(15.5%)	33(37.5%)	1 0.295(0.128-0.679)	0.253(0.092-0.695)	0.008*
	No	49(84.5%)	53(62.5%)			
Presence of complication	No	38(67.9%)	64(72.7%)	1 1.492(0.702-3.169)	0.993(0.393-2.513)	0.989
	Yes	18(32.1%)	24(27.3%)			
Occupation	Employed	2(3.5%)	10(11.6%)	1 0.4(0.068-3.940) 1.415(0.508-3.940) 0.308(0.054-1.759) 4.5(1.313-15.420)	0.595(0.088-3.997) 1.202(0.373-3.880) 0.142(0.013-1.527) 5.562(1.391-22.230)	0.593 0.758 0.107 0.015*
	unemployed	29(50%)	41(47.6%)			
	Merchant	2(3.5%)	13(15%)			
	Daily laborer	7(12%)	14(16.5%)			
	Retired	18(31%)	8(9.3%)			
Residential area	Aldiss Ababa	51(88%)	79(91.8%)	1 0.646(0.214-1.950)	0.776(0.206-2.916)	0.707
	Out of Addis	7(12%)	7(8.2%)			
Salt restricted	No	22(37.9%)	33(37.5%)	1 1.019(0.513-2.023)	1.396(0.568-3.431)	0.468
	Yes	36(62.1%)	53(62.5%)			
BP control	Uncontrolled	51(87.9%)	65(75.6%)	1 0.425(0.168-1.077)	0.323(0.105-0.996)	0.049*
	Controlled	7(12.1%)	21(24.4%)			
Number of medications	<3 drugs	28(63.6%)	81(81%)	1 1.286(0.470-3.516)	1.478(0.945-2.313)	0.087
	≥3drugs	16(36.4%)	19(19%)			

4.10. Examples of drug therapy problems identified from study participants

Table 11: Examples of drug therapy problems identified from hypertensive patients attending follow up clinic of ALERT Centre, Addis Ababa, Ethiopia, October 2018 -February 2019

No	Descriptions of DTP	Type of DTP
1	A 72 year old male patient with hypertension and gouty arthritis was on enalapril 10mg Bid, HCT 25 mg, allopurinol 100mg and indomethacin 25 mg. His average BP was 153/96 and ASCVD risk score was 22.08%. Enalapril and allopurinol have drug interaction. This patient is candidate for statin therapy	Drug interaction and needs addition of statin
2	A 59 year old male patient with hypertension and Type 2 DM was on ASA 81 mg, enalapril 10mg Bid ,atorvastatin 40mg ,atenolol 25 mg and metformin 1gm Bid . His average BP 132/90, ASCVD score 70 % and FBS 217 . There is no compelling indication for atenolol use in this patient	Ineffective drug and DI between ASA and metformin
3	A 50 year old male patient with hypertension was on ASA 81 mg, atorvastatin 40 mg, enalapril 10 mg and nifedipine 20 mg Bid. His average BP and ASCVD risk score were 160/100, 3.13 % respectively. Use of atorvastatin and aspirin were unnecessary because of low risk in this patient. The dose of enalapril should be escalated to lower the elevated BP.	low dose of enalapril and no medical indication
4	A 65 year old female patient with hypertension and osteoarthritis was on enalapril 10 mg BID, nifedipine 20 mg and diclofenac 50 mg .The patient experienced constipation due to nifedipine.	ADR
5	A 60 year old female patient with hypertension and Type 2 DM was on HCT 25 mg, glibenclamide 5mg Bid ,metformin 500 mg Bid ,atorvastatin 40 mg and ASA 81 mg. His average BP, ASCVD risk score, FBS were 120/75, 10 % and 237mg/dl respectively. Aspirin and glibenclamide and/or metformin) have drug interaction.	No medical indication and drug interaction
6	A 60 year old female patient with hypertension and dyslipidemia was on HCT 25 mg, enalapril 10 mg and atorvastatin 40 mg. The patient experienced enalapril induced dry cough.	ADR
7	A 70 year old male hypertensive patient with 45.01% of ASCVD risk score was on HCT 25 mg and enalapril 5 mg. This patient needs both statin and antiplatelet therapy.	Needs addition of statin and ASA 81 mg
8	A 63 year old male patient with hypertension and IHD was on ASA 81 mg, enalapril 10mg Bid, atenolol 50 mg and atorvastatin 80 mg. His average BP was 113/76 so dose of antihypertensive should tapered.	Dose too high
9	A 65 year old male with hypertension with ACS was on ASA 81 mg, clopidogrol 75 mg, metoprolol 25 mg, enalapril 10mg and atorvastatin 40mg.his average BP was 140/85. Aspirin and clopidogrol has drug interaction which increases risk of bleeding.	Drug interaction
10	A 75 year old male with hypertension, asthma and degenerative valvular heart disease was on nifedipine 20 mg, enalapril 10 mg, metoprolol 25 mg, ASA 81 mg, spironolactone 25mg and salbutamol puff. This patient experienced gynecomastia secondary to spironolactone	ADR and drug interaction between ASA and spironolactone

5. Discussion

The current study was aimed to determine magnitude of DTPs and CVD risk among hypertensive patients on follow up at ALERT Centre. The findings of this study revealed 73.1% of the study participant had at least one DTP. The most common type of identified DTP was needs additional drug therapy and DI. The level of medication non-adherence was 51.5% and the main reason for non-adherence was forgetfulness. About 40.3% of study participants who had lipid profile had 20 % or high risk of ASCVD.

In this study the prevalence of controlled BP was 55.7% which was consistent with 50.3% in study from Jimma (Asgedom et al., 2016) and 50.4% in Gondar (Animut et al., 2018), but higher than 30.1% in Zewditu Memorial hospital (Yazie et al., 2018), 47.3% in Jimma university (Tesfaye et al., 2017) and 26.8% in Malaysia (Rampal et al., 2008). The reason could be majority of study participants in Yazie *et al.* had DM, advanced age and other cardiovascular disease, which contribute to poor BP control. In Tesfaye *et al.* study non adherence to low diet salt and physical activity was reported which might influence the BP control and in Rampal *et al.* study BP control was assessed by single follow up. The finding of an elevated BP should always lead physicians to search for the cause(s), particularly the commonest reasons poor adherence to the prescribed treatment regimen, persistence of a white-coat effect, and occasional or more regular consumption of salt, drugs, or substances that raise BP or oppose the antihypertensive effect of treatment like alcohol or non-steroidal anti-inflammatory drugs (Williams et al., 2018). As compared to the current study a higher BP control was found in French (64.7% to 74.5%) and Italian study (56.8% to 68.3 %)(Wu et al., 2015) and Gondar (86.4%)(Abegaz et al., 2018). This could be due to the difference in study design and settings (cross sectional vs retrospective cohort), affordability of more effective medications and high level of adherence, which could enhance BP control attainment. The treatment goal also influenced by knowledge and experience of physicians and the guidelines were used.

In this study HCT + Enalapril was frequently prescribed dual therapy and Enalapril was frequently prescribed monotherapy which was similar with studies conducted in Ethiopia, Dire Dawa (Hussen and Daba, 2017) and Adama (Hussein et al., 2014). From the five major drug classes of hypertension treatment: angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARBs), beta-blockers (BBs), calcium channel blockers (CCBs) and diuretics any class can be initiated or combined since they are proven to reduce BP, cardiovascular events, major cardiovascular outcomes and mortality. There are compelling or

possible contraindications for each class of drug and preferential use of some drugs for some condition (Williams et al., 2018).

In the current study, about 73.1% of the study participants had at least one DTP and 1.5 DTPs per patient. The finding of this study is in line with studies done in Ethiopia: 75.51% in Dessie (Belayneh et al., 2018), 72% in Bonga (Gizaw and Dubale, 2017) and 71.2% in Dire Dawa (Hussen and Daba, 2017). However it was lower than other studies done in Ethiopia like, 80.7% in Adama (Hussein et al., 2014), 1.8 DRPs per patient in Harar (Ayele et al., 2018), 82% in Jimma (Yimama et al., 2018), 88.66% in Jimma and Felege Hiwot referral hospital (Tegegne et al., 2015) as well as 88.8% in Malaysia (Redzuan et al., 2017), 11.2 DRPs per patient in Jordan (Al-azzam et al., 2016), 2.88 DRPs per patient in Indonesia (Zazuli et al., 2017) and in 90.5% Malaysia (Huri and Wee, 2013). Such variations could be due to difference in study designs (interventional vs. observational; prospective vs. retrospective), different methods to assess DTPs classification systems and characteristics of study participants and multiple comorbidities. But the current study reported higher than studies done in Cyprus (63%)(Gok et al., 2016), India 1.25 DRPs per patient (Shareef et al., 2014), Sweden 66% (Peterson and Gustafsson, 2017), Indonesia (45.8%) (Nasution and Tanjung, 2016). This discrepancy might be due to difference in patients' level of education and awareness, the health care system and facilities, study method and settings (four primary health centers), small sample size, difference in clinic set up and professionals working in the area.

The commonest DTP identified was needs additional drug therapy (32.1 %) followed by DI (25.8%), dosage too low (12.3%), ADR (11.4%), unnecessary drug therapy (8.6%), ineffective drug (6.9 %) and dose too high (2.9%). Needs additional drug therapy was most frequently identified type of DTP. This finding was consistent with study done in Jimma (29.35%) (Yimama et al., 2018) and Dessie (35.85%) (Belayneh et al., 2018). However it was lower as compared to studies done in Ethiopia, Dire Dawa (62.4%) (Hussen and Daba, 2017), Jimma and Felege Hiwot referral hospital (90.69%) (Tegegne et al., 2015). This difference might be explained by some of these studies recruited study participants with higher number of uncontrolled BP, infections (urinary tract infection and pneumonia), cardiovascular complications and comorbidities which might need additional drug therapy and difference in study design (cohort vs cross sectional). But it was higher than studies conducted in Ethiopia, Ambo (15.9%) (Albachew et al., 2015) and Sweden (9%) (Peterson and Gustafsson, 2017),

Indonesia (22.3%) (Zazuli et al., 2017). This might be due to our study included ten-year ASCVD risk, which detected most patients need antiplatelet and statin preventive therapy.

DI (25.8%) was the second most frequently identified types of DTP. DI is a major factor that may affect patient's clinical outcome by contributing to increased risk of adverse drug events, lower antihypertensive effect of medications and a higher health care cost. This finding was lower as compared to studies carried out in Ethiopia, Adama (58.7%) (Hussein et al. 2014), India (49.05%) (Shareef et al., 2014) and Malaysia (33.7%) (Redzuan et al., 2017). The variations might be due to difference in classification system of drug interaction, difference among study subjects (some studies included all cardiovascular patients that will increase number of medication use) and different study design. For instance, Hussein *et al.* classified minor and moderate drug interactions as DI, which increased prevalence, but our study considered only major interactions. The most common DIs were between aspirin and HCT resulting in an increased risk of nephrotoxicity and decreased antihypertensive effects, HCT and indomethacin decrease antihypertensive effect, enalapril and spironolactone, increasing risk of hyperkalemia; and aspirin use in combination with spironolactone, resulting in an increased risk of nephrotoxicity. These interactions are unavoidable unless single medication is used. But this is impractical to achieve treatment goal and manage different conditions that exist concurrently. Usually benefits of combining medications outweighs the risk patients encountered due to DI. It is important to monitor closely for early detection of toxicity due to significant drug interactions and design proper alleviating mechanisms.

Dosage too low (12.3%) was the third commonly identified type of DTPs. This finding was comparable with studies done in Ethiopia, Dessie (13.2%) (Belayneh et al., 2018) and Jimma (15.8%) (Yimama et al., 2018). Hypertensive patients may need increased doses of their medication to achieve BP goal. The recent guideline recommend to initiate combinations of monotherapies at low dose then if the BP goal is not achieved dose increase might be considered after excluding nonadherence (Williams et al., 2018).

ADR was identified in present study from patients' medical record that were confirmed by physicians but any complaints from the patients were not considered. Among study participants, 11.4 % of them had ADRs associated to medication they were taking. This finding is in line with studies done in Ethiopia which are (9.43%) in Dessie (Belayneh et al., 2018), (9.993%) in Ambo (Albachew et al., 2015) and (8%) in Sweden (Peterson and Gustafsson, 2017). But it is lower than studies conducted in Ethiopia which are (19%) in Harar (Ayele et

al., 2018), (48.6%) in Adama (Hussein et al., 2014), (18.86 %) in India (Shareef et al., 2014) and (23.9%) in Malaysia (Redzuan et al., 2017). This variation might be due to some of the studies were performed on cardiovascular inpatients, lesser comorbidities in current study and only ADRs confirmed by physicians were considered which may underestimate the result. In this study the most frequently encountered ADRs were headache, peripheral edema and dry cough. This finding is similar with study done in Ethiopia, Adama (Hussein et al., 2014) and Jimma (Tegegne et al., 2015).

In the present study unnecessary drug therapy was found in (8.6%) of study participants. This was comparable with study conducted in Ethiopia, which is (10.7%) in Harar (Ayele et al., 2018) (5.66%) in India (Shareef et al., 2014) and (5%) in Sweden (Peterson and Gustafsson, 2017). But lower than previous findings in Ethiopia which are (30.19%) in Dessie (Belayneh et al., 2018), (24.5%) in Ambo (Albachew et al., 2015). Such variation might be due to difference in professionals working and guidelines they used. Most of study participants in Dessie Ethiopia were taking antibiotics and it was conducted prospectively in medical ward, which enable to check daily basis.

In the current study ineffective drug accounted (6.9 %) of all DTPs. This is lower than study findings from Jimma, Ethiopia (27.94%) (Yimam et al., 2018). The variation might be explained by DM was most common comorbidity in Jimma study that were taking amlodipine and HCT but guidelines recommend to use ACEI and nondihydropyridine CCB.

The identification of predictors of DTPs is important, as it helps to identify and prevent patients who are at risk, and need for close monitoring of drug therapy. The result of this study showed alcohol use, number of medications and BP control were statistically significantly associated with DTP occurrence. Previous studies identified different factors that are associated to occurrences of DTPs. Some of them including both number and presence of comorbidities, age, marital status, number of drugs, education level and uncontrolled BP (Yimam et al., 2018; Hussein et al., 2014; Hussien and Daba, 2017; Tegegne et al., 2015; Zazuli et al., 2017; Al-azzam et al., 2016). But in other study number of drugs, age and sex were not associated to presence of DTPs (Albachew et al., 2015). This discrepancy might be due to difference in factors and relates to diseases, drugs and behavior that may influence patients' taking the drugs.

Adherence to antihypertensive medication is vital in order to achieve BP control. Patients with poor adherence are highly susceptible to develop further complications and cause uncontrolled BP (Cutler et al., 2008; Asgedom et al., 2018).

The present study revealed that 51.5 % of study participants were non-adherent to their medications. This finding is in line with study findings (54.2%) in Palestine (Al-ramahi, 2014) and (54%) in Saudi Arabia (Khayyat et al., 2017). In comparison with current study there are studies reported lower prevalence, which is (35.4%) in Gondar (Ambaw et al., 2012) (37.8%) (Gebreyohannes et al., 2019), (38.2%) in Jimma (Asgedom et al., 2018), (30.8%) in Black Lion hospital (Hareri et al., 2013), (32.8%) in Dire Dawa (Hussen and Daba, 2017), (40.5%) in Adama (Hareri et al., 2014), (36.8%) in Palestine (Zyoud et al., 2013), (26.4%) in Jimma, Ethiopia (Yenesew et al., 2015), (22.4%) in Lebanon (Mohammad et al., 2015) and (12.3%) in Saudi Arabia (Ghobain et al., 2016). This discrepancy might be due to difference in adherence assessment tool for example in Ghobain *et al.* study patients labeled as nonadherent if they missed their medications for a total of 7 days during the previous month. In addition, better patients' knowledge and awareness about treatment in different study settings (private vs public) could affect level of adherence. Number of comorbidities and subsequent drug uses may cause regimen complexity and combinations of antihypertensive agents can worsen the situation for which patients suffer from difficulty of remembering and understanding drug information.

On the contrary there are several literatures that revealed higher level of nonadherence in Ethiopia, which is (68.13%) in Dessie (Gelaw et al., 2014), (67.7%) in Cameroon (Adidja et al., 2018), and (86.7%) in Brazil (Dosse et al., 2009). This variation might be due to most study participants in Ethiopia study had adverse effects and uncontrolled BP. The study conducted in Brazil a multidisciplinary team care report form and telephone interview was used and patient compliance to non-drug therapy was measured, which resulted in a higher prevalence.

The main reasons for non-adherence were forgetfulness followed by disbelief in drug effectiveness, fear of side effect, unavailability of drug product and patient feeling as better. This finding was supported by studies done in Ethiopia , Gondar (Gebreyohannes et al., 2019), Jimma (Yenesew et al., 2015), Adama (Hussein et al., 2014), Dire Dawa (Hussen and Daba, 2017), Saudi Arabia (Patel et al., 2015) and Palestine (Al-ramahi, 2014).

In this study physical activity, salt restriction and duration of antihypertensive medication were statistically significant with adherence. Another studies also revealed that physical activity, comorbidities and alcohol intake were associated with antihypertensive medication adherence (Asgedom et al., 2018 ; Al-ramahi, 2014; Ambaw et al., 2012; Belayneh et al., 2018 ; Anuwer et al., 2015).

Performing risk assessments to increase individual awareness of ASCVD risk is the first step in providing comprehensive cardiovascular risk reduction, this process also informs patients regarding the benefits and risks of interventions shown to reduce ASCVD risk. The cornerstone of any primary prevention strategy is lifestyle management, which includes following a healthy eating pattern, engaging in regular physical activity, maintaining a healthy weight, and avoiding tobacco products. Additionally, certain pharmacological interventions including aspirin and statins, have indications for primary prevention and are considered in select patient groups based on their ASCVD risk (Dixon et al., 2018).

In the current study the ten-year ASCVD risk score among 144 patients who had lipid profile was calculated and 40.3% of them had 20% or higher risk. This finding was lower than study done in USA (Navar et al., 2017) which revealed 60.6 % of study participants had 20% or higher risk and Wong et al. study revealed 55% of United State persons with hypertension were at high 10-year risk of CVD by Framingham risk assessment criteria or had pre-existing CVD (Wong et al., 2009). The variation could due to difference in race, high number of diabetic, male patients and smokers in Navar *et al.* study and difference in risk assessment in Wong *et al.* study. In the present study predictors for ASCVD risk were assessed and occupation, alcohol use and BP control were found to be statistically significant and associated to ASCVD risk of 20% or higher. Retired study participants were 5.56 times more likely to have 20% or higher ASCVD risk as compared to study participants who were employed (AOR=5.562 ,CI 1.391-22.230). This might be due to most patients are retired when their age is advanced that increase the CVD risk and their income is limited. This finding is in line with study done in Canada (Setayeshgar et al., 2013).

6. Limitation of the study

- This was cross-sectional study not followed patients prospectively and interventions to DTPs were not yet made
- Non-adherence and social habits might be underestimated in this study since it was assessed based on patients' self-reporting
- ADRs were retrieved from medical records without established causal relationship and taken only from medical chart without considering patients' complaint for ADR that could underestimate its prevalence
- DTPs were identified by the principal investigator which might cause bias

7. Conclusion

The prevalence of DTPs among hypertensive patients was high. The most common type of identified DTP was needs additional drug therapy. Alcohol use, number of drugs and BP control were statistically significant with the occurrence of DTPs. The rate of medication non-adherence was high and the main reason for non-adherence was forgetfulness. Physical activity, salt restriction and duration of treatment were significantly associated with level of adherence. The ten-year ASCVD risk among participants who had lipid profile was high. Occupation, alcohol use and BP control were statistically significant to ASCVD risk of 20% or higher.

8. Recommendations

Based on findings from this study, the following recommendations are provided:

- There should be clinical pharmacy services for timely detection, prevention and resolution of DTPs
- There should be use of medication reminders, single pill combination and education on importance of medication adherence to improve patient adherence
- Ensure availability of medicines with affordable costs in a hospital
- Physicians should monitor patients for signs of adverse drug effects , doing laboratory tests as necessary like lipid profile and estimating cardiovascular disease risk score
- There should be awareness on hypertension and educating people risk factors such as harmful use of alcohol, sedentary lifestyles and unhealthy diets.

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Annex I: English version of information sheet

Dear participant, Good Morning/Afternoon

Introduction

My name is ----- I am a member of study that is conducted at ALERT Centre, Addis Ababa, Ethiopia entitled “assessment of drug therapy problems and adherence among ambulatory hypertensive patients at ALERT follow up clinic. The study is being conducted by Miftah Shafi from Addis Ababa University, school of Pharmacy, department of clinical pharmacy and pharmacology, postgraduate program. I kindly request you to take part in this study and Your cooperation and willingness is vital in assessing drug therapy problems, adherence .The study will be carried out through recording medical findings from your medical chart and interviewing (if needed). The interview may take 10-15 minutes, so you are kindly asked to provide important information as honestly as you can. Your name will not be written in this form and will never be used in connection with any information we take from the chart and you tell us. There is no possible risk associated with participating in this study except the time spent to deliver information for us. All information taken from your medical chart or given by you will be kept strictly confidential. Your Participation is voluntary and you are not forced to participate in the study. If you feel discomfort with the study, it is your right to drop it. If you have any question regarding this study or would like to be informed of the results after its completion, please feel free to contact the principal investigator by information given below

Name: Miftah Shafi

Phone no: +251927173018

Email:miftahshafi@gmail.com

I, _____, have read the above information. I freely agree to participate in this study. I understand that I am free to refuse to answer any question and to withdraw from the study at any time. I understand that my responses will be kept anonymous.

Participant Signature _____ Date _____

Thank you for your participation

Annex II: Data abstraction format from patient interview (English version)

I. Socio-demographic characteristics			
1.Age(in years): -----			
2.Gender	<input type="checkbox"/> Male	<input type="checkbox"/> Female	Pregnant: <input type="checkbox"/> yes <input type="checkbox"/> No
3.Marital status:	<input type="checkbox"/> Single	<input type="checkbox"/> Married	<input type="checkbox"/> Divorced <input type="checkbox"/> Widowed
4.Educational status	<input type="checkbox"/> No formal edu. <input type="checkbox"/> elementary	<input type="checkbox"/> Grade 9-10 <input type="checkbox"/> Grade10-12	<input type="checkbox"/> College diploma <input type="checkbox"/> University degree and above
5.Residence(current)	<input type="checkbox"/> Addis Ababa <input type="checkbox"/> out of Addis Ababa		
6.Occupation	<input type="checkbox"/> Employed <input type="checkbox"/> Unemployed <input type="checkbox"/> merchant <input type="checkbox"/> laborer <input type="checkbox"/> Retried <input type="checkbox"/> Other(specify)_____		
7.Social habit	Cigarette Smoke	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> previous history of smoking	
	Caffeine use	<input type="checkbox"/> Yes <input type="checkbox"/> No	
	Alcohol use	<input type="checkbox"/> Yes <input type="checkbox"/> No	
	Kat chewing	<input type="checkbox"/> Yes <input type="checkbox"/> No	
	Salt restriction	<input type="checkbox"/> Yes <input type="checkbox"/> No	
8.Physical activity	<input type="checkbox"/> Yes <input type="checkbox"/> No if yes, for how long?		<input type="checkbox"/> < 30minutes/day <input type="checkbox"/> ≥30minutes/day
9. Source of your medication?	<input type="checkbox"/> Free <input type="checkbox"/> paid		

II. Assessment of adherence (MMAS-8)

No	Items	No	Yes
1	Do you sometimes forget to take your medicine?	0	1
2	People sometimes miss taking their medicines for reasons other than forgetting. Thinking over the past 2 weeks, were there any days when you did not take your medicine?	0	1
3	Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it?	0	1
4	When you travel or leave home, do you sometimes forget to bring along your medicine?	0	1
5	Did you take all your medicines yesterday?	1	0
6	when you feel like your symptoms are under control, do you sometimes stop taking your medicine?	0	1
7	Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?	0	1
8	How often do you have difficulty remembering to take all your medicine? 0. Never 1. Rarely 2. Once in a while 3. Sometimes 4. Usually 5. All the time	0	1
	Total score		

If you have any problems that challenges your medication adherence please select your reason (more than one answer is possible)

- Fear of adverse events
- Disbelief in drug effectiveness
- Directions not understood
- Patient forgets to take
- Patient felt better
- product not available
- Patient felt better worse
- Drug product too expensive
- Other specify-----

Annex III: Data abstraction format from patient medical chart

Card no: ----- Age (in year) _____ Weight (kg): _____ Height
(m) _____ BMI (kg/m²) _____ Systolic BP _____ Diastolic BP _____

Total cholesterol _____ Triglycerides _____ LDL _____ HDL _____

Blood glucose _____

1. Duration of hypertension treatment -----

2. Comorbidity Yes No

3. List of co morbidities

DM Asthma Ischemic heart disease

4. Stoke Arthritis Valvular heart disease

5. HF Dyslipidemia If other specify -----

Complications Yes No

6. Type of complication HHD Nephropathy peripheral neuropathy
 if other specify _____

7. Past Medications (dose, frequency, regimen)

8. Drug allergy:

9. Current medications (dose, frequency ,regimen)

10. Review of Systems (ROS) (abnormal findings only):

11. Abnormal organ function tests& electrolytes

12. Pertinent investigations and imaging

13. Vital sign (abnormal values, start from recent results)

14. BP measurements of last three visits

15. Assessment of adverse drug reaction (undesirable effect)

15.1. Was any adverse drug reaction to the prescribed medicines occurred? Yes No:

15.1.1. If yes would you describe the manifestation of the events -----?

- Headache
- Dry cough
- Ankle edema
- Constipation
- Hyperkalemia
- Hypotension
- Epigastric pain
- Gynecomastia
- If other specify –

16. Is there any drug interaction Yes No

Annex IV: Modified DTPs registration Format

Drug therapy problem category	Drug therapy problems cause
1. Unnecessary drug therapy	<input type="checkbox"/> Duplicate therapy <input type="checkbox"/> No medical indication at this time <input type="checkbox"/> Non drug therapy more appropriate <input type="checkbox"/> Treating avoidable adverse reaction <input type="checkbox"/> If other specify-----
2. Needs additional drug therapy	<input type="checkbox"/> Preventive therapy <input type="checkbox"/> Untreated condition <input type="checkbox"/> Synergistic therapy <input type="checkbox"/> If other specify-----
3. Ineffective therapy	<input type="checkbox"/> More effective therapy available <input type="checkbox"/> Condition refractory to drug <input type="checkbox"/> Dosage form inappropriate <input type="checkbox"/> Contraindication product <input type="checkbox"/> If other specify -----
4. Dosage too low	<input type="checkbox"/> Ineffective dose <input type="checkbox"/> Needs additional monitoring <input type="checkbox"/> Frequency inappropriate <input type="checkbox"/> If other specify-----
5. Adverse drug reaction	<input type="checkbox"/> Undesirable effect <input type="checkbox"/> Unsafe drug for the patient <input type="checkbox"/> Drug interaction <input type="checkbox"/> Allergic reaction <input type="checkbox"/> If other specify-----
6. Dosage too high	<input type="checkbox"/> Dose too high <input type="checkbox"/> Needs additional monitoring <input type="checkbox"/> Duration too long <input type="checkbox"/> If other specify -----
7. Drug interaction	<input type="checkbox"/> Precence of major or sever drug interaction among current medications

Annex V: Amharic version (የአማርኛ መጠይቅ ቅፅ)

ቅፅ 1: የስምምነት ቅፅ

ውድ ያቃለ መጠይቅ ተሳታፊ፤ እንደምን አደሩ/ዋሉ

ስሜ ----- ይባላል ፤ በአዲስ አበባ ዩንቨርሲቲ ጤና ሳይንስ ኮሌጅ ፈርማሲ ትምህርት ቤት በፋርማኮሎጂ እና ክሊኒካል ፋርማሲ ትምህርት ክፍል በፈርማሲ ፕራክቲስ የሁለተኛ ዲግሪ ተማሪ ስሆን፤ በአሁኑ ሰዓት እዚህ አለርት ሆስፒታል ህክምና በሚካታተሉ የደም ግፊት ታካሚዎች በመድሀኒት ህክምና ተያያዥ ችግሮች እና መድሀኒትን ባግባቡ በመውሰድ ዙሪያ ጥናት እያካሄድኩ እገኛለሁ፤ ስለዚህ የእናንተ ተሳትፎ እና ትብብር ለዚህ ጥናት በጣም አስፈላጊ በመሆኑ በጥናቱ ላይ እንድትሳተፉ በትህትና እጠይቃለሁ። ጥናቱም የሚካሄደው እናንተን ቃለ-መጠየቅ በማድረግ እና የህክምና ማህደራችሁን በመከለስ ይሆናል። ቃለ-መጠየቁ ከ 10-15 ደቂቃ ሊወስድ ስለሚችል በተቻለ መጠን ጥያቄዎችን ትእግስት በተሞላበት መንፈስ እንድትመልሱ በትህትና እጠይቃለሁ። እናንተ የምትሰጡት መረጃ ከመድኃኒት ጋር እና ተያያዥ ጉዳዮች ችግሮችን ለመፈታት ጠቃሚ ነው። በዚህ ጥናት ላይ እናንተ የምትሰጡት መረጃ በሚስጥር አንደሚያዝና ስማችሁን በማንኛውም ሁኔታ እንደማይጠቀስ ለረጋግጥላችሁ እወዳለሁ። የናንተ ተሳትፎ እዚህ ጥናት ላይ ሙሉ በሙሉ በፍቃደኝነት የተሞላ እና ማንም ሳትፈልጉ እንድትሳተፉ አያስገድዳችሁም። አንዴ ጥናቱ ላይ ከገባችሁ በኋላ በአጋጣሚ ያልተመቻችሁ ነገር ካለ በማንኛውም ሰዓት ከጥናቱ ራሳችሁን ማግለል ትችላላችሁ። ጥናቱን በተመለከተ ማንኛውም ግልጽ የልሆነ ነገር ፣ ስጋት፣ ካጋጠማችሁ ከታች በተቀመጠው አድራሻ ዋናውን አጥኚ መጠየቅ ትችላላችሁ።

ስም: ሚፍታህ ሻፊ

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እኔ _____ ከላይ የተገለፀውን መረጃ አንብቤ ተረድቻለሁ፤ በጥናቱም ለመሳተፍ ሙሉ ፍቃደኛ ነኝ።

የተሳታፊ ፊርማ _____ ቀን _____

ውድ ጊዜዎን ሰጥተው ስለተሳተፉ አመሰግናለሁ!!

ሀ. የታካሚ ማህበረሰባዊ ባህሪያቶች መረጃ በተመለከተ (መመሪያ: ለመረጡት ምላሽ የx ምልክትን ያድርጉ)

ክፍል 1: የመላሾች ማህበረሰባዊ ሁኔታ			
1. እድሜ: -----			
2. ፆታ	<input type="checkbox"/> ወንድ	<input type="checkbox"/> ሴት	<input type="checkbox"/> እርጉዝ: <input type="checkbox"/> አዎ <input type="checkbox"/> አይደለም
3. የጋብቻ ሁኔታ	<input type="checkbox"/> ያላገባ <input type="checkbox"/> ያገባ	<input type="checkbox"/> የሞተበት <input type="checkbox"/> የፈታ	
4. የትምህርት ደረጃ	<input type="checkbox"/> ማንበብና መጻፍ የማይችል <input type="checkbox"/> 2ኛ ደረጃ	<input type="checkbox"/> መሰናዶ <input type="checkbox"/> ኮሌጅ ዲፕሎማ	<input type="checkbox"/> የመጀመሪያ ደረጃ <input type="checkbox"/> ዲግሪና ከዛ በላይ
5. የመኖሪያ ቦታ	<input type="checkbox"/> አዲስ አበባ	<input type="checkbox"/>	ከአዲስ አበባ ዉጪ
6. ሥራ ምንድነው?	<input type="checkbox"/> የመንግስት ሰራተኛ <input type="checkbox"/> ጡረታ	<input type="checkbox"/> ስራ -አጥ <input type="checkbox"/> ሌላ(ይገለፅ)-----	<input type="checkbox"/> የቀን ሰራተኛ <input type="checkbox"/> ነጋዴ
7. ማህበራዊ ልማድ:	ስጋረ የጨሰሉ?	<input type="checkbox"/> አዎ	<input type="checkbox"/> አላጨሰም <input type="checkbox"/> ከዚህ በፊት አጨሰ ነበር
	አልኮል ይጠጣሉ?	<input type="checkbox"/> አዎ	<input type="checkbox"/> አልጠጣም
	የጨው አጠቃቀም?	<input type="checkbox"/> የተወሰነ	<input type="checkbox"/> የልተወሰነ
	ቡና ይጠጣሉ?	<input type="checkbox"/> አዎ	<input type="checkbox"/> አልጠጣም
	ጫት ይቅማሉ?	<input type="checkbox"/> አዎ	<input type="checkbox"/> አልቅምም
8. የአካል ብቃት እንቅስቃሴ ያደርጋሉ?	<input type="checkbox"/> አዎ <input type="checkbox"/> አይደለም	አዎ ካሉ	<input type="checkbox"/> በቀን ከ 30 ደቂቃ ያነሰ <input type="checkbox"/> በቀን 30 ደቂቃ
9. የህክምና ወጪዎን የሚሸፍነው?	<input type="checkbox"/> በነጻ	<input type="checkbox"/> በግዢ	

ክፍል2: ሞሪስኪ” መድኃኒትን በታዘዘው መሰረት በአግባቡ ስለመውሰድ መለኪያ- 8

ጥያቄዎች	አይደለም	አዎ
1 አንዳንድ ጊዜ መድኃኒትዎን ረስተው ሳይወስዱ ቀርተው ያዉቃሉ?	0	1
2 ሰዎች አንዳንድ ጊዜ ከመርሳት በተጨማሪ ባሉት የተለያዩ ምክንያቶች መድኃኒታቸውን ሳይወስዱ ይቀራሉ። ባለፉት ሁለት ሳምንታት፣ መድኃኒትዎን ሳይወስዱ የቀሩበት ቀኖች ነበሩ?	0	1
3 መድኃኒትዎን እየወሰዱ ህመም ሲባባስ ሐኪምዎን ሳያጠየቁ መድኃኒትዎን አቋርጠው ያዉቃሉ?	0	1
4 በጉዞ ወይም በሌላ ምክንያት ከቤትዎ ርቀው ሲጓዙ አንዳንድ ጊዜ መድኃኒትዎን ረስተውት ሳይወስዱ ያዉቃሉ?	0	1
5 በትላንትናው ዕለት ሁሉንም መድኃኒትዎን ወስደዋል?	1	0
6 ህመም ሲሸልዎት (የህመም ስሜቶች ሲጠፉ) አንዳንድ ጊዜ መድኃኒትዎን አቋርጠው ያዉቃሉ?	0	1
7 መድሀኒቶችን በየቀኑ መውሰድ ለአንዳንድ ሰዎች ምችት ይነሳቸዋል። እርስዎ በህክምና ክትትል ወቅት በየቀኑ ወይም አንድም ጊዜ ሳያዘንፉ መድሀኒት በትክክል ለመውሰድ ተሰላችተው ያዉቃሉ?	0	1
8 ሁሉንም መድሀኒቶች መውሰድ አለመውሰድዎን ማስታወስ የከበደዎት ጊዜ አለ? በፍፁም <input type="checkbox"/> አልፎአልፎ <input type="checkbox"/> አንዳንድ ጊዜ <input type="checkbox"/> አብዛኛው ጊዜ <input type="checkbox"/> ሁል ጊዜ <input type="checkbox"/>	0	1
አጠቃላይ ድምር		

2.1. መድሀኒትዎን በአግባቡ ካልወሰዱ እባክዎ ምክንያቱን ይግለጹ (ከ አንድ በላይ መልስ መምረጥ ይቻላል)

- የጎረቤት ጉዳትን በመፍራት
- ያድነኛል ብዬ ስለማለስብ
- ስለመድሀኒቱ አወሳሰድ በቂ መረጃ ስለሌኝ
- መድሀኒቱን ስወስድ ህመሜ ስለሚባባስብኝ
- መድሀኒቱን ማግኘት ስላልቻልኩ
- መድሀኒቱን ስውጠው ስለሚያስቸግረኝ
- ስለምረሳው
- የምወስዷቸው መድሀኒቶች ብዙና ግራ የሚያጋቡ ስለሆኑ
- ተሽሎኛል ብዬ ስለማስብ
- መድሀኒቱ ውድ ስለሆነ
- ሌላም ካለ ይግለጹ-----

Annex VI: Ethical clearance

<p>በ ፋርማሳ ት/ቤት የኢትዮጵያ ሪፐብሊክ</p>	<p>አዲስ አበባ ዩኒቨርሲቲ Addis Ababa University</p> 	<p>School of Pharmacy Ethical Review Board</p>
		<p>ቀን Date: August 13, 2018</p> <p>ቁጥር Ref. No: ERB/SOP/38/10/2018</p>
<p>To: Miftah Shafi School of Pharmacy</p>		
<p>Re: <u>Ethical Clearance</u></p>		
<p>It is to be recalled that you submitted a study proposal entitled "Assessment of Drug Therapy Problems, Adherence and Treatment Satisfaction among Adult Hypertensive Patients at ALERT Hospital: A Cross-sectional Study" for ethical approval by the School's Ethical Review Board (ERB). The Board thoroughly reviewed the study proposal based on its operational guidelines and found it to fulfill all ethical requirements stipulated in the guidelines. This is, therefore, to inform you that the proposal is ethically approved for implementation.</p>		
<p>With best regards,</p> <p> Daniel Bisrat (D) Secretary, ERB</p> 		
<hr/>		
<p>☎ 00251156 02 12 ✉ 1176</p>	<p>ቴሌኮን Telex: 21205</p>	<p>ፋክስ Fax: 00251(11)1558566</p>
<p>ካብል Cable: AAUNIV</p>		