Assessment of Drug Therapy Problems and Medication Adherence among Ambulatory Hypertensive Patients on Follow up at Tikur Anbessa Specialized Hospital

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This is to certify that the thesis prepared by Melaku Tileku Tamiru, entitled with: ***"Assessment of Drug Therapy Problems and Medication Adherence among Ambulatory Hypertensive Patients on Follow up at Tikur Anbessa Specialized Hospital"*** and submitted in partial fulfillment of the requirements for the Degree of Master of Pharmacy 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 Medication Adherence among Hypertensive Patients on follow-up at Tikur Anbessa Specialized Hospital

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Hypertensive patients are at high risk of drug therapy problems (DTPs), as there is multiple drug use for their comorbidities. To date, studies regarding DTPs in hypertensive patients are limited in Ethiopia. Thus, this study aimed to assess DTPs and medication adherence among ambulatory hypertensive patients on follow up at Tikur Anbessa Specialized Hospital (TASH). A hospital based cross sectional study was employed in 388 participants who fulfilled the inclusion criteria. Participants were interviewed and their medical chart was reviewed through a structured data collection formats. DTPs were assessed using Cipolle/Morely/Strand's DTPs classification system. Data were reported as mean/percentage and multivariate logistic regression was performed to identify associated factors with DTPs. Out of 388 study participants, 283 of them had at least one DTP, of which 49.5% and 40.3% had drug interactions and adverse drug reactions (ADRs), respectively. Factors associated with DTPs, were old age (Adjusted Odds Ratio [AOR] =1.05, 5%CI:1.02-1.08), longer duration of treatment (AOR=1.06,95% CI:1.01-1.10), presence of complaints (AOR=2.23, 95%CI:1.06-4.71), ≥3 comorbidities (AOR=2.27, 95%CI:1.06-4.88), ≥5 drugs use (AOR=2.15, 95%CI:1.02-4.50), statins use (AOR=2.62, 95%CI:1.09-6.30) and aspirin use (AOR=3.79, 95%CI:1.11-12.87). About 45% of the study participants were non-adherent to their antihypertensives. Factors for non-adherence were monthly income of <500 Ethiopian birr (AOR=1.68, 95%CI: 1.03-2.72), ≥5 drugs use (AOR=2.36, 95%CI: 1.02-5.47), use of antidiabetics (AOR=1.95, 95%CI: 1.09-3.51) and non-steroidal anti-inflammatory drugs use (AOR=0.43, 95%CI: 0.20-0.91). DTPs were common among ambulatory hypertensive patients in TASH, indicating a need of multidisciplinary team that involved pharmaceutical care providers to identify and resolve DTPs in this setting.

Key words: Hypertension, drug therapy problems, medication adherence, Ethiopia

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List of Abbreviations and Acronyms

ADRs	Adverse Drug Reactions
AOR	Adjusted Odds Ratio
BP	Blood Pressure
CI	Confidence Interval
CVD	Cardio Vascular Disease
DDIs	Drug-Drug Interactions
DTPs	Drug Therapy Problems
eGFR	estimated Glomerular Filtration Rate
JNC	Joint National Committee
LMICs	Low and Middle Income Countries
MDRD	Modification of Diet in Renal Disease
MMAS	Morisky's Medication Adherence Scale
NCD	Non Communicable Disease
NSAIDs	Non-Steroidal Anti-inflammatory Drugs
OR	Odds Ratio
PCNE	Pharmaceutical Care Network of Europe
SD	Standard Deviation
SPSS	Statistical Package for Social Sciences
TASH	Tikur Anbessa Specialized Hospital
WHO	World Health Organization

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1. Introduction

1.1. Background

Hypertension is a chronic non-communicable disease (NCD) in which the blood pressure (BP) in the arteries is persistently elevated. It is defined as a systolic BP equal to or above 140 mmHg and/or diastolic BP equal to or above 90 mmHg (1). Hypertension can be classified into two major types: Primary Hypertension and Secondary Hypertension. Primary Hypertension is due to non-specific lifestyle and genetic factors. Lifestyle factors such as physical inactivity, high salt intake, poor fruit and vegetables intake, obesity, drinking of alcohol and cigarette smoking are known to increase Primary Hypertension. Secondary Hypertension is due to identifiable cause such as chronic kidney disease, endocrine disorders or drugs. About 90% to 95% cases are of Primary and the rest 5% to 10% are of Secondary Hypertension (2).

The worldwide prevalence of hypertension has significantly increased from about 972 million (26.4%) in 2000 (3) to 1.39 billion (31.1%) in 2010 (4). By 2025, it is estimated that this number will escalate to more than 1.56 billion (60%) (5). Hypertension in Africa had risen from 55 million in 1990 to 130 million in 2010, and if action is not taken, could increase to nearly 220 million by 2030 (6). Men have higher BP than women in most countries in the world. However, it is more common in older ages. There is a crude increase in the prevalence of hypertension in the last four decade by 90%, majorly in low and middle income countries (LMICs). From 2000 to 2010, prevalence of hypertension decreased by 2.6% in high-income countries, but increased by 7.7% in LMICs (7). A community based survey from nine regions of the country showed the prevalence of hypertension among Ethiopian population to be 15.8%. The prevalence is higher in the urban population (19.7 %) than rural (14.8 %). The prevalence in females (16.3 %) and males (15.5 %) is similar (8).

Hypertension raises the incidence of cardiovascular diseases (CVDs) and their consequences. For instance, in 2015, out of 56 million total deaths, an estimated 40 million (70%) were due to NCDs, of which CVDs accounted for 17.7 million deaths (45% of NCD deaths) (9), and 55% of the 17.7 million deaths were linked to hypertension (3). If nothing is done about it, by 2020, three-fourth of all deaths in Africa will be attributable to hypertension (6). Unless BP isn’t controlled optimally, it lead to cardiovascular, cerebrovascular and kidney diseases (10).

Most hypertensive patients suffer from other comorbidities which require proper combinations of antihypertensive agents and other medications (11). Some comorbidities such as diabetes and dyslipidemia are also associated with uncontrolled hypertension (12, 13). It also has financial implications for national and local treatment plans. This is because the majority of hypertensive patients will require combinations of drugs to achieve BP control (11). Combination therapy with multiple medications can lead to the occurrence of drug therapy problems (DTPs) such as adverse effects, drug-drug interactions, inappropriate selection of drugs and inappropriate dosage of drugs (14). Another study indicated the association between the presence of DTPs and hypertension is highly significant (15).

There are variations in the definitions and classification system of DTPs in different literatures. Cipolle/Morley/Strand classification system is one of them which defines DTPs as any undesirable event experienced by a patient that involves, or is suspected to involve, drug therapy, and that interferes with achieving the desired goals of therapy and requires professional judgment to resolve. The problems may occur in the whole drug therapy chain. In this classification, DTPs are classified as: Need for additional drug therapy, Unnecessary drug therapy, Ineffective drug, Dosage is too low, Adverse drug reaction, Dosage is too high and Non-adherence (16).

If not resolved, DTPs have clinical consequences. Non-adherence for example, may lead to treatment failure, reduced quality of life, and increased morbidity and mortality (17). Ineffective drug use can be a challenge in patients' management, for example, optimal levels of blood glucose, cholesterol or BP cannot achieved during treatment (18), which will pose a serious medical and economic problem for society. Fortunately, numerous studies showed that majority of DTPs (50-80%) are often preventable (19).

Pharmaceutical care practitioners need to prevent, identify and resolve DTPs, if occurred, and increase patients' quality of life (20, 21). Identification of DTPs among ambulatory hypertensive patients is critically important to ensure patients' safety and treatment optimization. Hence, this study was conducted to assess the types and number of DTPs that occur in hypertensive patients on follow up at Tikur Anbessa Specialized Hospital (TASH).

1.2. Statement of the problem

Health is a human right and the attainment of health is a most important social goal in the world. Medicines play vital role for diagnosis, prevention and treatment of diseases to maintain health (22). However, access to medicines for NCDs, including hypertension is still a challenge, and development of new drugs remains far from the health needs of developing countries (23). In addition, drug therapy is more complex and is challenging to prescribe and use drugs appropriately (24). Use of drugs that are not needed and/or prescribing drugs without adequate scrutiny regarding their efficacy, safety, affordability, and suitability can lead to DTPs (25, 26).

A number of DTPs exist because of the availability of many drugs, complex drug regimen, high burden of diseases and number of patients (27). Antihypertensive, Antidiabetics and lipid modifying drugs are the most common drug classes that are mostly involved in DTPs (28). Hypertensive patients use those and other medicines for their multiple comorbidities (11), which showed significant correlation with DTPs (14). In addition, the presence of DTPs in hypertension, diabetes, dyslipidemia, ischemic heart disease, heart failure, and gout treatment is highly significant (15). Furthermore, the equipment used to measure BP has changed with most monitors now being digital rather than a level of mercury rising on a measure. This may result in inappropriate record that may affect treatment trend (29) and can be a source of DTP. Hence, the frequency of DTPs in hypertensive patients has been reported to be high (30), which can reach up to more than 90% (31-33).

DTPs are reasons for hospitalization in 65% of patients with CVDs including hypertension (34), which may result in reduced quality of life, and increased morbidity and mortality (17, 35-37). One-third of the patients visiting emergency clinics had at least one DTP (38) and about 5 to 10% of hospital admissions were due to DTPs (39). The costs of hospital admissions due to DTPs are substantial as well (40). For example, drug related morbidity and mortality in the ambulatory setting in the USA was estimated to cost $76.6 Billion in 1995 (22), which had raised to $177.4 Billion in 2001 (41). The cost may be reflected in absenteeism, low productivity, high health care cost, and low quality of life (42, 43). Therefore, DTPs incur economic costs and are of major concern due to their psychosocial and physical burdens (44).

Attention to DTPs has been given after the incidence of aplastic anemia following treatment with chloramphenicol (45) and birth defects after the use of thalidomide (46). Since then, research in DTPs has been intensified in developed nations (24). Conversely, there is a scarcity of published data on DTPs in developing nations (47). In addition, despite their consequences, the level of impact of DTPs is not considered to be huge by clinicians, as it did not comprise a huge part of their workload, although such events could be emotionally distressing (24).

Most of the DTPs are preventable (48) and measures taken can improve patient outcomes, save lives, and enhance patients' quality of life (49). Although ADRs have been most frequently studied category of DTPs, in the long run, other DTPs may be as important as ADRs (50). Hence, a broad approach to the issue of DTPs is needed. This is because by identifying all types of DTPs including the potential DTPs, precautions may be taken to prevent them from becoming overt clinical problems. In addition, a wider definition of DTP could provide a basis for understanding the whole spectrum of DTPs.

The fact that daily life in a follow-up clinic for hypertension in a hospital is characterized by high patient turnover, lack of time, high speed and unplanned events, which are in many ways a chaotic situation, give limited room to evaluate drug treatment. In addition, when treatment with a new drug is started, it is difficult to optimize dosage because of the short hospital stay since steady state often has not been reached. Hence, it is hard to evaluate the long-term drugs effect and drug interactions with already established drug regimens. This makes it necessary to focus on DTPs. Previous studies have mainly addressed DTPs as a cause of hospitalization (51-58). However, DTPs that arise in the tertiary care hospital setting have rarely been described (24).

A study of DTPs provides valuable insights to reduce the incidence of DTPs. The data from this study can feed into decision making pertaining to reduction of DTPs through formulating and implementing management strategies based on the findings. Therefore, the primary aim of this study was to determine the prevalence of DTPs, medications involved in experiencing DTPs and factors associated with DTPs among hypertensive patients on follow up at TASH.

1.3. Literature review

1.3.1. Drug therapy problems

DTPs are a major public health issue for chronic patients (59). Findings from a meta-analysis of ninety five studies indicated that the prevalence of medication-related hospitalizations has been reported to be as high as 54%, and cardiovascular drugs were involved in DTP and frequently implicated for hospitalization (60).

Studies assessing DTPs in high income countries have identified that, psychotropic drugs, NSAIDs and other analgesics, and vitamins/minerals to cause DTPs in addition to cardiovascular drugs (61). About 63 % of patients had DTPs in Northern Cyprus (62) and the rate was increased to 66% in Sweden (61). Mining of the literature demonstrated that DTPs associated with safety, particularly related to ADRs (46%-54%) are the most common ones followed by effectiveness (22-28%), and necessity (26%) (62, 63). Adherence seems to have a wide range (19%-72%) in different studies (62, 64). ADRs have been a cause for 6.5% of the emergency visits in Germany (65), and often lead to 0.6% of all hospital admissions in Argentina (66), of which 2.8% of them occur due to drug-drug interactions (DDIs) (67). DDIs are likely to be highly underestimated as medication-related issues, as they are commonly reported as ADRs. Complex disease states also may make recognizing a DDI more challenging, further contributing to underreporting, though the clinical impact of a DDI can sometimes be life-threatening (68).

Studies that came out from the middle income countries have indicated that, the association between the presence of DTPs and hypertension, diabetes, dyslipidemia, ischemic heart disease, heart failure, and gout is highly significant (15). Most commonly involved drugs in DTPs were aspirin, clopidegrol, simvastatin, amlodipine and metformin (69). Another study revealed that 19.8% of drug-related cases were caused by cardiovascular drugs (70). Prevalence of DTPs was ranging from 45.8% in Indonesia (71) to 90.5 % in Malaysia (69). The most frequent type of DTP in Indonesia was a need for additional drug therapy (47%) followed by ineffectiveness (21.2%), non-adherence (13.6%), ADR (9.1%), unnecessary drug therapy (7.6%) and dose too low (1.5%). A slight variation from the Indonesian study was noted in another study conducted in Jordan, Middle East and North Africa (15). This study reported need for additional drug therapy (41.73%) and non-adherence (13.45%) to be most common DTPs. Overdose of drugs

was also demonstrated to be a DTP responsible for most of the hospital admissions in India (70). The Malaysian study alluded to the fact that insufficient awareness (26%), drug choice problems (23%), dosing problems (16%) and DDIs (16%) have been the most commonly observed DTPs (69).

A retrospective evaluation of case notes of hypertensive and/or diabetic patients, who attended two tertiary health institutions, was carried out in Niger. Data were collected using a data collection form which included information like medications prescribed (in the first and the last four months of clinic visits). Average numbers of drugs and DTP per patient (Mean ± SD) at the first month of data evaluation and the fourth month of therapy were compared, and showed that unnecessary drug therapy in the first and fourth-month (23.6% vs. 29.4%) was the most commonly observed DTP, followed by wrong drug therapy (23.4% vs. 22.9%), need for additional drug therapy (20.9% vs. 17.4%), non-adherence (15.4% vs. 13.8%), drug interactions (12.9% vs. 9.6%), dosage too low (1.5 % vs. 5.2 %), ADR (1.4 % vs. 1.3 %), and dosage too high (0.9 % vs. 0.4 %) (72).

The prevalence of DTP was found to range from (72%-89%) in different hospital settings (73, 74). Whilst drug interaction (57.3%) was reported to be the most frequent DTP in Adama hospital (75), need additional therapy had been the prevalent DTPs in Felege Hiwot and Jimma (90.7%) (76), Felege Hiwot (66.28%) (31), and Gebretsadik Showa hospital (33.1%) (74). Unnecessary drug therapy (24.5%) was also the most common type of DTP in Ambo hospital (73). ADRs and non-adherence were second most commonly observed DTPs in different hospital settings (31, 73, 75), while other categories of DTPs were reported as less important.

1.3.2. Factors associated with drug therapy problems

A systemic review indicated that majority of DTP studies were conducted in high income countries (39). Number of drugs were found to be directly associated with number of DTPs in a study done at Norway (77), and Singapore (78), while old age and renal impairment were additional risk factors for DTP occurrence in Sweden (61). In a qualitative study from an expert panel, it was showed that polypharmacy, cognitive situation (confusion), missing information, non-adherence, polymorbidity, visual, renal and hepatic impairment, ADR, language issues,

impaired manual skills, self-medication and drugs like antiepileptics, antidiabetics, anticoagulants, NSAIDs, diuretics, tricyclic antidepressants, anticholinergics, benzodiazepines, opioids, corticosteroids and digoxin were important risk factors for DTP occurrences (79).

Other studies carried out elsewhere produced varied results. Male gender, old age, renal impairment, polypharmacy, poor BP control, CVDs, longer hospital stay and drugs such as antihypertensives, lipid-modifying and antidiabetics were found to be significantly associated with the occurrence of DTPs in Malaysia (69). Education was significantly associated with DTPs in some studies (15) but not in others (71). Other factors, including older age, not married, not having health insurance, and co-morbidities (type and number), and number of drugs were associated with DTPs in Jordan (15) as well as local studies (73, 75).

1.3.3. Medication adherence and associated factors

There is currently no universally agreed method and/or tool used to evaluate medication adherence, and is a potential source of substantial heterogeneity (80). In a survey done among 2746 clinicians in 150 cities across India, majority (93.5%) of them said that one-fourth of patients had uncontrolled BP and was due to non-adherence (81).

In a recent review by Abegaz *et al* (82), 45.3% of patients with hypertension globally were non-adherent to their medication, with a non-adherence rate as high as 62.5% reported among African patients. There are also adherence problems in European countries. For instance, in a cross-sectional study conducted in Portugal, 36.8%, 17%, and 46.2% of the participants had poor, moderate and high adherence. Forgetfulness (31.4%) is the major reason for non-adherence (83). A qualitative study done in Spain implied factors for non-compliance included fears and negative images of antihypertensive drugs; lack of basic knowledge about hypertension; clinical encounter was viewed as unsatisfactory because of its length; few explanations given by the physician and low physician–patient interaction (84).

The prevalence of non-adherence was 86.76% in Brazil. Emotional factor (69.1%) followed by could not tell the reason (10.3%) and eating habits (8.8%) (85) were major reasons for non-adherence. About 50%, 27.1%, and 22.4% of the participants had high, medium, and low

adherence in Lebanon. Having controlled BP and taking a combination drug were predictors of high adherence, while forgetfulness, drug regimen complexity, and side effects were for low adherence (86). A study from Malaysia revealed that good adherence was observed in 53.4% of the patients sampled. Female patients were more adherent to their medication, while increasing the number of drugs and their daily dose frequencies negatively affected adherence (87). About 36.2%, 26.8%, 36.8% of the participants had high, medium, and low adherence, respectively in Palestine (88), while it was about 16.9%, 28.9%, and 54.2% in another study from this country. Young age, living in a village, health status level below excellent, forgetfulness, fear of getting medication, adverse effect, and dissatisfaction with treatment had a significant association with non-adherence (89). The prevalence of adherence was 49.8% in Vietnam. Awareness of complications related to hypertension was the main reason for adherence (90).

A prospective study carried out in Ghana showed the non-adherence rate of 31.3%, for which forgetfulness (45.4%) was the major cause followed by side effects (20.8%), feeling very well (16%), financial problems (10.4%), and too busy work schedules and forgot to report for reviews and remember to take medicines on time (7.6%) (91). About 54% of the participants were adherent in Nigeria. Patients with formal education, higher monthly income, those on single drugs were more adherent. The major causes for poor adherence were ignorance on need for regular treatment (32.7%) and financial problems (32.7%) followed by drug side effects (12.1%), unavailability of drugs (8.0%), polypharmacy and non-attendance at scheduled clinic day (4.8%), normal BP on previous clinic visit (3.6%), forgetfulness (3.0%), and busy schedule (1.8%) (92). Another study in Nigeria reported that the prevalence of non-adherence was 34.6%. Most of the patients (90.1%) sometimes forget taking medicines or do not bring medicines along when they leave home (94.3%). The highest rates of on-adherence were reported in totally dependent patients (62.5%). High depression scores, low disability scores and the presence of peptic ulcer disease were significantly correlated with non-adherence (93).

The prevalence of non-adherence was 32.8%, 35.4%, 38.2%, 45.8%, 68.13%, and 68.6% in Debre Markos, Gondar, Jimma, Adama, Dessie, and Nedjo, respectively (94-99). In a cross sectional study conducted in Debre Markos, a favorable attitude towards antihypertensive medications, good patient-provider relationship, one or no comorbidities, a long duration of treatment, and a low

medical cost had associations with good adherence (94). In a cross-sectional survey done in Gondar, sex (being female), knowledge about hypertension and its treatment (right), distance from the hospital (being closer) and number of comorbidities (with no or one) were associated with good adherence (95). In a study conducted in Jimma, presence of comorbidity, alcohol intake, self-purchasing of medications and combination of antihypertensive medications were associated with non-adherence (96). In a cross-sectional study in Adama, the most common reason for non-adherence was financial problem (44.9%) followed by negligence, forgetfulness, adverse effects, old age, disability and use of social drugs (97). A cross sectional study conducted in Dessie showed that the major reasons for non-adherence were economic problem (74.7%) and lack of information (48.13%). Other reasons reported included loss of hope, interference with daily routine activities and hobbies, adverse effects, loss of any pleasant activity, and use of social drugs, distance, forgetfulness and taking extra dose of medication (98). A cross-sectional study carried out at Nedjo showed that old age, illiteracy, income of <500 birr, duration of treatments ≥5 years, physical inactivity and knowledge deficit about hypertension and its treatment were significantly associated with non-adherence. The major reasons for non-adherence were forgetfulness, followed by inability to buy medications (99).

2. Objective

2.1. General objective

- This study was aimed to assess DTPs and medication adherence among hypertensive patients on follow-up at TASH.

2.2. Specific objectives

- To determine the prevalence of DTPs among hypertensive patients
- To identify the most common drugs involved in DTPs among hypertensive patients
- To identify contributing factors for DTPs among hypertensive patients
- To determine the rate of adherence among hypertensive patients
- To identify factors associated with non-adherence among hypertensive patients

3. Methods

3.1. Study setting

The study was conducted in TASH, a referral public tertiary care hospital established in 1972 in Addis Ababa, Ethiopia. It is a training center for postgraduate and undergraduate medical students, and other health sciences students. It is also an institution where specialized comprehensive clinical services that are not available in other public or private institutions are rendered. It also has the lion share of health care delivery in the country. This hospital offers diagnosis and treatment for approximately 370,000 - 400,000 patients a year (100). Among the specialty clinics in TASH, renal referral clinic is one of them and serving for a comprehensive kidney related cases including hypertension. The clinic provides the service to the population both within and outside of Addis Ababa three days per week (every Monday, Tuesday and Thursday). The clinic has four senior physicians, eight nurses and one support staff members.

3.2. Study design and study period

A hospital based cross sectional study design was employed. The data were collected for the period of four months (from February 1, 2018 to May 30, 2018) and data from patients' medical chart from June 1, 2017 to May 30, 2018 were used for the study.

3.3. Source and study population

All patients with hypertension who visited the renal clinic of TASH formed source population of the study. All adult patients with hypertension on follow-up clinic at TASH during the study period and fulfilling the inclusion criteria were a study population of the study.

3.4. Inclusion and exclusion criteria

Inclusion criteria:

Patients diagnosed with hypertension aged 18 years and above

Ambulatory hypertensive patients who were taking antihypertensive drugs for at least 1 year

Exclusion criteria:

Patients who had incomplete medical records

Patients who could not respond for example, too sick to be interviewed

Patients who refused to participate in the study were excluded.

3.5. Sample size determination and sampling technique

The sample size required was calculated using single proportion sample size estimating formula.

$$n = \frac{\left(Z_{\alpha/2}\right)^2 P(1-P)}{d^2}$$

(Where n = required initial sample size, $Z\ a/2$ = critical value for normal distribution at 95% confidence interval which equals 1.96 (Z value at alpha = 0.05), P = proportion of success; (p=0.5), q = proportion of population with hypertension not having DTPs (q=0.5), and d = marginal error (5%=0.05): Therefore, substituting all values in the above formula, n =384. This cross-sectional study aim to estimate the prevalence of unknown parameter (s) in this hospital and is considered as a baseline data from the target population using a random sample, an adequate sample size was needed to estimate the population prevalence with a good precision. This can be estimated of course from previous studies published in the study domain to estimate the assumed P value. However, there is no DTP assessment study in a tertiary care hospital of the country. Those studies done in other hospitals in Ethiopia couldn't necessarily reflect TASH's trend. Therefore, P value were taken to be 0.5 as optimum and larger sample size was an essential component in the study.

An approximate population of the study (based on appointment period on follow-up clinic registration book) within the data collection period were 1920 (N), which was an average of 40 patients per day. Considering 10% contingency for non-response rate, the final targeted sample size of the study was calculated to be 423 ambulatory hypertensive patients on follow-up. Systematic random sampling technique was used to collect the samples. Sampling interval (k^{th}) was determined by dividing the total number of hypertensive patients that came within the study period (four month) by the allocated sample size. Total number of patients within four months= 1920; Sample size=423. Hence sampling interval was calculated as follows:

$$K = \frac{1920}{423} = 4$$

The first patient was selected through simple random sampling then every 4^{th} patient, selection continued from the patient registration list until the required sample was reached.

3.6. Study variables

Dependent variables:

Drug Therapy Problems (Need for additional drug therapy, Unnecessary drug therapy, Ineffective drug, Inappropriate dosage, Adverse drug reactions, Drug interactions) and Non-adherence

Independent variables:

Socio-demographic characteristics (age, gender, level of education, residence and marital status), social habits (physical activities, kchat chewing, coffee drinking, smoking and alcohol use), presence of comorbid condition and complications, number of prescribed medications, duration of the hypertension and its treatment, hospitalizations due to uncontrolleld BP, source of medication and use of traditional medicine, BMI, eGFR and other clinical characteristics.

3.7. Data collection instruments and procedures

A structured questionnaire was prepared according to the objectives of the study and the local situation of the study area in English. The questionnaire was then translated to Amharic and back to English to assure consistency of the tool. Discrepancies in the translation were resolved by mutual agreement with the medication therapy management project team. Primary data were then collected using an interviewer administered questionnaire (Annex VII) on socio-demographic and clinical characteristics and secondary data were collected retrospectively using structured data abstraction formats (Annex V) from medical chart to record laboratory results, current medications, co-morbidities, treatments and other relevant medical and medication histories. This was complemented by self-administered key informant questionnaire (Annex I). Appropriateness of drug therapy was evaluated using various references and guidelines: Guidelines on Clinical and Programmatic Management of major NCDs, Joint National Committee (JNC-VIII), American Heart Association/American College of Cardiology and American Diabetes Association (2). Micromedex drug interaction checker was used to identify DDIs and absolute contraindications. Actual and potential major DDIs were taken as a significant DDIs while others were omitted. ADRs were identified from the patient reports and from medical charts which were already recorded by the attending physician.

Nowadays, different classifications of DTPs are used with discrepancies (14, 101-113). Most DTPs classification systems only have a problem and intervention section. Only some classifications like Cipolle/Morley/Strand classification have a separate section for categorizing the causes of DTPs. Because of the multifaceted nature of various DTPs, it is hard to select one. Cipolle/Morley/Strand classification includes problems in the whole drug therapy chain from patient's perspective. This system is in use in America (16). The Ethiopian Federal Ministry of Health also requested pharmacists working in wards and clinics to report DTPs as per a form that adopted this classification system. Hence, this classification system was used in the study because of these backgrounds in order to define, identify, classify and record DTPs using the pretested data collection abstract formats.

As many drugs are eliminated through kidney, inappropriate use during renal impairment may result in adverse events that are challenging in clinical practice. In this study, patients were divided into five stages of renal impairment according to the National Kidney Foundation. Accordingly, the Modification of Diet in Renal Disease (MDRD) was applied to calculate eGFR so that could be classified into the different stages. This was done because prevention of renal damage is a very important aim of antihypertensive therapy. Although drugs such as calcium channel blockers, beta blockers, angiotensin converting enzyme inhibitors and statins are commonly used reno-protective drugs, long term use would make them to be a risk, particularly in renal impairment, making management a challenge. Thus, the balance between efficacy and adverse effects should be determined for their optimum use.

In order to describe the risk of drugs to the individual patient, a drug risk ratio was introduced for each drug, which was the number of DTPs in relation to the number of times the medication was used. It can be simply calculated as frequency of the drug's involvement in DTP divided by the frequency of that drug used as per the prescription. This ratio was used to identify drugs that are prone to create DTPs and to quantify this tendency among the various drugs. Drugs with the highest drug risk ratio are those that most frequently expose the patient to risk when taking these drugs. On the other hand, frequently used drugs with a lower drug risk ratio can be used as they are considered to be safe. However, a drug risk ratio of 0.26, for instance, means that, a DTP may occur in one fourth of the times the drug is used.

Modified Morisky's Adherence Scale (MMAS-8) was used to measure patients' adherence to their medication as it is reliable and valid in patients with hypertension. MMAS-8 is an 8-item self-report measure of adherence. Items 1 through 7 have response choices "yes" or "no", whereas item 8 has a 5-point likert response choices. Each 'no' response is rated as '1' and each 'yes' is rated as '0' except for item 5, in which each response 'yes' is rated as '1' and 'no' is rated as '0'. Item 8 concerning the difficulty to remember taking medications is scored "Never/Rarely = 0, Once in a while = 1, sometimes = 2, usually = 3 and all the time = 4. The higher scores the higher adherence. The total scores range from 0 to 8 and grouped into three levels: high adherence (score = 8), medium adherence (score of 6 to < 8), and low adherence, score< 6.

3.8. Data quality management

Training was given to the data collectors (two nurses and two clinical pharmacists) to familiarize them with the data collection instrument and on how to collect the necessary data from patient medical charts and how to conduct patient interview. Subsequent support was given by the principal investigator as needed. Pre-test was done on 5% of the sample for completeness of variables one week before the actual data collection started. Based on the results obtained from pre-test, amendment was made on the assessment tools and way of assessment based on the inputs found on pre-test. The principal investigator was closely supervising the data collection on a daily basis. At the end of each data collection days, the principal investigator checked the completeness of filled questionnaire and recorded information to ensure its quality. An immediate correction was made for any errors identified during data collection. The actual DTPs were identified by the principal investigator.

3.9. Data analysis

Variables and database were coded, set and entered using Epi Info version 7.2.1. The data were then cleaned, transferred to Excel and exported to Statistical Package for Social Science (SPSS) version 25.0 for analysis. Descriptive statistics included 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. Tables and charts were used to present the results. Bivariate and multivariate logistic regression analysis was performed to investigate associations and factors associated with the occurrence of DTPs, respectively. After checking the absence of collinearity among variables, variables in bivariate analysis with *p*-value ≤ 0.20 were further analyzed in multivariate logistic regression to control the effect of confounders. Statistical significance was considered at p value <0.05.

3.10. Ethical considerations

Ethical clearance certificate was obtained from College of Health Sciences, Addis Ababa University, Institutional Review Board with a protocol number of 002/17/SPharma. Written informed consent was obtained from study participants for the interview and to extract data from their medical charts. Each participant was informed about the purpose of the study and its risk (time to be spent). Study participants were also told that they have full right to refuse participation to interview at any time, and their refusal by no means affects the service they get from the institution. Confidentiality and privacy of study participants was ensured during interview and all information accessed from medical chart were kept and restricted from any access. Thus, identifiers like name and address of the patient was not recorded in the data abstraction formats.

3.11. Operational definition

Adverse Drug Event (ADE): Any undesirable event experienced by a patient whilst taking a drug, regardless of whether or not the drug is suspected to be related to the event (114).

Adverse drug reaction: Any undesirable experience that has happened to the patient while taking a drug at normal doses used clinically is suspected to be caused by the drug (114).

Alcohol use- drinks any alcoholic beverage regularly for more than 1 drink in female and 2 drinks in male per day (1unit =300ml) (115).

Age Group: Patients with age ≥60 years, between 40 and 59 years and age of 25 to 39 years are elderly, middle adult and younger adults based on WHO age classification (116).

Body Mass Index (in kilograms per square meters): interpreted as underweight (BMI<18.5), normal weight (18.5 - 24.9), overweight (25.0 - 29.9) and obese (≥30.0) (117).

Comorbidity: a condition existing concomitantly but independently with hypertension

Controlled BP: BP<150/90 mmHg in hypertensive patients aged 60 or older, or BP <140/90 mmHg aged less than 60 years and in all ages with diabetes or chronic kidney disease (2).

Drug Interaction: Drug Interactions can be either kinetic, e.g. enzyme induction or inhibition or dynamic, e.g. two drugs negatively affecting the same organ.

Drug Risk Ratio: the number of DTPs associated with a drug in relation to the number of times the drug is used.

Drug Therapy Problem (DTP) is any undesirable event experienced by a patient that involves, or is suspected to involve, drug therapy, and interferes with achieving desired goals of therapy (16). (Further breakdown of the categories and their details, annex VI)

Free Source of Medications: medicines were received through government sponsorship or any employer's organization sponsorship through a credit system.

Non-Adherence: is the extent of deviation of drug taking behavior of a patient from the agreed recommendations by health care provider which was measured with Morisky's 8- item scale in which when the MMAS-8 score ≤6, he/she is considered as non-adherent

Physical Activity: doing exercise for at least 30 minutes per day for 5 days per week or walking for 30 minutes per day throughout the week (2).

Renal Risk Drugs: Drugs with recommendations for precautions in reduced renal function.

Reno-Protective Drugs: Renal risk drugs that also have the property of protecting renal function.

4. Results

4.1. Socio-demographic characteristics of study participants

From 410 study participants enrolled in this study, a total of 388 study participants were included for analysis and 22 were excluded because of incompleteness of the data. More than half (55.4%) of the participants were females. The mean ± SD age of the study participants was 53.61 ± 13.66 years and nearly half (46.9%) of them were in the middle adulthood age (40-59 years). Majority (62.9%) of the participants were married. Most (83.0%) of the study participants were living in Addis Ababa. Almost one-third (31.7%) of the study participants had a tertiary level of education and nearly half (45.4%) of the study participants were employed. Only 3.1% and 10.6% of the study participants were regularly smoking cigarettes and drinking alcohol, respectively. However, almost all (90%) participants reported physical inactivity based on wider acceptable definition of physical inactivity (Table 1)**.**

Table 1: Socio-demographic characteristics of ambulatory hypertensive patients on follow up at TASH, Addis Ababa, Ethiopia, February 1- May 30,2018 (n=388)

Variables	Categories	Study Participants		
		Frequency	**Percentage (%)**	Mean ± SD
Gender	Male	173	44.6	
	Female	215	55.4	
Age (years)				53.61±13.66
	15-24	11	2.8	
	25-39	48	12.4	
	40-59	182	46.9	
	≥ 60	147	37.9	
Marital status				
	Single	60	15.5	
	Married	244	62.9	
	Divorced	32	8.2	
	Widowed	52	13.4	
Employment status				
	Employed	176	45.4	
	Unemployed	212	54.6	
Place of residence				
	Addis Ababa	322	83.0	
	Out of Addis Ababa	66	17.0	
Educational status				
	No formal education	50	12.9	
	Primary (1-8)	112	28.9	
	Secondary (9-12)	103	26.5	
	College/University	123	31.7	
Monthly income (birr)				
	< 500	128	33.0	
	500-1200	82	21.1	
	> 1200	178	45.9	
Smoking status				
	Current smoker	12	3.1	
Khat chewing status				
	Regular user	4	1.0	
Alcohol drinking				
	Regular user	41	10.6	
Physical activity				
	Regular activity	43	11.1	

SD: standard deviation.

4.2. Clinical characteristics of study participants

The clinical characteristics of patients with hypertension are described in Table 2. The mean duration of hypertension treatment was 9.68 ± 8.61 years. Of the 388 study participants, 94.1% had comorbid conditions with a mean ± SD of 2.36 ± 1.23 comorbidities per patient. One fifth (22.7%) of the participants were found to have a single comorbidity, while 24.7% and 22.9% of participants had two and three comorbidities respectively. A maximum of four comorbidities were encountered in 23.7% of the study participants. The most common comorbid condition based on the physician's documented diagnosis was diabetes mellitus 126 (32.5%) followed by dyslipidemia 122 (31.4%) and chronic kidney disease 114 (29.4%). Moreover, 179 (46.1%) participants had developed hypertension related complications. Out of 238 complications, the most commonly encountered complication was hypertensive heart disease (30.1%), followed by nephropathy (17.5%), stroke (10.8%) and retinopathy (2.3%). Hospitalization due to high BP, at least, once within the last year was reported by 27.3% of the participants.

Table 2: Clinical characteristics of ambulatory hypertensive patients on follow up at TASH, Addis Ababa, Ethiopia, February 1- May 30, 2018 (n=388)

Variables	Categories	Study participants		
		Frequency	Percentage (%)	Mean ± SD
Duration of hypertension treatment (years)				9.68 ± 8.61
	1-5	159	41.0	
	5-10	96	24.7	
	≥10	133	34.3	
BMI (kilogram per meter square)				25.29 ± 4.31
	<18.5	13	3.4	
	18.5 - 24.9	190	49.0	
	25.0 - 30.0	132	34.0	
	≥ 30.0	53	13.7	
Hospitalization within the last 1 year (n,%, yes)		106	27.3	
Duration of appointment for follow-up				2.28 ± 1.14
	≤ 1 month	114	29.4	
	> 1 month	274	70.6	
Average BP Control	Controlled	281	72.4	
	Uncontrolled	107	27.6	
eGFR by MDRD (ml/min/1.73m^2)				63.47 ± 25.05
	≥90	12	3.1	
	55-89	26	6.7	
	30-54	109	28.1	
	15-29	196	50.5	
	<15	45	11.6	
Presence of comorbid conditions (n,%, yes)		365	94.1	
	Diabetes mellitus	126	32.5	
	Dyslipidemia	122	31.4	
	Chronic kidney disease	114	29.4	
	Ischemic heart diseases	72	18.6	
	Gout	62	16.0	
	Peripheral neuropathy	58	14.9	
	HIV/AIDS	28	7.2	
	Others*	96	24.7	
No of comorbidities per patient				2.36 ± 1.23
	1-2	184	47.4	
	≥3	181	46.6	
Presence of hypertension complications (n,%, yes)		179	46.1	
	Hypertensive heart disease	119	30.1	
	Nephropathy	68	17.5	
	Stroke	42	10.8	
	Retinopathy	9	2.3	
Number of complications per patient				0.61 ± 0.77
	1-2	169	94.4	
	≥3	10	5.6	

Others*:HF, AF, VHD, PUD, Arthritis, UTI, BPH, Psychiatric and Neurological problems, Renal diseases, Asthma and Thyroid disorders, eGFR: estimated glomerular filtration rate, MDRD: Modification of Diet in Renal Disease, BMI: Body mass index

4.3. Pattern of prescribed medications in patients with hypertension

In this study, the mean number of drugs per day was 4.05 ± 2.04 per patient. Of the 388 study participants, 43.8% of them took dual antihypertensive therapy, while very few (0.5%) of the participants were on five agents. The most frequently prescribed agent for hypertension was enalapril (8.0%) followed by nifedipine (7%), enalapril + amlodipine (6.7%), Other agents, including statins (36.6%), antidiabetics (25.5%) and aspirin (25.0%) were also the most frequently prescribed drugs (Table 3).

Table 3: Prescribed medications among ambulatory hypertensive patients on follow up at TASH, Addis Ababa, Ethiopia, February 1- May 30, 2018 (n=388)

Treatment Categories		Study participants (n, %)		
		Frequency	Percentage (%)	Mean ± SD
Antihypertensive drug use	Monotherapy	107	27.6	
	Dual Therapy	170	43.8	
	Triple therapy	85	21.9	
	Quadruple therapy	24	6.2	
	Five agents	2	0.5	
Antihypertensive regimen	Enalapril	31	8.0	
	Nifedipine	27	7.0	
	Enalapril + Amlodipine	26	6.7	
	Hydrochlorothiazide + Amlodipine	22	5.7	
	Amlodipine	22	5.7	
	Hydrochlorothiazide + Enalapril	21	5.4	
	Hydrochlorothiazide + Nifedipine	18	4.6	
	Enalapril + Nifedipine	17	4.4	
	Hydrochlorothiazide	16	4.1	
	Enalapril + Nifedipine + Hydrochlorothiazide	13	3.4	
	Others*	175	45.1	
Other medications	Statins	142	36.6	
	Antidiabetics	99	25.5	
	Aspirin	97	25.0	
	Amitriptyline	53	13.7	
	Non-steroidal anti-inflammatory drugs	39	10.1	
	Proton pump inhibitors	34	8.8	
	Highly active antiretroviral therapy	28	7.2	
	Steroid (Prednisolone)	28	7.2	
	Tramadol	13	3.4	
	Allopurinol	12	3.1	
	Antibiotics	12	3.1	
	Others**	203	52.3	

Number of medication per patient				4.05±2.04
	<5	238	61.3	
	≥5	150	38.7	
Source of Medicines	Through Sponsorship	181	46.6	
	Through Payment	207	53.4	
Use of herbal products	Occasionally	23	5.9	

*Other antihypertensive therapy regimens; **Anticonvulsants, antipsychotics, thyroid drugs;

A total of 1570 medications were used by the study participants in general, of which 808 (51.46%) were antihypertensive medicines. The mean number of drugs used per day was 4.05 ± 2.04 per patient. Only 38.7% of the study participants took more than half (928, 59.1%) of the total drugs used, reflecting that comorbidities that required drug treatment can significantly increase the number of drugs used. Commonly prescribed antihypertensive drug classes were calcium channel blockers (258), diuretics (239), angiotensin converting enzyme inhibitors (201), beta blockers (97), angiotensin receptor blockers (9) and others (10). The most frequently prescribed specific antihypertensive drugs considering their class were enalapril (96.5%), atenolol (81.4%), hydrochlorothiazide (66.1%), amlodipine (58.5%), nifedipine (41.5%) and furosemide (30.5%).

4.4. Number of drug therapy problems among the study participants

Out of 283 study participants with DTPs, one DTP was identified in 37.1% participants followed by two DTPs in 29.7% and more than three DTPs in 33.2% of the participants. A total of 602 DTPs were identified. The average number of DTP per patient was 1.55 ± 1.33.

Table 4: Number of DTP occurrences among hypertensive patients on follow up at TASH, February 1 - May 30, 2018 (n=283)

No. of DTP occurrences	Patients with DTPs	Proportion/Sample (n=388)	Proportion/Patients with DTPs (n=283)	Total no. of DTPs in each occurrence
One	105	27.1	37.1	105
Two	84	21.6	29.7	168
Three	47	12.1	16.6	141
Four	47	12.1	16.6	188
Total	283	72.9*	100.0	
Total number of identified DTPs in 283 study participants				**602**

*Total was not 100% as 105 (27.1%) of the study participants had no DTP and were excluded.

4.5. Experienced drug therapy problems and causes

The most frequent DTP category identified was drug interaction (49.5%), followed by ADR (40.3%) and a need for additional drug therapy (32.8%). The most frequently identified cause of DTP was experiencing undesired drug effect (19.8%) followed by more effective alternative drug availability (17.0%) and unsafe/contraindicated drug use (16.6%).

Table 5: Drug therapy problems and causes among ambulatory hypertensive patients on follow up at TASH, Addis Ababa, Ethiopia, February 1- May 30, 2018 (n=388)

Drug related needs	DTP Category	Cause of DTP	Proportion out of patients with DTP
Indication	Unnecessary drug therapy	Non drug therapy indicated	17 (6.0)
		Duplication of drug therapy	12 (4.2)
		No medical indication	2 (0.7)
		Treating avoidable ADR	1 (0.35)
		Total	**32 (11.3)**
	Needs additional drug therapy	Untreated medical condition	40 (14.1)
		Preventive/Prophylactic drug	28 (9.9)
		Synergistic/potentiating drug	25 (8.8)
		Total	**93 (32.8)**
Effectiveness	Ineffective drug therapy	More effective alternative is available	48 (17.0)
		Dosage form inappropriate	20 (7.1)
		Not effective for condition	1 (0.35)
		Total	**69 (24.5)**
	Dosage too low	Wrong dose	42 (14.8)
		Frequency inappropriate	2 (0.7)
		Total	**44 (15.5)**
Safety	ADR	Undesirable drug effect	56 (19.8)
		Unsafe for patient/ contraindication	47 (16.6)
		Contraindications present	7 (2.5)
		Allergic reactions	4 (1.4)
		Total	**114 (40.3)**
	Dosage too high	Wrong dose	4 (1.4)
		Total	**4 (1.4)**
	Drug Interaction (Total)		**140 (49.5)**
Total number of identified DTPs			**602**
Total number of participants with DTPs			**283 (72.9)**
Average number of main DTPs per patient			**1.55 ± 1.33**

Unmet Drug-Related Needs were considered as DTPs.

It was found that about 60 (21.2%) patients with DTPs had undesirable side effects and allergic reactions, which could possibly be associated with hypertension treatment. Based on the records on the patient medical chart, the most common type of undesired drug effect obtained was pedal edema (32, 11.3%) followed by dry cough (14, 4.9%), headache (13, 4.6%) and postural hypotension (13, 4.6%).

Table 6: Types and Prevalence of undesirable drug effects identified from hypertensive patients on follow up at TASH, February 1- May 30, 2018 (n=283)

Type of undesired drug effects	Frequency (n, %) out of patients with DTP/s
Pedal edema	32 (11.3)
Dry cough	14 (4.9)
Headache	13 (4.6)
Postural hypotension	13 (4.6)
Fatigue	10 (3.5)
Leg/foot pain	8 (2.8)
Gastrointestinal disturbances	7 (2.5)
Sexual dysfunction	6 (2.1)
Others	14 (4.9)

Others: angioedema, flushing, itching, insomnia, dizziness, bradycardia, gynecomastia, urinary frequency, electrolyte disturbance, hyperuricemia, dyslipidemia

A total of 260 potential major DDIs in 140 (36.1%) of the study participants were identified with a mean ± SD of 0.67 ± 1.12 per patient. One DDIs was found in 77 patients, two in 34 patients, three and four in 13 patients each and five in 5 patients. The top five potential DDIs in descending order of prevalence were as follows: Hydrochlorothiazide used concomitantly with aspirin may yield an increased risk of nephrotoxicity; concomitant use of aspirin and metformin may increase the risk of hypoglycemia toxicity; use of aspirin with furosemide may increase risk of nephrotoxicity; amlodipine used with simvastatin concomitantly may raise the risk of myopathy; aspirin use with glinbenclamide may result hypoglycemia and using amitriptyline and aspirin concurrently may result in increased risk of bleeding. Other major DDIs together with their prevalence is shown in Table 7.

Table 7: Types and Prevalence of drug interactions identified from hypertensive patients on follow up at TASH, February 1- May 30, 2018 (n=388)

Type of Adverse Drug Interaction	**Frequency (n, %)**
Aspirin + Hydrochlorothiazide	42 (30.0)
Aspirin + Metformin	39 (27.9)
furosemide + Aspirin	23 (16.4)
Amlodipine + Simvastatin	22 (15.7)
Aspirin + Glinbenclamide	20 (14.3)
Aspirin + Amitriptyline	18 (12.9)
Enalapril + Allopurinol	8 (5.7)
Enalapril + Spironolactone	8 (5.7)
Aspirin + Spironolactone	5 (3.6)
Amitriptyline + Indomethacin	5 (3.6)
Diclofenac + Hydrochlorothiazide	5 (3.6)
Others	60 (42.9)
Total Potential Drug interaction	**260**
Total Participants with Potential Drug interaction	**140 (100.0)**

4.5.1. Medicines involved in experiencing drug therapy problems

The most frequent antihypertensive drug class involved in DTPs was calcium channel blockers (0.44) followed by beta blockers (0.37), angiotensin converting enzyme inhibitors (0.33), and diuretics (0.23) (Figure 1). Other than antihypertensive agents, Aspirin (0.80) and Antidiabetics (0.44) were the most commonly reported drugs for the occurrence of DTPs followed by statins and amitriptyline with a drug risk ratio of 0.4 each. The top antihypertensive drug involved in DTPs was Nifedipine (0.74) followed by Atenolol (0.42) and Enalapril (0.34). In the contrary, Furosemide was the most frequently used antihypertensive drug with the lowest drug risk ratio (0.07).

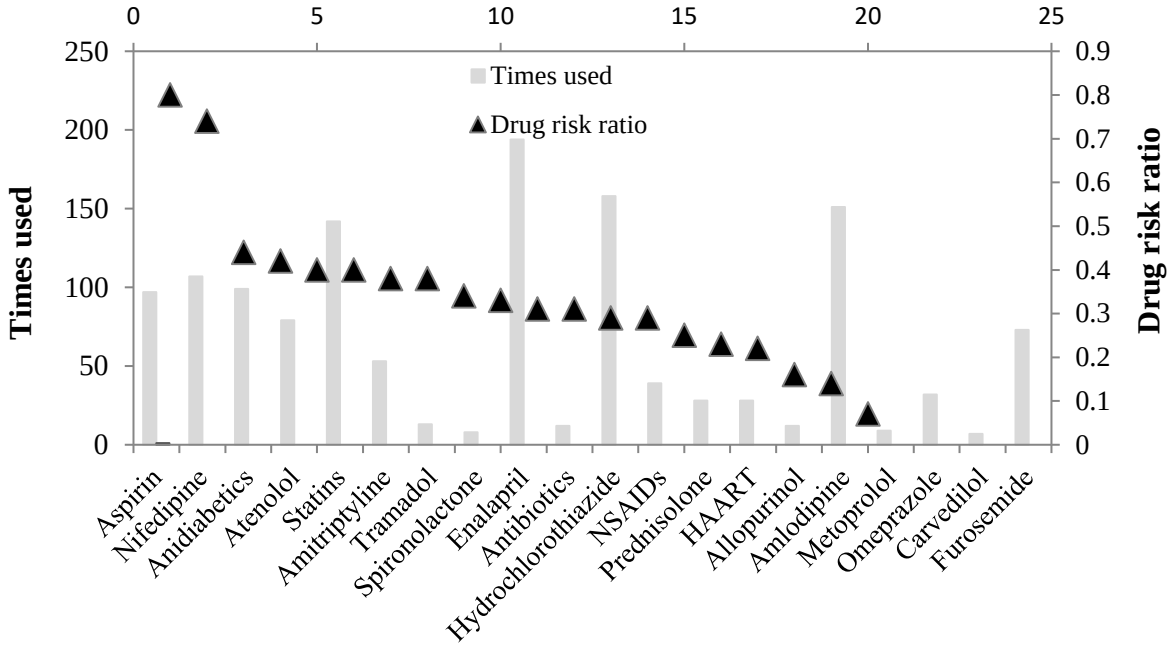

Figure 1: Times used and drug risk ratio for most utilized drugs (left) and for the drugs with highest drug risk ratio (right) among ambulatory hypertensive patients on follow up at TASH, Addis Ababa, Ethiopia, February 1- May 30, 2018 (n=388)

4.5.2. Examples of various types of the identified drug therapy problems

Table 8: Examples of various types of the identified drug therapy problems

Percentages and examples of the various type of the identified DTPs	
DTP categories	**Examples**
Indication DTPs (32.2%)	A hypertensive patient with known heart failure was on only enalapril. But, patient has uncontrolled BP, she needs additional therapy such as carvedilol
	Patient needs to start aspirin as secondary prophylaxis for CAD
	A CKD and dyslipidemia was existed in a patient with uncontrolled BP. But, he was only on atorvastatin and Nifedipine; he needs additional drug such as enalapril
Efficacy DTPs (17.8%)	It is more effective to use fibrate instead of statin, since patient has hypertriglyceridemia: LDL= 63 mg/dl but TG = 186 mg/dl
	It is more effective to use angiotensin converting enzyme inhibitor to treat hypertension in patient with diabetes than using atenolol
	A potent statin has been indicated and simvastatin 40 mg Po/d had been used in post myocardial patient but there is more effective alternative like atorvastatin 40 mg daily
Safety DTPs (29.4%)	Dose of amlodipine that should be used in hypertensive patient should not exceed 10 mg daily so reduce the dose of amlodipine from 20 mg to 10 mg
	The maximum recommended dose of atenolol in hypertension is 100 mg/day but patient receives 50mg PO TID, so dose reduction for atenolol is needed
	In a patient with GFR 15-35 ml/min the maximum dose of atenolol that can be used should be 50 mg daily not 100 mg daily so reduce the dose.
	Enalapril causes cough to the patient, so change to angiotensin receptor antagonist like candesartan
	Nifedipine causes ankle edema to the patient
Inappropriate dosing (12.4%)	Patient had been taking amlodipine 5mg PO BID but amlodipine is a long acting calcium channel blocker to be administered on daily basis.
	Patient took different drugs but because of many reasons when there is a change to some other drugs, equivalent doses weren't considered

4.5.3. Factors associated with the occurrence of drug therapy problems

As illustrated in Table 9, in bivariate analysis, factors that were associated with DTPs were old age, male gender, being ever married, longer duration of treatment, comorbidities (presence and number), complaints and complications, use of nifedipine, hydrochlorothiazide with amlodipine, hydrochlorothiazide, antidiabetics, and living in Addis Ababa ($p< 0.2$).

According to the multivariate logistic regression analysis (Table 9), nine variables were significantly associated with the occurrence of DTP.

From the Adjusted Odds Ratio (AOR) for age (AOR=1.049, 95% CI: 1.021-1.077, $p<0.001$), it was showed that old age was significantly associated with DTPs. Marital status also played a role, as being ever married participants were 3 times more likely than never married to have DTP. Longer duration of treatment (AOR=1.057, 95% CI: 1.011-1.104, $p=0.015$) was also identified as a risk for the occurrence of DTP.

The occurrence of DTP was 2.3 times higher in those patients with subjective complaints than those with no complaints (AOR=2.229, 95%CI: 1.056-4.707, $p=0.036$). In addition, an increase in the number of comorbidity (AOR=2.272, 95% CI: 1.057-4.884, $p=0.036$) had a strong positive relation with developing DTPs. A one unit increase in the comorbidity will make the patient 2.3 times riskier to develop DTPs. Taking different antihypertensive drug therapy regimens were not statistically associated with DTPs. The occurrence of DTP were 2 times higher in those participants on ≥5 drugs than those taking <5 drugs (AOR=2.146, 95%CI: 1.024-4.50, $p=0.043$). When patients took other medications for their additional compelling indication, the risk of DTP may probably be increased. The occurrence of DTP were 2.6 times higher in those participants taking statins than those who didn't take (AOR=2.62, 95%CI: 1.087-6.304, $p=0.032$). Moreover, the occurrence of DTP was 3.8 times higher in those taking aspirin than those who didn't take (AOR=3.79, 95%CI: 1.114-12.87, $p=0.033$).

Table 9: Bivariate and multivariate analysis of factors associated with drug therapy problems among patients with hypertension on follow up at TASH, Addis Ababa, Ethiopia, February 1- May 30, 2018 (n=388)

Covariates	Categories (n, %)	Drug Therapy Problem		Odds Ratios		
		No (n=105)	Yes (n=283)	Crude (95% CI)	Adjusted (95% CI)	P-value
Age	Mean ± SD		53.61±13.66	1.08(1.058-1.102)**	1.049(1.021-1.077)	**<0.001**
	<60	80(33.2)	161(66.8)	1.00		
	=>60	25(17.0)	122(83.0)	2.425(1.461-4.026)**		
Gender	Male	35(20.2)	138(79.8)	1.903(1.192-3.039)**	1.701(0.881-3.285)	0.114
	Female	70(32.6)	145(67.4)	1.00		
Marital status						
	Never married	31(51.7)	29(48.3)	1.00		
	Ever married	74(22.6)	254(77.4)	3.669(2.078-6.480)**	2.959(1.444-6.062)	**0.003**
Place of residence						
	Addis Ababa	82(25.5)	240(74.5)	1.586(0.89-2.754)*	0.896(0.431-1.863)	0.768
	Outside Addis Ababa	23(34.8)	43(65.2)	1.00		
Level of education	No and/or Primary	39(24.1)	123(75.9)	1.254(0.737-2.136)		
	Secondary	31(30.1)	72(69.9)	0.924(0.520-1.642)		
	Tertiary	35(28.5)	88(71.5)	1.00		
Employment status	Unemployed	55(25.9)	157(74.1)	1.133(0.723-1.775)		
	Employed	50(28.4)	126(71.6)	1.00		
Monthly income	<500 Birr	33(25.8)	95(74.2)	1.093(0.653-1.830)		
	500-1200 Birr	23(28.0)	59(72.0)	0.974(0.544-1.746)		
	>1200 Birr	49(27.5)	129(72.5)	1.00		
Regular Coffee intake	No	40(28.2)	102(71.8)	1.00		
	Yes	65(26.4)	181(73.6)	1.092(0..688-1.734)		
Regular Alcohol intake	No	96(27.7)	251(72.3)	1.00		
	Yes	9(22.0)	32(78.0)	1.360(0.626-2.955)		
Regular physical activity	No	96(27.8)	249(72.2)	0.687(0.317-1.485)		
	Yes	9(20.9)	34(79.1)	1.00		

(Continue)

(Continued)

Table 9: Bivariate and multivariate analysis of factors associated with drug therapy problems among patients with hypertension on follow up at TASH, Addis Ababa, Ethiopia, February 1- May 30, 2018 (n=388)

Covariates	Categories	Drug Therapy Problem		Odds Ratios		P-value
		No (n=105)	Yes (n=283)	Crude (95% CI)	Adjusted (95% CI)	
Duration of treatment	Mean ± SD		9.68 ± 8.61	1.098(1.057-1.141)**	1.057(1.011-1.104)	**0.015**
	1-5 years	32(27.1)	86(72.9)	1.00		
	6-10 years	54(39.4)	83(60.6)	0.572(0.336-0.973)**		
	>10 years	19(14.3)	114(85.7)	2.233(1.186-4.204)**		
Comorbidities						
	No	12(52.2)	11(47.8)	1.00		
	Yes	93(25.5)	272(74.5)	3.191(1.362-7.475)**	2.084(0.984-4.414)	0.055
Complication						
	No	70(33.5)	139(66.5)	1.00		
	Yes	35(19.6)	144(80.4)	2.072(1.298-3.308)**	1.411(1.031-2.458)	0.501
Complaints						
	No	27(40.9)	39(59.1)	1.00		
	Yes	78(24.2)	244(75.8)	2.166(1.246-3.765)**	2.229(1.056-4.707)	**0.036**
No of Comorbidities						
	1-2	66(35.9)	118(64.1)	1.00		
	>=3	27(14.9)	154(85.1)	3.190(1.920-5.302)**	2.272(1.057-4.884)	**0.036**
No of complication						
	1-2	70(33.5)	139(66.5)	1.00		
	>=3	35(19.6)	144(80.4)	2.072(1.298-3.308)**	1.659(1.332-1.305)	0.232
Antihypertensive drugs						
	Nifedipine	13(48.1)	14(51.9)	2.715(1.231-5.989)**	0.512(0.182-1.44)	0.204
	Hydrochlorothiazide	8(50.0)	8(50.0)	2.835(1.036-7.760)**	0.525(0.12-2.005)	0.346
	Hydrochlorothiazide + Amlodipine	11(50.0)	11(50.0)	2.894(1.215-6.893)**	0.377(0.124-1.15)	0.086
Antidiabetics use	No	92(31.8)	197(68.2)	1.00		
	Yes	13(13.1)	86(86.9)	3.089(1.640-5.822)**	0.618(0.25-1.523)	0.296
Statin use	No	94(38.2)	152(61.8)	1.00		
	Yes	11(7.7)	131(92.3)	7.365(3.781-14.35)**	2.62(1.087-6.304)	**0.032**

Continue

Continued

Table 9: Bivariate and multivariate analysis of factors associated with drug therapy problems among patients with hypertension on follow up at TASH, Addis Ababa, Ethiopia, February 1- May 30, 2018 (n=388)

		Drug Therapy Problem		Odds Ratios		
Covariates	**Categories**	**No (n=105)**	**Yes (n=283)**	**Crude (95% CI)**	**Adjusted(95% CI)**	**P-value**
Aspirin						
	No	101(34.7)	190(85.3)	1.00		
	Yes	4(4.1)	93(95.9)	12.36(4.414-34.60)**	3.79(1.114-12.87)	**0.033**
Number of medicines						
	Mean ± SD			1.558(1.348-1.80)**		
	<5	88(37.0)	150(63.0)	1.00		
	>=5	17(11.3)	133(88.7)	4.590(2.597-8.110)**	2.146(1.024-4.50)	**0.043**
No of antihypertensive						
	Mean ± SD		2.09 ± 0.90	1.725(1.345-1.299)**	1.364(0.91-2.046)	0.134
Source of drugs						
	For free	40(22.1)	141(77.9)	1.614(1.021-2.550)**	1.477(0.822-2.65)	0.192
	Paid	65(31.4)	142(68.6)	1.00		

Variables in bivariate analysis with p≤0.20 and ≤0.05 indicated by * and **, respectively. Statistically significant in multivariate analysis set at: p≤0.05, set in **bold** typeface. CI: Confidence interval at 95 %,

4.6. Medication adherence

According to the Morisky's 8 items assessment scale, high adherence was found in 56 (14.4%), medium adherence in 185 (47.7%), and low adherence in 147 (37.9%) participants. However, an early study considered poor adherence during hypertension treatment if patient adherence rate is below 80% (118). Hence, a modification on MMAS-8 interpretation was made and those who scored ≥7 out of 8 were included as adherent and the others as non-adherent. Accordingly, 176 (45.4%) of the participants were found to be non-adherent to their antihypertensive medications. The mean ± SD score in this study was also 5.95 ± 1.71. This shows that nearly half of the total study participants were categorized under poor adherence to their medication.

Forgetfulness to take medicines appropriately was the most prevalent reason for poor adherence (118, 45.9%) followed by directions not understood (114, 29.4%), drug products prescribed were unaffordable (61, 15.7%). (Table10).

Table 10: Possible reasons for non-adherence reported by ambulatory hypertensive patients on follow up at TASH, February 1- May 30, 2018 (n=388)

Reason for Non-Adherence	Frequency (n, %)
Patient forgets to take	118 (30.4)
Directions not understood	114 (29.4)
Cannot afford drug product	61 (15.7)
Patient felt better	12 (3.1)
Patient felt worse	12(3.1)
Fear of Adverse events	21 (5.4)
Patient Prefers not to Take	17 (4.4)
Drug product not available	12 (3.1)
Regimen complexity	9 (2.3)
Disbelief in drug effectiveness	8 (2.1)
Patient not aware of medication changes	4 (1.0)
Patient can't swallow/administer	2 (0.5)

4.6.1. Determinants of poor medication adherence

As illustrated in Table 11, in bivariate analysis, factors associated with poor medication adherence were living in Addis Ababa, having lower income, receiving a higher number of antihypertensive tablets daily or a higher dosing frequency, physical inactivity and taking amlodipine and NSAIDs ($p< 0.2$).

The multivariate logistic regression showed that residence in Addis Ababa, lower monthly income, polypharmacy, antidiabetics and NSAIDs use had a statistically significant association with non-adherence ($P < 0.05$).

The odds of being non-adherent for patients who lived in Addis Ababa increased by 2.2 times (AOR=2.160, 95%CI: 1.209-3.862, *p*=0.009) as compared to patients who lived outside of Addis Ababa. Being non-adherent for patients with a monthly income of <500 Ethiopian birr (AOR=1.675, 95%CI: 1.032-2.719, *p*=0.037) was increased by 1.7 times as compared to patients with a monthly income of >500 Ethiopian birr. The odds of being non-adherent for patients on ≥5 drugs were increased by 2.4 times (AOR=2.361, 95%CI: 1.019-5.471, *p*=0.045) as compared to those patients who took <5 drugs. The use of antidiabetics medication (AOR=1.953, 95%CI: 1.087-3.507, *p*=0.025) increased the occurrence of poor adherence by 2 times while NSAIDs used by participants (AOR=0.425, 95%CI: 0.199-0.908, *p*=0.027) had a protective effect on non-adherence.

Table 11: Bivariate and multivariate analysis of factors associated with medication non-adherence among ambulatory patients with hypertension on follow up at TASH, Addis Ababa, Ethiopia, February 1- May 30, 2018

		Non-Adherence		Odds Ratio		
Covariates	**Categories**	**Yes**	**No**	**Crude(95% CI)**	**Adjusted(95%CI)**	**P-value**
Residence	Addis Ababa	137(42.5)	185(57.5)	1.951(1.139-3.341)*****	2.160(1.209-3.862)	**0.009**
	Out of Addis Ababa	39(59.1)	27(40.9)	1.000	1.000	
Employment status	Employed	89(50.6)	87(49.4)	1.000	1.000	
	Unemployed	87(41.0)	125(59.0)	1.470(0.983-2.199)	1.370(0.833-2.255)	0.215
Monthly income	<500	113(41.5)	159(58.5)	1.673(1.080-2.591)*	1.675(1.032-2.719)	**0.037**
	>500	63(54.3)	53(45.7)	1.000	1.000	
Number of antihypertensive	Mean ± SD		2.09 ± 0.90	0.797(0.637-0.998)*	0.912(0.693-1.199)	0.508
Physical Activity	No	150(43.5)	195(56.5)	1.988(1.041-3.798)*****	0.516(0.259-1.027)	0.060
	Yes	26(60.5)	17(39.5)	1.000	1.000	
Herbal products	No	161(44.1)	204(55.9)	1.000	1.000	
	Yes	15(65.2)	8(34.8)	0.055(0.174-1.017)	0.472(0.177-1.259)	0.134
Coffee drinking	No	72(50.7)	70(49.3)	1.000	1.000	
	Yes	104(42.3)	142(57.7)	1.404(0.927-2.127)	1.457(0.929-2.287)	0.101
Total number of drugs	<5	101(42.4)	137(57.6)	1.000	1.000	
	>=5	75(50.0)	75(50.0)	0.737(0.489-1.111)	2.361(1.019-5.471)	**0.045**
Amlodipine	No	171(46.7)	195(53.3)	1.00	1.000	
	Yes	5(22.7)	17(77.3)	2.982(1.077-8.252)*****	2.767(0.904-8.474)	0.075
Enalapril + Nifedipine	No	165(44.5)	206(55.5)	1.000	1.000	
	Yes	11(64.7)	6(35.3)	0.437(0.158-1.206)	0.394(0.138-1.127)	0.082
Antidiabetics	No	137(47.4)	152(52.6)	1.000	1.000	
	Yes	39(39.4)	60(60.6)	1.387(0.871-2.207)	1.953(1.087-3.507)	**0.025**
Amitriptyline	No	147(43.9)	188(56.1)	1.000	1.000	
	Yes	29(54.7)	24(45.3)	0.647(0.361-1.158)	0.336(0.385-1.385)	0.336
Non-steroidal anti-inflammatory drugs	No	150(43.0)	199(57.0)	1.000	1.000	
	Yes	26(66.7)	13(33.3)	0.377(0.187-0.758)*	0.425(0.199-0.908)	**0.027**

Percentages were calculated per row. *****Variables in bivariate analysis ≤0.05, statistical significance was set at p≤0.05. Kg/m^2: kilogram per square meter

5. Discussion

More than half of patients in the follow up unit receive appropriate agents for their medical condition; the remaining have at least one irrational antihypertensive agent in their regimen (81). This irrational use may lead to DTPs. Identification and resolution of common types of DTPs contributes to reduction of drug related hospitalizations, morbidity and mortality. Therefore this study was carried out in a large tertiary care teaching hospital to assess the magnitude of DTPs and its contributing factors in ambulatory hypertensive patients.

The findings of a high prevalence of DTPs (72.9%), almost three-fourths of the patients had one or more DTPs, highlights the benefit of establishing a multidisciplinary team with the task of making a holistic assessment of drug therapy. TASH is a specialized and comprehensive patient care service center, and the segregation into departments with high clinical expertise on each disease will provide good and focused treatment of conditions that caused patients to visit clinics for follow-up. However, the specialization may have less focus and expertise on comorbidities at one follow-up clinic, which may lead to DTP. Therefore, hypertensive patients need to get special attention to their drugs as they often have a number of comorbid conditions and would be on many drugs. Such situations present a challenge to clinicians to handle stable long-term drug regimens. This could be due to the fact that in many times, patients got different residents with possible variations in their patient care and treatment approach during their follow-up period.

The DTPs (602) identified in this study include potential and/or actual DTPs though whether a potential DTP should be included has been debated in the literature (103, 112, 119). But, a potential DTP should be considered as a DTP, as it will mostly lead to the occurrence of actual DTPs, if not dealt properly. Many studies showed that a large amount of DTPs are preventable, which supports the need to take potential DTPs into consideration (49, 55). In the literature, considerable differences in DTP frequency have been reported (120-122). Such variations could be due to lack of standardized method for identifying and classifying DTPs. This poses difficulty for quality assurance as there is no unified classification system for clinical documentations and restricts the possibility to compare across different practices, hospitals, countries. Hence,

international agreement on the definition and classification of DTPs and recommendations for easy, practical and reliable operationalization is needed (123).

For clinicians, feedback on their own practices should often be more educational and encouraging than comparisons across borders while there are many differences in therapeutic trends, health care systems and health cultures. Tools to be used in quality procedures aimed at improving the current status of the service should be prepared and standardized to quantify DTPs and might possibly serve as a quality indicator. International agreement on the DTP notion seems to take time (123), hence preparing a national standard would be advantageous.

The finding of this work (prevalence of DTPs was 72.9%) is concordant with some studies done in Ethiopia (72%) (74) and Sweden (66.0%) (61). However, it is lower as compared with others done in Ethiopia, Jimma and Bahir Dar (88.66%) and Adama (80.7%) (75, 76) as well as in Malaysia (90.5%) (69) and Brazil (91.7%) (33). Such variations could be due to study designs (interventional vs. observational; prospective vs. retrospective), DTPs definition (potential vs. actual DTPs inclusions), DTPs classification systems and characteristics of study participants (includes inpatients vs. outpatients). But a higher prevalence was detected when compared with studies done in Jordan (41.73%) (15) and Indonesia (45.8%) (71). This discrepancy might be due to participants' level of education and awareness, the health care system and resources allocated, study settings (five teaching hospitals) with a different expertise, hospitals' infrastructure and client satisfaction rate.

Studies from sub-Saharan Africa has showed a steady increase in the prevalence of hypertension, due to low treatment and control rates from 9.7% in 1990 to 30.8% in 2010, with regional variations ranging from 15% to 70% (6, 7, 124). In clinical practice, taking five BP readings in a row may not be exactly the same. Thus, what matters is whether the reading is near 120/80 or 130/85 or 140/90 or 150/95 or 160/100, and so on. To report BP as controlled according to specific cutoff numbers, it is needed to follow a certain protocol. However, if clinicians want to be satisfied as the treating physician that no new action is needed, then they can use their own judgment considering the age and condition of the patient. In practice, the frequency of better control is at least 50% and more in multiple measurements. Accordingly, 72.4% of the study participants had a controlled BP based on at least 50% of the measures taken from available patients' consecutive clinic visits. This is preferred, as measurement of office BP alone is not

enough, clinicians also emphasize on the importance of home BP monitoring to predict the cardiovascular mortality and morbidity while white coat hypertension is considered as well.

The present study showed that the most frequently encountered DTPs in decreasing order were drug interactions, ADRs and need for additional drug therapy.

Drug interaction is defined to occur when the effects of one drug are changed by another drug, food, drink or some chemical agent. Drug interactions can fall in one of these group; drug combinations that should always be avoided, drug combinations that should usually be avoided (special precautions/close monitoring), drugs can be combined with action to be taken to reduce risk (changing timing or routes of administration) and drug combinations where no action is needed as the risk is small (125, 126). The presence of large number of drug interactions makes almost impossible for each prescriber to remember all potentially hazardous drug combinations. Developing explicit lists of interactions by specialists in the field and updating timely is vital so as to reduce clinically significant drug interactions.

More than three-fourth (78.6%) of patients in this study had a moderate-to-severe reduction of eGFR. Patients in stages three, four and five must be considered to have impaired renal function (90% of patients in this study) as this may increase the occurrence of drug interactions and ADRs. The most commonly found drug interactions in this study, use of aspirin with diuretics and oral hypoglycemic agents even during severe renal impairment would make patients to easily experience nephrotoxicity and hypoglycemia, respectively. Calcium channel blockers use with statins was also found to be common which can enhance the risk of statin exposures (risk of myopathy). This is because precautions are recommended when those drugs and classes of drugs that are eliminated through kidney are to be used in patients with renal impairment as the drugs are riskier to kidney (68). Another common type of drug interaction found was aspirin combination with tricyclic antidepressants that can increase the risk of bleeding. All of these findings were consistent with a study done in Saudi Arabia (70).

Generally, when a major drug interactions occurred, interventions to be made can be but not limited to: start/stop the drug, increase and decrease the dose, change the drug product, institute a monitoring plan, provide personalized patient instructions or education, refer patients to a specialist, removal of barriers to obtain medicine or care and others. In line with other studies

(79), this study found that higher drug risk ratio was found with aspirin, antidiabetics and statins. Risk appears to be lower, but comorbidities will force the use of high risk drugs that would eventually increase DTPs (27, 32, 79).

Monotherapy can be used to control high BP but if not controlled, a combination therapy (43.8% of participants in this study) can be instituted that can increase the risk of ADRs. A similar finding was reported in Nigeria (127, 128). Hence, ADRs may lead to problems that can limit therapeutic options and adherence. ADR (42.7%) is the third most common DTP encountered in a study done at Adama, Ethiopia (75). This is in agreement with the results of the current study (29.4%), albeit the extent appeared to be lower. The lower prevalence of ADR could be attributed to the approach used, as complaints were not included as ADR unless confirmed and documented by a physician. ADR (54%) was the most commonly encountered DTP in Northern Cyprus (62). The reason for its higher prevalence was the employment of prospective observational study, pharmacist interventions, interventions evaluation and classification using PCNE DTP classification tool V6.2, which could quantify DTPs more. Among 15.5% of study participants with undesired side effects and allergic reactions, peripheral edema accounted for 11.3% followed by dry cough (4.9%), headache (4.6%) and hypotension (4.6%). A similar pattern was reported from India (129), but headache (16.7%) took the top spot in other local study (130). This difference might be because the study was done on patients at health centers, with lesser comorbidities, that didn't require angiotensin converting enzyme inhibitors.

Consistent with the findings of this study, other research conducted in Asia (15, 71), as well as locally (31, 74, 76, 98) have reported high frequencies in the need for additional drug therapy. These findings indicate that meticulous attention is required when it is used in clinical practice. This report also provides evidence that hypertensive outpatients have a high incidence and wide variety of DTPs. The effectiveness of integrating a clinical pharmacist in the multidisciplinary hypertension management program should be prospectively evaluated and emphasized (71), On the other hand, ineffective drug therapy, inappropriate dosing, and unnecessary drug therapy types of DTPs identified in this study were less prevalent compared to other studies (33, 73, 76). Variations were there because of methodological dissimilarities.

Several factors have been shown to have association with DTP in the literature. Some of them, including old age, being ever married, longer duration of treatment, number of drugs, number of

comorbidities, and taking statins and aspirin have been consistently shown to have a significant association (15, 32, 50, 61, 75, 79), but there is a conflicting report for level of education, gender, and types of antihypertensive drug therapy regimens (27, 71, 76, 78, 98). This difference could be attributed to heterogeneity of the factors and relates to diseases, drugs and behavior that may affect patient's taking the drugs. For example, the method of categories used by researchers, the treatment approach of clinicians and patients' life style may have a pivotal impact on the variability. In clinical practice, it is often easier to deal with one risk factor, for example renal impairment, at a time. However, in reports and surveys for health administration, it may be practical to use the mean number of risk factors per patient in a particular setting as an indicator of the risk of DTPs. Hence, this information can be used to identify high-risk patients in need of pharmaceutical care services.

Non-adherence is one main reason for poor BP control (81). About 45% of the study participants in this study were non-adherent to their antihypertensive medications. A comparable finding was obtained in studies conducted in Beirut (49.5%) (86), Malaysia (46.6%) (87), Vietnam (50.2%) (90), Nigeria (45.8%) (92) and Ethiopia (45.8%) (97). Another recent review done by Abegaz et al (82) showed a non-adherence rate of 45.3% globally. This is consistent with the present finding. Lower prevalence was found as compared with other studies done in Ethiopia: Dessie (68.13%) (98) and Nedjo (68.6%) (99), Brazil (86.76%) (85) and Palestine (54.2%) (89). Those studies done in Ethiopia illustrated that most of the patients claimed to have adverse effects and symptoms of high BP for which patients may be reluctant to take their medicines because of fear of adverse effects and lack of information on risk factors, causes and complications of the disease. In the study done in Brazil, a multidisciplinary team care report form and telephone interview was used and patient non-drug therapy compliance was assessed, which could obviously resulted in a higher prevalence. Dissatisfaction and poor patient-provider relationship rate may bring such variations. Information provision, written leaflet and good communication with clinicians could improve some reasons of non-adherence such as forgetfulness and dissatisfaction with treatment so as to control BP and avoid complications (131, 132).

But, a higher prevalence was found than three studies done in Ethiopia; Jimma (38.2%) (96), Gondar (35.4%) (95), Debre Markos (32.8%) (94) and in Nigeria (34.6%) (93), Ghana (31.3%) (91) and Portugal (36.8%) (83). This might be due to number of comorbidities and subsequent

drug uses may incur regimen complexity, and combinations of antihypertensive agents use can worsen the situation for which patients' got a difficulty in remembering and understanding drug related information. Such significant associations had been mentioned in many studies done previously (87, 92, 95, 96).

Several factors have been shown to have association with non-adherence in the literature. Some of them, including living in Addis Ababa, a monthly income of <500 Ethiopian birr, number of medications, and use of antidiabetics and NSAIDs have been consistently shown to have a significant association (79, 86, 87, 95, 96, 99, 133). On the other hand, comorbidities, complications, age, level of education, physical activity status and social drug uses (89, 95, 98, 99, 134) were also associated with poor adherence, though, they were not in this study. The difference could be due to variability in the study participants, adherence measurement tool, health care systems and policies, and knowledge, skill and patient care approaches of the health care professionals. This in turn is because; non-adherence is not limited to medication alone. It can also take many other forms, which include the failure to keep appointments, to follow recommended dietary or other life style changes, and to follow other aspect of treatment or recommended preventive health practices, which all can be the reason for the differences.

Different studies have been extensively reported reasons for non-adherence. In this study, forgetfulness is the most commonly reported reason for non-adherence followed by lack of understanding directions. This is in line with many studies (86, 89, 91, 93, 99). Unavailability of medicines and their expensive price were also reasons, similar to the ones reported in other studies (92, 95, 98, 134). Patient sometimes may fear drug side effects and/or felt better or worse, which may result to missed doses. These finding came to be third most common reason for non-adherence as well in different studies (86, 91, 92). A randomized controlled trial done in Jordan showed that changes in patient's behavior, attitudes and beliefs would improve adherence (135). Another trial conducted in Spain showed knowledge and adherence can be increased through personalized information and written leaflets. However, educational intervention had no significant impact on patients' adherence to medications (132).

6. Limitations of the study

This study only describes the current situation of DTPs without doing interventions, assessing the acceptance rate of physicians to these interventions, and assessing the extent of implementation of interventions and their impact. DTPs were not evaluated by the multidisciplinary team, chaired with physicians who would be best to make the final decision about acknowledgement of DTPs. This could influence assessment of the DTPs. These points were not attempted because clinical pharmacy services are not yet implemented in follow up clinics and this study is expected to provide an evidence for decision makers to show the need for clinical pharmacy services. Future work is suggested to cover those points and to fully evaluate clinical pharmacy services, to provide more evidence to ensure the success and benefits of implementation of clinical pharmacy services in reducing DTPs. This cross sectional study may also suffer from biases particularly social desirability bias, especially on self-reported sensitive issues like cigarette smoking status, khat chewing status, alcohol intake status, adherence status and reasons for non-adherence. All patients may not be actively screened for comorbidities and complications, this entailed to underestimate reports; computer screening may highly overestimates DDIs and it was difficult to standardize local alcoholic drinks and local bottles used; salt addition habits and sedentary life styles.

Despite these limitations, many factors associated with DTPs were assessed and data were collected both from patients' medical chart and patients themselves to get complete information. Therefore, considering the study findings during clinical practice will help in ensuring the proper use of medicines to reduce the risk of adverse drug events, promote cost-effectiveness, and achieve desired therapeutic outcomes. Furthermore, the study is an evidence for the need of pharmaceutical care provision in order to identify, prevent, and resolve DTPs early so as to maintain safe medication.

7. Conclusion and recommendations

7.1. Conclusion

At the follow-up clinic in a hospital, new drugs are often added while others may be withdrawn to the drug regimens. Consequently, it is of practical interest to know what will happen after the patient leaves the hospital. The findings of this study indicated that hypertensive patients on follow up have a high risk of developing DTPs, which will affect desired therapeutic outcomes. The identification of several risk factors for DTPs may be helpful in finding patients at risk, which can then be singled out for special attention to avoid overt DTPs. Patients' adherence to antihypertensive drugs can be improved through focusing on the identified determinants and reasons for poor adherence, and acting proactively. Such interventions could avoid treatment failures from occurring in therapy due to DTPs including non-adherence. As a result, there would be much savings on the medicines budget both from the patient as an individual and the government as a whole since hospital admissions and cost of treatment will be reduced.

7.2. Recommendations

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

- ✓ Implementation of clinical pharmacy services is a recommended strategy to identify and resolve DTPs in this setting.
    - Early identification and resolution of DTPs through pharmaceutical care providers may be vital in minimizing DTPs and maximizing the quality of the service given.
- ✓ Clinicians should emphasize on the negative clinical and societal impact of DTPs and contributing factors so as to achieve the desired goal of pharmacotherapy.
- ✓ Maintaining the accessibility and availability of affordable medicines in a hospital may avoid the risk of unaffordability and unavailability so as to improve adherence
- ✓ Adherence strategies should be established

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Annexes

Annex I: Participants' Information Sheet

Name of principal investigator: Melaku Tileku Tamiru

Name of study area: Renal referral clinic of Tikur Anbessa Specialized Hospital

Research budget covered by: Addis Ababa University

Research objective: To assess DTPs and medication adherence among ambulatory hypertensive patients on follow-up at Tikur Anbessa Specialized Hospital.

Significance of the study: drug therapy problems lead to poor health outcomes, increased healthcare costs and reduced quality of life; thus, they must be quantified, identified and resolved based on possible interventional strategies.

Risks: The only threat for the interviewee could be spending time (a maximum of 30 minutes).

Participant right: Interviewees cannot participate and/or withdraw or skip answering questions at any time from the interview.

Beneficial: The study is beneficial to improve the quality of clinical care through future interventions based on the findings of this study

Confidentialities: The study will not include patient's name and/or address and data will be accessed and interview will be made only by ethically conducted, well trained and experienced health care professionals and analyzed by the principal investigator.

Agreement: participants are expected to be fully voluntary to participate in the study.

Whom to contact: If you have any kind of difficulties about the study, fell-free to contact the principal investigator: Melaku Tileku: Cell Phone: **0911595338/melakutileku@gmail.com.**

Annex II: Informed Consent

Addis Ababa University, College of Health Sciences, School of Pharmacy, Department of Pharmacology and Clinical pharmacy, Study on 'assessment of drug therapy problems and medication adherence in patients with Hypertension at ambulatory care clinic of Tikur Anbessa Specialized Hospital"

Greeting: Hello, my name is_____. I am here today to collect data on the assessment of the drug therapy problems and medication adherence among ambulatory Hypertensive patients on follow-up at Tikur Anbessa Specialized Hospital. The study is being conducted by Mr. Melaku Tileku, from Addis Ababa University, College of Health Sciences, School of Pharmacy, Department of Pharmacology and Clinical pharmacy, Post graduate program. The purpose of this study is to assess drug therapy problems and medication adherence in hypertensive patients at ambulatory care clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. So I am kindly requesting you to take part in this study by allowing your data to be accessed and included in the study.Your name will not be written in the data collection form and will never be used in connection with any information you tell us. There is no risk associated with participating in this study. All information regarding your medical condition will be kept strictly confidential. Your participation is voluntary and you are not obligated to participate in the study. If you don't feel good with the study, it is your right to withdraw any time you want. If you have questions regarding this study, please feel free to contact the principal investigator via his address:

Melaku Tileku, Tell: +251- 911595338, e-mail: melakutileku@gmail.com

Are you willing to participate in this study?

1. Yes ……..….. Include in the participant list

2. No …….…… Skip to the next participant

Annex III: Information to Data Collectors

Addis Ababa University, College of Health Sciences, School of Pharmacy, Department of Pharmacology and Clinical Pharmacy, Data collection tool to determine Drug Therapy Problems and Medication Adherence among ambulatory Hypertensive patients on follow-up

Dear data collector,

First of all I would like to thank you for your willingness to accept my request and to participate as a data collector in this study which will surely be of great significance in contributing to determine the magnitude and potential contributing factors of drug therapy problems among ambulatory hypertensive patients on follow-up at TASH. This data will then enable the concerned bodies to emphasize on the identified problems and the associated factors to formulate and implement interventional strategies like Medication Therapy Management services as a part of pharmaceutical care services in order to identify, resolve and prevent them for the future. Finally, I would like to be grateful in advance. Your effort to maintain the quality of data through honest and effective data collection procedures will have a significant output of the present study. I promise you to timely respond any challenges you may face during the data collection period.

The principal investigator!

Annex IV: Interview Guide

First of all, thank you for your willingness to participate honestly on this interview.

My name is_____. I would like to interview you today on drug therapy problems and your medication adherence status while you are taking antihypertensive medications for your medical problems. Confidentiality regarding this interview will be strictly maintained. At any time during the interview, please feel-free to ask me if you have any questions, you can skip any question which is (are) not comfortable to you or you can stop the interview at any time for any reason even. I would like to assure you that there is no problem upon the interview except spending your time (a maximum of 30 minutes).

I thank you very much for your time and willingness to answer these questions honestly!

Annex V: Data abstraction formats

Part I: Socio-Demographic Characteristics					
1.Age (in years)		2.Sex Male ☐ Female ☐		Pregnancy: ☐ Yes ☐ No	
3.Marital status		Single ☐	Married ☐	Divorced ☐ Widowed ☐	
4.Educational status		No formal ☐ Grade 1-8 ☐	Grade 9-10 ☐ Grade 10-12 ☐	College diploma ☐ University degree and above ☐	
5. Residence (current)		Addis Ababa ☐ Out of Adds Ababa ☐		6. Monthly income, ETB	
7. Job type		Employed ☐ Unemployed ☐ ☐ house wife ☐ merchant ☐ Student ☐ daily laborer ☐ farmer Others----------			
8. Social habits	Cigarette Smoker	Yes ☐ No ☐		Coffee drinking Yes ☐ No ☐	
	Alcohol Drinker	Yes ☐ No ☐		Kchat chewing Yes ☐ No ☐	
9.Physical Activity	Walk ☐ Yes ☐	No ☐, if yes, for how long?		<30minutes /day ☐ >30minutes/day ☐	
	Sport ☐ Yes ☐	No ☐ if yes, for how long?		Daily ☐ 1-3d/week ☐ 4-6d /week ☐	

Part II: Clinical characteristics			
1.Duration of hypertension		2.Duration of treatment	
3.Hospitalization within 1 year	Yes ☐ No ☐	If, yes due to what , specify _____	
4.Number and types of Antihypertensive/day (write with their full regimen)	Number_____ Antihypertensive agent, List:		
5.Other Drugs (including OTC, herbals)	No ☐ Yes ☐ If yes list them and their purpose of use (indications)		
6.Comorbid condition	No ☐ Yes ☐ If yes list here		
7.Complication	No ☐ Yes ☐ If yes list here		
8.Known drug allergy	No ☐ Yes ☐ If yes, Specify the drug		

Part-III: 8-Items Morisky Medication Adherence Scale- (MMAS-8)

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

What makes you **not to take** your medicines appropriately? (More than one answer is possible)

- ☐ Directions not understood
- ☐ Patient prefers not to take
- ☐ Patient forgets to take
- ☐ Drug product too expensive
- ☐ Patient cannot swallow/ administer
- ☐ Drug product not available
- ☐ Patient felt better
- ☐ Patient felt worse
- ☐ Regimen complexity
- ☐ Fear of adverse events
- ☐ Patient not aware of medication changes
- ☐ Disbelief in drug effectiveness
- ☐ Others, specify----------

Part IV: Data abstraction formats on taken patient histories, laboratory investigations, physical examinations and diagnostic imaging techniques

Card Number_____ Unique ID/Code_____Age (in years) _____

Weight (kg) _____ Height (cm) _____ Body mass index (BMI) [kg/m^2] _____

1. Past medical conditions and medications

Indication	Drug product (Generic Name)	Full Dosage regimen	Date (dd/mm/yy)		Response Effectiveness/ safety profile
			Started	Stopped	

2. Past medical history (hospitalizations, surgical procedures, injuries, pregnancies and so on)

PMH: _____

PSH: _____

Injuries: _____

3. Physical Examination (PE)/**vital** signs: Consecutive record of visits

	First visit				**Second Visit**				**Third visit**			
Date(dd/mm/yy	BP	PR	RR	T^0	BP	PR	RR	T^0	BP	PR	RR	T^0
SaO_2												

Any Pertinent physical examination and/or Review of systems findings:

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4. Pertinent **laboratory and imaging** series results (Findings for three consecutive results).

Lab Investigations		Date(dd/mm/yy)	Date(dd/mm/yy)	Date(dd/mm/yy)
Parameters				
Blood glucose level	HbA1c (%):			
	FBS(mg/dL):			
	RBS(mg/dL):			
Lipid panels	TC: mg/dl			
	LDL: mg/dl			
	TG: mg/dl			
	HDL: mg/dl			
RFTs	BUN/Scr			
	eGFR			
LFTs	AST			
	ALT			
	ALP			
	Bil/Alb			
Coagulation profile	PT			
	INR			
	PTT			
Serum electrolyte	Na^{+}/Cl^{-}			
	$Mg^{2+/}K^{+}$			
	$Ca^{2+/}Po_4^{3-}$			
CBC	WBC/N/L			
	RBC/Hgb/Hct			
	MCV/MCH			
	Plt			
Others				

Any diagnostic tools/Imaging techniques/modalities with findings			
Technique	Date(dd/mm/yy)	Date(dd/mm/yy)	Date(dd/mm/yy)

5. Current medical conditions and medications

	For the current working diagnosis (including Comorbidities and complications)				
Indication	Product name (Generic Name)	Full Dosage regimen	Date(dd/mm/yy)		Response Effectiveness/ safety profile
			Started	Stopped	

6. Adverse Drug Events

Drug Regimen	**Adverse drug reaction**	**Event**	**date**
	Drug allergies (drug, timing, reaction-rash, shock, asthma, nausea, anemia and others)		
	Other alerts/health aids/special needs (sight, hearing, mobility, literacy, disabilities)		

Annex VI: Modified Drug Therapy Problems Registration Format

DTPs Categories	Common Cause of Drug therapy problem
1. Unnecessary drug therapy	□ No medical indication of the drug is found □ Duplication of drug therapy is existed □ Non drug therapy should be indicated □ Drug is used in treating avoidable ADR □ Others ,specify_____
2. Needs additional drug therapy	□ Untreated medical condition is existed □ Preventive/ prophylactic drug needed □ Synergistic/ potentiating drug needed □ Others, specify_____
3. Ineffective drug product	□ More effective alternative drug is available □ Condition is already refractory to drug □ Dosage form is inappropriate □ The drug is not effective for condition □ Others, specify_____
4. Inappropriate Dosage	□ Wrong dose (too small or too high) of the drug □ Frequency is inappropriate (short or long) □ Duration of drug use is too short or too long □ Others, specify_____
5. Adverse drug reaction	□ Undesired effect from the drug is found □ Unsafe drug for patient is existed □ Dosage is administered or changed too rapidly □ Allergic reactions is found/reported □ Contraindication to the drug is present
6. Drug Interactions	□ There is (are) Major drug interaction (s)

*Adopted from (16)

Annex VII: Questionnaire: Amharic Version (የአማርኛ መጠይቅ ቅፅ)

ቅጽ 1: ጥናቱን በተመለከተ ለታካሚ የሚሰጥ መረጃ

የተመራማሪው ስም: መላኩ ትልቁ

ጥናቱ የሚካሄድበት ቦታ: ጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል

የጥናቱን በጀት የሚሸፍን ተቋም: አዲስ አበባ ዩኒቨርስቲ

የጥናቱ ዋና አላማ:በተመላላሽ የደም ግፊት ህመማን ህክምና ወቅት ከመድሀኒት ጋር የተያያዙ ችግሮችን መለየትና እና የመድሀኒቶችን ትክክለኛ አወሳሰድ በተመለከተ ግምገማ ማድረግ።

የጥናቱ ጠቀሜታ: ጥናቱ ለጤና ባለሙያዎችና ለፖሊሲ አውጪዎች ከመድሀኒት አጠቃቀም ጋር የተያያዙ ችግሮችን እንዲለዩ ከማገዙም በላይ ታካሚዎች መዳሐኒታቸዉን በትክክል እንዲወሰዱ የበኩላቸዉን አስተዋፆ እንዲያበረክቱ ይረዳል። በተጨማሪም በተመሳሳይ ዙርያ ወደፊት ለሚሰሩ ጥናቶች ግብዓት በመሆን መሰረታዊ መረጃ ይሰጣል።

የጥናቱ ሂደት: መረጃ ሰብሳቢዎች የተሳታፊውን ፍቃድ ካገኙ በኋላ በመጠይቁ መሰረት ቃለመጠይቅ ያደርጋሉ፤ ከታካሚ ካርድ ላይ የተመዘገበውን መረጃ አንዳስፈላጊነቱ ይወስዳሉ።

ጉዳት: ጥናቱ የተወሰነ ጊዜን ከመሻማቱ በስተቀር የሚሰከትለዉ ጉዳት የለም።

የተሳታፊው መብት: ተሳታፊው ቃለ መጠይቁን በፈለገው ሰዓት ማቋረጥ እንዲሁም ያልፈለገውን ጥያቄ ያለመመለስ መብት አለዉ።.

ጥቅም: የጥናቱ ዉጤት ለወደፊቱ የተሻለና ጥራት ያለው አገልግሎት ለመስጠት ይረዳ ዘንድ ግብዐት ሆኖ ያገለግላል።

ማበረታቻ: በጥናቱ ላይ ተሳታፊ በመሆን የሚሰጥ ማበረታቻ ባይኖርም በጥናቱ ላይ ተሳትፎ በማድረግ ከሚገኘዉና ከሚሰበሰቡ መረጃዎችም በሆስፒታሉ ያለዉን አገልግሎት ለማሻሻል የጎላ ፋይዳ አለዉ ።.

ምስጢራዊነቱ: ጥናቱ የተሳታፊዎችን ስም፣ አድራሻ እና ሌሎች ያስተላለፏቸውን መልዕክቶች በተገቢው መልክ በሚስጢር ይጠብቃል።

ስምምነት: ታካሚው በሙሉ ፍላጎት ተሳታፊ እንደሚሆን ይጠበቃል።.

ለተጨማሪ መረጃ የዚህን ጥናት አስተባባሪ፤ ተመራማሪ ወይም አማካሪ ማነጋገር ይችላሉ።

1. የጥናቱ ተመራማሪ ፡ መላኩ ትልቁ፣ +251-911-595-338 ፤ኢሜል: melakutileku@gmail.com
2. የጥናቱ ዋና አማካሪ፡ ፕሮፌሰር ኤፍሬም እንግዳወርቅ፡ ኢሜል: ephrem.engidawork@gmail.com

ቅጽ 2: በጥናቱ ለሚሳተፉ የስምምነት ማረጋገጫ

በአ.አ.ዩ ጤ/ሳ/ኮ ፋርማሲ ት/ቤት ፋርማኮሎጂ እና ክሊኒካል ፋርማሲ ት/ት ክፍል በጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል በተመላላሽ የደም ግፊት ህመማን ህክምና ወቅት ከመድሀኒት ጋር የተያያዙ ችግሮችን መለየትና እና የመድሀኒቶችን ትክክለኛ አወሳሰድ በተመለከተ በተመላላሽ የህክምና ክፍል የሚደረግ የግምገማ ጥናት

ሠላምታ፡- ሰላም፣ ስሜ ---------- ይባላል፡፡ ዛሬ እዚህ የተገኘሁ በተመላላሽ የደም ግፊት ህመማን ህክምና ላይ ባሉ ከመድሀኒት ጋር በተያያዘ ሊፈጠሩ የሚችሉ ችግሮችን ለመለየት እና የታካሚዎቸነ የመድሐኒት አወሳሰድ ሁኔታ ለመገምገም በተመላላሽ የመታከሚያ ክፍሎች ለሚደረግ የግምገማ ጥናት መረጃዎችን ለመሰብሰብ ነዉ፡፡ ጥናቱ እየተካሄደ ያለዉ በአ.አ.ዩ ጤ/ሳ/ኮ ፋርማሲ ት/ቤት ፋርማኮሎጂ እና ክሊኒካል ፋርማሲ ት/ት ክፍል ከድኅረ-ምረቃ መርሐ ግብር አቶ መላኩ ትልቁ በተባለ ግለሰብ ነዉ፡፡ ከላይ እንደተገለፀዉ የዚህ ጥናት ዓላማ በሆስፒታሉ ስለሚኖረዉ በተመላላሽ የደም ግፊት ህመማን ህክምና ላይ ባሉ ከመድሀኒት ጋር በተያያዙ ችግሮችን መለየትና እና የታካሚዎቸነ የመድሐኒት አወሳሰድ ሁኔታ ጥናታዊ ግምገማ ማድረግ ሲሆን ስለመዲሃኒቶች አጠቃቀም መሠረታዊ መረጃን ማጠናቀርም የጥናቱ አካል ነዉ፡፡ ስለሆነም እርስዎ መድሐኒትዎን በተመለከተ በሚደረግልዎት የህክምና መረጃ በጥናቱ ዉስጥ እንዲካተት እንዲፈቅዱልኝ እጠይቅዎታለሁ፡፡ የእርስዎን ማንነት የሚገለጽ (ለምሳሌ ስም) በመረጃ መሰብሰቢያ ቅጹ ላይ ካለመካተቱም በላይ ሌሎች መረጃዎችም ምሥጢራዊነታቸዉ የተጠበቀ መሆኑን አረጋግጥልዎታለሁ፡፡ የእርስዎ መረጃ በጥናቱ ዉስጥ እንዲካተት ፈቃጅም ከልካይም እርስዎ ብቻ ነዎት፡፡ በማንኛዉም ጊዜ ስለጥናቱ ጥያቄ ከተፈጠረብዎት ዋናዉን ተመራማሪ መጠየቅ/ማግኘት እንደሚችሉ ለመግለጽ እወዳለሁ፡፡

የዋናዉ ተመራማሪ አድራሻ፡- አቶ መላኩ ትልቁ ስ.ቁ: +251-911595338፤ ኢ-ሜይል: melakutileku@gmail.com

በጥናቱ ሊይ ለመሳተፍ ፍቃደኛ ነዎት? ፍቃደኛ መሆንዎን በፊርማዎ ቢያረጋግጡልን?

1. አዎ (ፊርማ.....) ወደ ተሳታፊዎች ዝርዝር ይጠቃለሉ
2. አይደለም .... ወደ ቀጣይ ተሳታፊ ተሻገር

ሀ. <u>የታካሚዉ አጠቃላይ መገለጫዎች</u> (መመሪያ፡ ለመረጡት ምላሽ በየ √ ምልክትን ያድርጉ)

1. አጠቃላይ መገለጫዎች					
1.እድሜ በዓመት፤		2.ፆታ፤ ወንድ ☐	ሴት ☐	ነፍሰ-ጡር: አዎ ☐	አይደለሁም ☐
3.የጋብቻ ሁኔታ፤	ያላገባ/ች ☐	ያገባ/ች ☐	አግብቶ/ታ የፈታ/ች ☐	ሚስቱ/ባሏ የሞተችበት/ባት ☐	
4.የትምህርት ደረጃ፤	ያልተማረ/ች ☐	ከ9ኛ-10ኛ ክፍል ☐	ኮሌጅ ዲፕሎማ ☐		
	ከ1ኛ-8ኛ ክፍል ☐	ከ11ኛ-12ኛ ክፍል ☐	ዩኒቨርስቲ ዲግሪ እና ከዛ በላይ ☐		
5.አሁን የሚኖሩበት ቦታ	አዲስ አበባ ☐	ከአዲስ አበባ ዉጪ ☐	6.በወር የሚያገኙት ገቢ በብር		
7. የስራዎ ሁኔታ	ስራ ያለው/ያላት ☐	ስራ አጥ ☐	ነጋዴ ☐	ተማሪ ☐	ገበሬ ☐ የቀን ሰራተኛ ☐
8.ማህበራዊ ልማድ	ሲጋራ ያጨሳሉ	አዎ ☐	አላጨስም ☐	ቡና ይጠጣሉ አዎ ☐	አልጠጣም ☐
	አልኮል ይጠጣሉ	አዎ ☐	አልጠጣም ☐	ጫት ይቅማሉ አዎ ☐	አልቅምም ☐
9. የአካል ብቃት እንቅስቃሴ ያደርጋሉ	የእግር ጉዞ ያዘወትራሉ	አዎ ☐	አላዘወትርም ☐ ፤ መልስዎ አዎ ከሆነ በቀን ለምን ያህል ጊዜ	ከ30 ደቂቃ በታች ☐	ከ 30 ደቂቃ በላይ ☐
	ስፖርት ያዘወትራሉ	አዎ ☐	አላዘወትርም ☐ ፤ መልስዎ አዎ ከሆነ በሳምንት ለምን ያህል ጊዜ	በየቀኑ ☐	1-3ቀናት ☐ 4-6ቀናት ☐

2. የታካሚዉን በሽታ (ዎች) እና መድሐኒቶች በተመለከተ ተጨማሪ መረጃዎች				
1.ህመመዎን ካወቁ ስንት ዓመት ሆንዎታል		2. የደም ግፊት መድሐኒት ለስንት ዓመት ወስዱ		
3. በደም ግፊትዎ ምክንያት ባለፈዉ ዓመት ዉስጥ ሆስፒታል ተኝተዉ ያዉቃሉ	አዎ ☐	አላውቅም ☐	መልስዎ አዎ ከሆነ ምክንያትዎን ይግለፁት	
4. በአሁኑ ሰዓት በየቀኑ የሚወስዷቸው የደም ግፊት መድሐኒቶች ዓይነት እና ብዛት	ብዛት _____ ስማቸዉን ጥቀስ/ሽ (ከነሙሉ አወሳሰዳቸዉና መጠናቸዉ)			
5. መድሃኒት የሚያገኙት በምን መልኩ ነዉ	በግዢ ☐	በነጻ ☐	በአሁኑ ሰአት የሚውሰዱት ጠቅላላ የመድኃኒት አይነት (ብዛት) ስንት ነው; ------	
6. ተጨማሪ የሚወስዷቸው መድሐኒቶች (የባህልና ያለሓኪም ትዕዛዝ የሚወሰዱ መድኃኒቶችን ጨምሮ)	ካሉ ይዘርዝሩ/ሯቸዉ ለምን እንደሚወሰዱ/ዷቸዉ ያብራሩት			
7. ተጨማሪ (ተያያዥ) ህመም አለብዎት ይዘርዝሩ/ሯቸዉ				
7.ህመሙ ያስከተለብዎት የተወሳሰበ የጤና ዕክል (ጉዳት) ካለ/ሉ ይዘርዝሩ/ሯቸዉ				

ለ. መድሐኒቶችን በታዘዘዉ መሰረት በአግባቡ ስለመዉሰድ መመዘኛ (ሞሪስኪ-ስምንት)

ተ.ቁ	ስለመድሃኒት አጠቃቀም የቀረቡ ጥያቄዎች	አይ	አዎ
፩	አንዳንድጊዜ ጊዜ መድሃኒትዎን መውሰድ ይዘነጋሉ እንዴ?	□1	□0
፪	አንዳንድ ጊዜ ሰዎች ከመዘንጋት ባሻገር በሆነ ምክንያት መድኀኒታቸውን ሳይወስዱ ይቀራሉ፡፡ ያለፉትን ሁለት ሣምንታት ሲያስቧቸው መድሃኒትዎን ያልወሰዱባቸው ቀናት ነበሩ?	□1	□0
፫	መድሃኒትዎን በሚወስዱበት ወቅት የበሽታው ምልክቶች የባሰብዎ ሲመስልዎ መድሃኒትዎን መውሰድ አቋርጠው ወይም አቁመው ያውቃሉ?	□1	□0
፬	ጉዞ ሲጓዙ ወይም ከቤትዎ ርቀው ሲሄዱ መድሃኒትዎን ከእርስዎ ጋር መውሰድ ዘንግተው ያውቃሉ?	□1	□0
፭	በትላንትናው ዕለት ሁሉንም መድሐኒት በትክክል ወስደዋል?	□0	□1
፮	የህመሙ ምልክቶች ቀንሰዋል ወይም ተሸሎኛል ብለው አንዳንዴ መድሐኒት መውሰድ አቋርጠው ያውቃሉ?	□1	□0
፯	መድኃኒቶችን በየቀኑ መውሰድ ለአንዳንድ ሰዎች ምቾት ይነሳቸዋል፡፡ እርስዎ በህክምና ክትትልዎ ወቅት በየቀኑ ወይም አንድም ጊዜ ሳያዛንፉ መድሐኒትዎን በትክክል ለመዉሰድ ተሰላችተዉ ያዉቃሉ?	□1	□0
፰	መድሃኒትዎን መውሰድ እንዳለብዎት ማስታወስ ምን ያህል ጊዜ አስቸግርዎት ያውቃል በፍፁም □ አልፎ አልፎ □ አንዳንድ ጊዜ □ አብዛኛው ጊዜ □ ሁልጊዜ □		
	ጠቅላላ ድምር		

ሐ. መድሐኒትዎን በአግበቡ ለመዉሰድ ያዳገትዎ ለምንድን ነዉ (ከ አንድ በላይ መልስ መምረጥ ይቻላል)

- ☐ የመድሃኒቱን አወሳሰዱ ስላልተረዳሁት
- ☐ መድሃኒቱን መዉሰድ ስላልፈለኩ
- ☐ መድሃኒቱን መዉሰድ ስላልፈለኩ
- ☐ ስለምረሳው
- ☐ የምወስዳቸው መድሃኒቶች ብዙና ግራ የሚያጋቡ ስለሆኑ
- ☐ መድሃኒቱ ውድ ስለሆነ
- ☐ የጎንዮሽ ጉዳትን በመፍራት
- ☐ ያድነኛል ብዬ ስለ ማላስብ
- ☐ መድሃኒቱን ስውጠው ስለሚያስቸገረኝ
- ☐ መድሃኒቱን ማግኘት ስላልቻለኩ
- ☐ መድሃኒቱን ስወስድ ህመሜ ስለሚባባስበኝ/
- ☐ መድሃኒቱን ስወስድ ህመሜ ስለተሻለኝ
- ☐ ሌላም ካለ ይገለፅ.....

<u>መ. የመድኃኒትዎ የጎንዮሽ ጉዳት (መድኃኒትዎን ሲወስዱ ያጋጠመዎት) ነገር</u>

3.1. በአሁን ሰዓት ወይም መድሃኒትዎን መውሰድ ሲጀምሩ ከመድሃኒቱ ጋር የተያያዙ ያልተለመዱ ሁኔታዎች/ የጎንዮሽ ጉዳት አጋጥሞዎት ያውቃል? አዎ ☐ አላጋጠመኝም ☐

3.2 መልስዎ አዎ ከሆነ ምን አጋጠመዎት (ከ አንድ በላይ መልስ መምረጥ ይቻላል)

የራስ ምታት ☐	መርሳት ☐
የድካም ስሜት ☐	ማቅለሽለሽ፣ ማስመለስ፣ ሆድ ቁርጠት፣ የጨጓራ ህመም ☐
ድብርት ☐	ራስን ማዞርና ብዥታ ☐
የዐይን ብዥታ ☐	የቆዳ ላይ ሽፍታና ማሳከክ ☐
ስንፈተ ወሲብ ☐	እንቅልፍ ማጣት ☐
ግራመጋባት ☐	የአፍ መድረቅ ☐
ደረቅ ሳል ☐	የሆድ ድርቀት ☐
የእግር እብጠት ☐	ፊት ማሳበጥ ☐
ሌላም ካለ ይግለፁ፡	