

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

A cross sectional study

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This is to certify that the thesis prepared by werkya mahammedsied entitled “assessment of drug therapy problems and contributing factors among adult ambulatory hypertensive patients in Ayder referral hospital Mekelle, northern, Ethiopia: A cross sectional study” 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 standard with respect to originality and quality.

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Abstract

Assessment of drug therapy problems and contributing factors among adult ambulatory hypertensive patients in Ayder referral hospital, Mekelle, northern Ethiopia, a cross sectional study

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Hypertensive patients are at high risk of Drug therapy problems (DTPs) as they often received multiple medications in order to achieve their target blood pressure. Currently studies concerning DTPs in patients with hypertension are limited in Ethiopia. Therefore, this study was aimed to assess the magnitude of DTPs and contributing factors among adult ambulatory hypertensive patients in Ayder referral Hospital. Institution based cross sectional study was conducted among 384 study subjects who fulfilled the inclusion criteria. Trained data collectors collected the data from patient interview and chart review using structured data collection format. DTPs were assessed using Cipolle's classification system. Logistic and multivariate regression analysis was performed to identify factors associated with DTPs. Data were reported as mean and percentage using tables and figures. DTPs were found in 52.8% of study subjects. A total of 277 DTPs were identified from 203 study subjects in which, 1 DTP was identified from 133(65.5%) patients, 2 in 66 (32.5%) patients and 3 in 4(1.97%) patients. The maximum number of DTPs found was 3 and the average number of DTPs per patient was 1.36. Unnecessary drug therapy was the top leading (32.5%) and dose too low (7.94%) was the least type of DTPs in the study subjects. ACEIs were the most frequent drugs involved in DTPs. The factor that was independently associated with DTPs was the total number of medications. The total number of medications taken by the patient per day was an important predictor of drug therapy problem AOR = 2.572 95% CI (1.062-6.229), P=0.01.

Keywords: Drug therapy problems, hypertension, Ambulatory, Mekelle, Ethiopia

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List of abbreviations and acronyms

ACEIs	Angiotensin converting enzyme inhibitors
ADRs	Adverse drug reactions
AOR	Adjusted odds ratio
ARH	Ayder referral hospital
ASA	Acetyl salicylic acid
BB	Beta blockers
BP	Blood pressure
BSL	Blood sugar level
CBC	Complete blood count
CCB	Calcium channel blockers
CHS	College of health science
CI	Confidence interval
COR	Crude odds ratio
CVDs	Cardiovascular diseases/ cardiovascular drugs
DDI	Drug-drug interaction
DBP	Diastolic blood pressure
DL	Dyslipidemia
DRP	Drug related problems
DTH	Dose too high
DTL	Dose too low
DTPs	Drug therapy problems
FMOH	Federal ministry of health
HCT	Hydrochlorothiazide

Hgb	Hemoglobin
HTN	Hypertension
HHD	Hypertensive heart disease
IDF	International diabetic federation
IEDT	Ineffective drug therapy
MMAS	Morisky Medication Adherence Scale
MDI	Major Drug interaction
Mm hg	Millimeter mercury
MRPs	Medication related problems
NADT	Needs additional drug therapy
OIS	Old ischemic stroke
PCNE	Pharmaceutical Care Network Europe
PPIs	Proton pump inhibitors
SBP	Systolic blood pressure
T2DM	Type 2 diabetes mellitus
UDT	Unnecessary drug therapy
VAR	Variable
WHO	world health organization

1. Introduction

1.1 Background

Hypertension is a state of elevated systemic blood pressure defined as a systolic blood pressure greater than or equal to 140 mm Hg and diastolic blood pressure greater than or equal to 90 mm Hg (Whelton *et al.*, 2017). Depending on whether the underlying cause is known or not it is classified as essential (when the cause is known) or secondary hypertension (where hypertension is due to systemic illness)(Wubayeet *al.*,2016). On the other hand, adult blood pressure can be classified as normal; if SBP < 120 mmHg, and DBP < 80 mmHg, Pre-hypertension: if SBP 120-139 mmHg or DBP 80-89 mmHg. Stage 1 hypertension: SBP 140-159 mmHg, or DBP 90-99 mmHg, Stage 2 hypertension if SBP $\geq$ 160 mmHg, or DBP $\geq$ 100 mmHg and Severe Hypertension if SBP $\geq$ 180/110 (Redzuan *et al.*, 2017, Wubayeet *al.*, 2016).

Hypertension is a significant worldwide health challenge because of its high prevalence and consequential cardiovascular disease risk factor (Tesfayeet *al.*,2009, Muluneh *et al.*, 2012, Soubeiga *et al.*, 2017). The prevalence varies in different countries, based on data from the national health and nutrition examination survey during 2015-2016, the prevalence of hypertension in the USA was 29.0% (Soubeiga *et al.*, 2017). According to WHO report hypertension was estimated to cause 7.5 million deaths, about 12.8% of the total annual deaths in Sub-Saharan Africa (Heleloet *al.*,2014).Similarly the prevalence of hypertension is increasing in Ethiopia even though the magnitude was different based on various study results (Gudina, 2013, Kibret & Mesfin, 2015).The result of pooled analysis of smaller studies showed that the prevalence of hypertension was estimated to be 19.6% (Kibret & Mesfin, 2015).

To reach optimal blood pressure control most of hypertensive patients need one or more antihypertensive medications (Rahmanet *al.*, 2008). Mixed drug therapy with several medication may lead to the occurrence of DTPs(Hanlon & Artz, 2001),the occurrence of DTP significantly affects health outcomes (Cramer *et al.*,2008). It may also affect quality of life, increase morbidity and mortality (Lassetter & Warnick, 2003). The resulting drug related morbidity and mortality could also cause severe medical and economic problem for the society.(Ernst & Grizzle, 2001).

According to the 1999 PCNE DTPs are defined as events or conditions involving or supposed to be involved in drug therapy that actually or potentially interfere with the desired health outcomes

(Gayathri *et al.*, 2018).DTPs can occur at every step of the medication use process (Cramer *et al.*, 2008). To date there is no uniform systems of classification for DTPs (Ruthset *al.*, 2007). However; according to (Cipolle *et al.*, 2012)there are seven distinct categories of DTPs (Table 1).

Table 1Categories and description of DTPs

Categories	Description
Unnecessary drug therapy	The drug therapy is unnecessary because the patient does not have a clinical indication at this time. It involved inappropriate combination/duplication of drug therapy.
Need additional drug therapy	Additional drug therapy is required to treat or prevent a medical condition in the patient. One or more drugs are missing according to established national/international guidelines.
Ineffective drug therapy	The drug product is not being effective at producing the desired response in the patient. Inappropriate drug selection according to established guidelines/formulary.
Dosage too low	The dosage is too low to produce the desired response in the patient. Sub-optimal dosing of drug therapy (including frequency and duration) according to established guidelines
Adverse drug reaction	The drug is causing an adverse reaction in the patient. Any noxious, unintended, and undesired effect of a drug, which occurs at doses in humans for prophylaxis, diagnosis, or therapy.
Dosage too high	The dosage is too high, resulting in undesirable effects experienced by the patient.
Non-adherence	The patient is not able or willing to take the drug therapy as intended.

The method of how DTPs are assessed and identified is important to make the decision more clinically rational. This is made by sequential assessment of an indication, effectiveness, dosing and safety profile of the product as well as medication adherence problems. The figure below summarizes the sequence (Cipolle *et al.*, 2012).

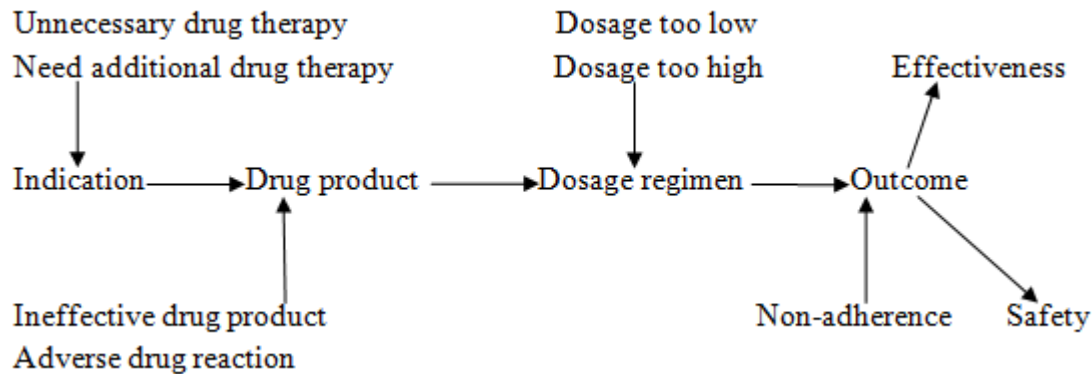


Figure 1 Drug therapy problem assessment and identification sequence

1.2 Statement of the problem

Most of DTPs occurred because of the rapid and increasing range of drug products, the rising number of diseases as well as patients (Cipolle *et al.*, 1998). Evidence from previous study has indicated the harmful outcomes associated with DTPs are main health issue that account \$76.6 billion in hospital costs, 17 million emergency department visits, and 8.7 million hospital admissions annually in the United States (Hsu *et al.*, 2016). However, majority of DRPs that attributed to hospital admissions are preventable (Al-arifi *et al.*, 2014).

Even though drug therapy in cardiovascular diseases can improve the well-being, its benefit can be affected by drug related problems (DRPs) (Abraham & Devi, 2013). DRPs are major public health concern worldwide and have been extensively increased over the past few decades and based on the result of some studies DRPs are cause of hospitalization (Al-azzam *et al.*, 2016).

One third of emergency visit in hospital is due to DTPs (Andreazza *et al.*, 2011).They also cause potentially preventable hospital admissions with considerable cost (Leendertse *et al.*, 2011). Previous study results showed that DTPs-related morbidity and mortality account for \$177 billion, with more than 1.5 million avoidable DTPs occurring each year in the United States (Renfro *et al.*, 2017).

Cardiovascular disease are issues of concern in developing countries like Ethiopia, the study result in government and private hospitals in Addis Ababa showed that more than half of the patients died were because of CVDs (Misganaw *et al.*, 2012).On other hand some study indicated that single- disease management is not as such potential strategy to care for patients that makes treatment of multiple disease more complex (Al Salmi, 2009) as a result medical outpatients with cardiovascular disease are exposed to DTPs (Yusuff & Tayo, 2011).The increased risk to DTPs is due to polypharmacy (Palaniappan *et al.*, 2015).

Hypertension is one of the chronic medical conditions associated with DTPs (Ombengi,*et al.*, 2016).The prevalence of DTPs among hypertensive patients requires considerable concern because it is associated with poor health related quality of life (Farha *et al.*, 2017). The goal of therapy in CVDs patients is to reduce mortality through optimization of drug therapy and quality of life by preventing DTPs (Al-azzam *et al.*, 2016).In order to make sure the safety and effectiveness of drug treatment early detection of DTPs by trained professions is required (Zazuli *et al.*, 2017).

This will be achieved through care full assessment of DTPs in addition to continuous clinical follow up among CVDs patients. Except those done in Adama general hospital and Ambo hospital there was scarcity of Studies done to assess the magnitude of DTPs and the associated factors in patients with hypertension in Ethiopia. Due to the reason that patients with CVDs have high incidence of DRPs and DTPs have potential impact on morbidity and mortality it is important to assess DTPs among hypertensive patients so that it would be easy to intervene and improve therapeutic outcome. In addition early detection of medical cases that are at high risk of developing DTPs would help policy makers to make decision on the inclusion of medication therapy management service in health plan design (Isetts *et al.*, 2008).

1.3 Literature review

1.3.1 Drug therapy problems

DTPs are main issues of safety for patients with chronic medical conditions and most of the patients with chronic medical illness are ambulatory (Krähenbühl-melcher *et al.*, 2007). Even though DTPs are well studied in the inpatient setting little is known in outpatient setting and the rate is higher in the outpatient setting in comparison to inpatient (Meyer-Masseti *et al.*, 2018).

A study done to identify patterns of DRPs in hypertensive patients with chronic heart disease in Chidambaram, Tamil Nadu, and South India found that a total of 75 DRPs were identified from 50 prescriptions. Among 75 DRPs 92 causes of DRPs was found on hypertension with chronic heart disease from which (56%) identified were drug use process, (42%) were unawareness of patients to drug treatment information and then followed by Subject/Psychological observed (86%) (Jainaf Nachiya *et al.*, 2014).

In Australia a study was done to examine the number and nature of DTPs in both home-dwelling and residential care-facility patients and identified 1,038 drug-related problems in 234 medication reviews. The number of problems identified was greater (4.9 ± 2.0 vs. 3.9 ± 2.2 ; $P < 0.001$) in reviews for home-dwelling patients compared with care-facility residents. However the number of clinically-significant problems identified was greater (2.1 ± 1.1 vs. 1.5 ± 0.7 ; $P < 0.001$) for home-dwelling patients (Stafford *et al.*, 2009).

Additionally Pooled analysis of two randomized controlled trials in Indiana University to determine the effect of pharmacist intervention on adverse drug events and medication suggested that pharmacist intervention to improve medication use in outpatients with cardiovascular disease decreases the risk of adverse drug events and medication errors (Murray *et al.*, 2009).

1.3.2 Prevalence of drug therapy problems

A prospective, observational study conducted among 189 patients with cardiovascular disease to assess the incidence of DRPs and provide pharmacist interventions for identified DRPs found a total of 416 DRPs (on average, 2.2 DRPs per each patient) and at least one DRPs was present among 130 patients (Movva *et al.*, 2015).

Another study done among 257 participants to assess DRPs in medical ward patients in Jimma University specialized hospital found a total of 316 DRPs. From the six classes of DRPs identified, 103 (32.6%) cases were related to untreated indication or need additional drug therapy, and 49 (15.5%) cases were related to high medication dosage, 49 (15.5%) cases, were related to unnecessary drug therapy, 44 (13.9%) cases were related to low medication dosage and 42 (13.3%) cases were related to ineffective drug therapy and noncompliance the least prevalent DRP was seen in 31 (9.8%) cases (Tigabu *et al.*, 2015).

Similarly cross sectional study done in Ambo general Hospital Ethiopia to determine presence of DTPs among 151 ambulatory hypertensive patient found that the mean of DTPs was 1.32 ± 0.47 and the total numbers of DTPs were 200. Most patients had one DTP and the most common DTP was indication related problem (Tegegne *et al.*, 2015).

1.3.3 Drugs involved in drug therapy problems

A study in south India to assess drug related hospital admission in tertiary care hospitals found that 19.8% of hospital admission was by cardiovascular system drugs (Sekhar *et al.*, 2011). In addition a systematic review on drug related hospital admission indicated that Anti-neoplastic agents, CVS drugs and CNS drugs were related to most of the DRPPs (Nivya *et al.*, 2015).

Another study conducted to describe the frequency, types, and temporal occurrence of DRPs in Taiwanese heart failure outpatients receiving case management found 796 DRPs among 141 out patients and the drugs most frequently causing a DRP were angiotensin converting enzyme inhibitors/angiotensin II receptor blockers, diuretics, warfarin, spironolactone, and B-blockers (Hsu *et al.*, 2016).

Similarly a prospective study conducted in University Kebangsaan Malaysia medical centre to identify the DRPs and the most common drugs associated with DRPs among hypertensive patients with multiple comorbidity showed that a total of 172 DRPs were identified with an average of 2.15 ± 1.5 DRPs per patient and the drugs that were most associated with DRPs were antihypertensive drugs (Redzuan *et al.*, 2017). Additionally study done to identify the major DRPs leading to hospital admissions in the elderly found that the most common drugs are cardiovascular and drugs for central nervous system (Somers & Petrovic, 2014).

On the other hand, a hospital based prospective observational study done in Jimma university specialized hospital among heart failure patients to assess the prevalence of DTPs and contributing factors found that the most frequently implicated medications in DTPs were beta-blockers (34.4%), angiotensin converting enzyme inhibitors (24.8%), statins (16.5%) and antithrombotics (13.1%) (Niriayo *et al.*, 2018).

1.3.4 Factors associated with drug therapy problems

A Cross-sectional study done in Swiss on cardiovascular out patients to describe DTPs and expense problems showed that the control of cardiovascular risk factors, quality of life and healthcare costs are statistically related to the presence of DTPs. From the total study patients included 91% had at least one DTP or expense problem. The odds ratios indicated that not being exposed to DTPs was associated with a higher chance of reaching the clinical target (OR: 3.4 95%CI:1.1–10.5; $P = 0.01$), of having a better physical quality of life than the median (OR: 2.5; 95%CI:0.9–7.3; $P = 0.05$) and having lower total health care costs (OR: 3.2; 95%CI:1.1–9.8; $P = 0.02$) (Niquille & Bugnon, 2010).

Similarly a cross-sectional study done in southern Brazil found that from 350 patients interviewed the frequency of DRPs was 31.6%. Quantitative ineffectiveness was observed in 30.9% of DRPs and the main cause of the DRP was an inadequate dosing regimen. Sixty-six DRPs (53.7%) were caused by the health system or the health professionals. Factors independently influencing the development of DRPs were educational level and the number of drugs being taken (Andreazza *et al.*, 2011).

On the other hand prospective cross-sectional study conducted to assess medication non adherence (part of DTPs) and its determinants in Ayder referral hospital and Mekelle general hospital among hypertension patients on follow up found that one fourth of the participants were completely non-adherent and only around half of them were adherent to their medications. The absence of family support, being at the pre hypertension class of blood pressure, living in Mekelle city and presence of hypertensive heart disease were shown to decrease adherence to antihypertensive medications (Ali *et al.*, 2014).

A retrospective study conducted at a tertiary hospital in Malaysia among 200 T2DM patients with hypertension found that 90.5% had at least one DRP, averaging 1.9 ± 1.2 problems per patient. The most common DRPs encountered were insufficient awareness of health and diseases (26%), drug choice problems (23%), dosing problems (16%) and drug interactions (16%). The most implicated drugs were aspirin, clopidogrel, simvastatin, amlodipine and metformin. The six domains of DRPs found to have statistically significant associations were renal impairment, poly pharmacy, cardiovascular disease, elderly status, and duration of hospital stay (Huri & Wee 2013).

Additionally study conducted in Taiwan to identify DTPs among geriatric out patients found that 87% had at least one DRP, being older, having orthostatic hypotension and taking more chronic medications were associated with higher likelihood of having at least one DRP (Chan *et al.*, 2012).

2. Objectives

2.1 General objective

This study aimed to assess the prevalence of DTPs and contributing factors among adult ambulatory hypertensive patients in Ayder referral hospital.

2.2 Specific objectives

- To measure the prevalence of DTPs among adult ambulatory hypertensive patients in Ayder referral hospital
- To determine the type of DTPs present among ambulatory hypertensive patients.
- To identify the most common drugs and drug classes involved in DTPs in ambulatory hypertensive patients and
- To assess the factors associated with DTPs in ambulatory hypertensive patients

3. Methods

3.1 Study setting

This study was conducted in Mekelle University, Ayder Referral Hospital located in Mekelle, the capital city of Tigray region, northern Ethiopia. The hospital is a training center for both post graduate and under graduate medical and other health sciences students at College of Health Sciences, Mekelle University. It is the only referral hospital in the region and serving up to 8 million populations in its catchment areas of the Tigray, Afar and southeastern parts of Amhara regions with 500 inpatient beds. It has four major departments (medical, surgical, emergency and intensive care unit) and other specialty units. Medical referral clinic was one of the specialty units of the hospital which provides medical services for registered, newly diagnosed and referral hypertensive patients. The clinic contains three nurses and two residents. The clinic had scheduled follow up (from Monday-Friday) for all ambulatory hypertensive patients. Based on the appointment chart about 256 patients per month or about 64 per week were getting services in the clinic.

3.2 Study design and study period

Institution based Cross-sectional study design was conducted for the period of three months from July 15/ 2017 to October 15 /2017.

3.3 Source and study population

All ambulatory hypertensive patients who visited medical referral clinic of Ayder referral hospital and receiving drug treatment were taken as source population. All adult ambulatory patients with hypertension and receiving drug therapy and also those meeting the inclusion criteria were study subjects of the study.

3.4 Inclusion and exclusion criteria

3.4.1 Inclusion criteria

- Patients diagnosed with hypertension and taking at least one antihypertensive drug
- Hypertensive patients who are willing to go through the interview
- Patients with hypertension who are 18 years and above
- Patients with hypertension who had regular follow up and took medication for at least the past one year.

3.4.2 Exclusion criteria

- Patients who were seriously ill to complete the interview
- Patients with pregnancy induced hypertension
- Patients who refuse to give consent
- Patients who do not start antihypertensive medication
- Patients with incomplete medical records

3.5 Sample size and sampling technique

Sample size was computed based on single population proportion formula by using the following assumption. The proportion (P) of DTPs in this study group was taken as 50% (P=0.5) to get possible large sample size, confidence level of 95 % chosen, Margin of error (d) = 5%. Using the following formula:

$$n = \frac{z_{\alpha/2}^2 p(1-p)}{d^2}, \text{ Hence } n = \frac{(1.96)^2 * 0.5(0.5)}{(0.05)^2} = 384$$

Taking the final sample to be 384 data was collected from patients who were available during the study period and that fulfill the inclusion criteria using convenience sampling technique.

3.6 Study variables

3.6.1 Dependent variables

- Drug therapy problems

3.6.2 Independent variables

- Socio demographic characteristics (age, gender, level of education, residence and marital status, physical activities, smoking, alcohol use and use of traditional medicine), clinical characteristics including (duration of therapy, number of prescribed drugs, comorbidity conditions, hospitalization, presence of complications).

3.7 Data collection procedure

A total of 384 patients with hypertension who have been on follow up at the medical referral clinic of Ayder referral hospital for at least 1 year were asked to participate in the study. To meet the objective of this study, the questionnaire was translated into Tigrigna version (Annex III, B) and to check the consistency of the translation before using the Tigrigna version back translation to the original language (English) was made by the principal investigator. Structured questionnaire that contains socio demographic characteristics, modified Morisky medication adherence questions and the modified Naranjio ADR probability scale questions for adherence and ADR respectively was used to collect data from patient interview, whereas drug and disease related conditions were collected from medical chart review.

The modified Morisky's medication adherence Scale (MMAS-8) (Morisky *et al.*, 1986) that was used to assess patients adherence status was an 8-item self-report measure of adherence that contains 8 questions. Each no response has value of 1 and each yes has value of 0 except for item 5 (reversed), in which each response yes was rated as 1 and no was rated as 0. Item 8 concerning the difficulty to remember taking medications was scored as Never/Rarely = 0, Once in a while = 1, sometimes = 2, usually = 3 and all the time = 4. The higher scores the higher the adherence. The summative score was classified into three levels as high adherence with a score of 8, medium adherence with score of 6 to <8 and low adherence with score of <6 (annex III A).

Medical chart review was made using data abstraction format (Annex III) following the interview starting one year back retrospectively up to the end of data collection period. The chart was reviewed daily after the interview. Data from chart review included patient medical history, medication history, prescribed medications with their indication, dosage regimen, documented ADR and pertinent laboratory values.

After the data was collected, the principal investigator had evaluated appropriateness of treatment by using JNC 8 guideline (for HTN) and references including Up-to-date v 21.2 and Micromedex for the related comorbidity diseases. Medscape drug interaction checker was used to identify drug-drug interactions. Identified DTPs were recorded and classified using DTPs registration format (taken from Cipolle *et al.*, 2012). Drugs involved in DTPs were also recorded.

3.8 Process of identification of drug therapy problems

For each study patient, interviewed a complete medication chart review was made to assess the magnitude of DTPs, and then the problems were generally classified in to seven distinct groups based on (Cipolle *et al.*, 2012) classification system (Table 1). This classification system was broadly accepted patient centered text book, which standardized guideline for clinicians while practicing pharmaceutical care service. Since the choice of anti-hypertensive drug class is influenced by many factors such as age, race, stage of hypertension and the presence of concomitant disease, DTPs were identified by considering the participant's age, comorbidity conditions, stage of hypertension, BP control, drug safety profile and the proper drug selection, dosage titration, indication for therapy, and untreated indication. Adverse drug reactions were identified based on modified Naranjo causality assessment tool for ADR. Before making decision for the appropriateness of medication therapy Patients' clinical characteristics and organ functions were also taken into consideration. The total number of drugs per patient per day was calculated from the medical record and only the patients' current medications were involved.

The presence of DTPs was identified based on each clinical condition of the individual patients during three visits period using international guidelines for clinical practice JNC 8 that clinicians were using in the hospital (James *et al.*, 2014). Deviations from the guideline because of clinical conditions of the patient were not considered as DTPs. The effects of white coat hypertension was not considered since the data was collected retrospectively starting from the date of patient contact back two visits. DTPs identification processes based on the clinical conditions and laboratory findings was done by the principal investigator.

3.9 Data quality assurance

In order to assure its quality, two clinical pharmacists who had basic knowledge on pharmaceutical care services were trained and oriented for one day. Data from chart review and patient interview were based on standardized data abstraction format. To maintain consistency the tool was pre tested on 8% of study population in Mekelle general hospital and all necessary amendments were made in the structure after the pretest then after filled questionnaires were examined for completeness and consistency during data management, storage and analysis by the principal investigator.

3.10 Data analysis

Data was checked, edited and cleaned for its completeness and consistency manually. The cleaned data was entered into a computer using Epi data manager and Epi data entry client statistical software package then exported to SPSS version 21 for analysis. Descriptive statistics including mean and standard deviation for continuous variables and frequency and percentage for categorical data were used to summarize socio-demographic and relevant clinical characteristics of the study participants. A test of association was done using binary and multivariate logistic regressions while P value < 0.05 was considered significant.

3.11 Ethical consideration

Letter of ethical clearance was obtained from the ethical review board of school of pharmacy, Addis Ababa University; a Letter for cooperation from department of internal medicine was taken to medical referral clinic of ARH. In addition written verbal consent from a patient was requested to extract data from patients' medical charts and interview. During data collection, name of the subjects were not included. Data analysis was done using a code number that have been given to each participant's data collection tool. Privacy of all information accessed from the patient's medical record was kept and restricted from any disclosure other than allowed to access them. The right of participants to withdraw from the interview at any time or not to participate in the study was respected and the purpose of the study was explained for each participant before conducting the interview.

3.12 Operational definitions of terms

Drug Related Problem- an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes (Van mill, 2017). DTPs in this study include; indication problems (needs additional drug therapy and unnecessary drug therapy), safety problems (dose too high and adverse drug reaction), effectiveness problems (dose too low and ineffective drug product) and non adherence.

Adverse drug reaction - any noxious, unintended, and undesired effect of a drug, which occurs at doses used in humans for prophylaxis, diagnosis or therapy (WHO,1972).

Cardiovascular disease- conditions that involve narrowed or blocked blood vessels that can lead to a heart attack, chest pain (angina) or stroke (Dipiro *et al.*, 2011).

Drug interactions- are interactions that can cause harm to patient and are well documented or can cause moderate harm without well documented studies (Delafuente, 2003).

Comorbidity – the coexisting of two or more medical conditions or disease processes that are additional to an initial diagnosis (Pickrell, 2003).

Coffee drinking habit – consumption of at least one cup of coffee per day

Employed: governmental, private (non/profitable, self-employed, laborers and farmer).

No formal education- a person not certified with any grade level of education

Hospitalization – hypertension related admission of a patient

Pharmaceutical care– a professional patient care practice, which, when provided as an organized service, is experienced, documented, evaluated, and paid for as medication management services (Cipolle *et al.*, 1998).

Physical activity-doing exercise for at least 30 minutes per day for 5 days per week (IDF 2017)

Polypharmacy - the use of multiple medicines in a patient (Masnoon *et al.*, 2017).

Unemployed - house wife and participants who had no their own income.

4. Results

4.1 Socio-demographic characteristics

In this study a total of 384 patients were included. Greater than half of the study subjects 227 (59.1%) were females and 157 (40.9%) were males. The mean age was 56.74 years with the maximum number of patients 204 (53.1%) being in the age group of 36 to 59 years, majority 323(84.1%) had coffee drinking habit, nearly half of them were alcohol consumers, more than half of them 222(57.8%) did not have history of traditional medicine use, greater than half of them (65.9%) were married; nearly half of them were with no formal education, majority (92.7%) were orthodox followers, most (81%) of the study participants reside in Mekelle city and more than 69 % of the study subjects had physical activity. The details of patients' demographic characteristics along with other related factors were shown in table 2

Table 2 Frequency distribution of Demographic characteristics of the study subjects, ARH Mekelle, northern Ethiopia, 2018 (N=384)

Demographic Characteristics of patients	Category	Number %
Sex	Male	157 (40.9)
	Female	227 (59.1)
Age group	18-35	16 (4.2)
	36-59	204 (53.1)
	>=60	164 (42.7)
	yes	323 (84.1)
Coffee drinking	No	61 (15.9)
	Yes	186 (48.4)
Alcohol consumption	No	198 (51.6)
	Yes	5 (1.3)
Chat chewing	No	379 (98.7)
	Yes	9(2.3)
Smoking status	No	375 (97.7)
	Yes	162 (42.2)
Use of traditional medicine	No	222 (57.8)

	Single	3(0.8)
Marital status	Married	253(65.9)
	Widowed	115(29.9)
	Divorced	13(3.4)
	No formal	175(45.6)
Educational status	education	
	Primary	107(27.9)
	school	
	Secondary	
	School	59(15.4)
	College&	
	above	43(11.2)
	Orthodox	356(92.7)
	Muslim	22(5.7)
Religion	Catholic	4 (1)
	Protestant	2(0.5)
Residence	Urban	311(81)
	Rural	73(19)
Physical activity	Yes	266(69.3)
	No	118(30.7)
Occupation	Employed	105(27.3)
	Unemployed	279(72.7)

4.2 Clinical characteristics

The mean duration of hypertension disease since diagnosis was 2 ± 0.88 years. Almost half of the study participants 185(48.2%) had history of hospitalization and majority 113(29.4%) had only one hospitalization, 165(42.96%) found to have 1-2 comorbidity 219(57.04%) were found without comorbidity condition and less than half of the study patients 167(43.5%) received less than or equal to two drugs per day. The details of disease and medication related conditions of the study subjects are shown in the following table (Table 3).

Table 3 Frequency and distribution of disease and medication related conditions of the study subjects ARH Mekelle, northern Ethiopia, 2018 (N=384)

Disease & medication related conditions	Category	Number (%)	Mean $\pm$ SD	Range
Hospitalization	Yes	185 (48.2)	1.52 $\pm$ 0.5	
	No	199 (51.8)		
	One	113 (29.4)		
	Two	49 (12.8)		
No of hospitalization	Three	12 (3.1)	1.59 $\pm$ 0.873	1 - 4
	>three	11 (2.86)		
	Yes	165 (42.96)		
Co-morbidity	No	219 (57.04)	1.51 $\pm$ 0.5	1 - 2
	Yes	66 (17.2)		
Complication	No	318 (82.8)		
	1-2 years	106 (27.6)		
	2-5 years	204 (53.1)		
	6-10 years	54 (14.1)	2 $\pm$ 0.885	1-5
Duration of hypertension	11-15 years	8 (2.1)		
	>15 years	12 (3.1)		
	1-2 years	119 (31)		
	2-5 years	206 (53.6)		
	6-10 years	46 (12)	1.9 $\pm$ 0.813	1-5
Duration of therapy	11-15 years	5 (1.3)		
	>15 years	8 (2.1)		
	<=2	167 (43.5)		
Total number of medication	3-4	122 (31.8)		
	>4	95 (24.7)		

4.3 Pattern of prescribed medications among the study subjects

The most frequently prescribed drug combinations were diuretics and ACEI 87 (22.6%) followed by diuretics alone 75(19.5). The percentage of classes of drugs prescribed in the study subjects during the study period was shown in the following figure.

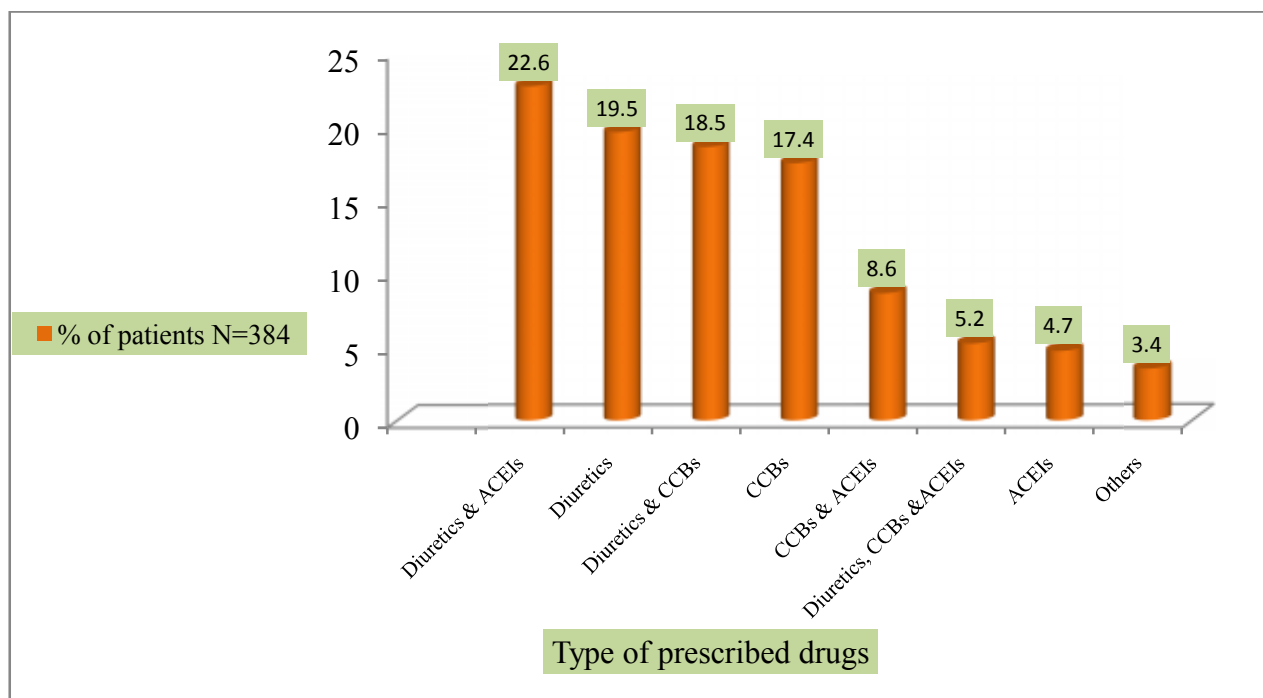


Figure 2 Percentage of classes of drugs prescribed among the study subjects ARH, Mekelle, northern Ethiopia, 2018, N=384

NB: CCB (calcium channel blockers), ACEIs (angiotensin converting enzyme inhibitors)

Others: Antibiotics, analgesics, anticoagulants, PPIs, Anti platelets, statins, minerals and vitamins.

4.4 Type of comorbidity among study subjects

As shown in figure 2 the most frequent comorbidity conditions among the study subjects were DM (22.4%) followed by hypertensive heart disease (20.6%) and the least frequent were others (HIV, hepatitis &schizophrenia) 3%.

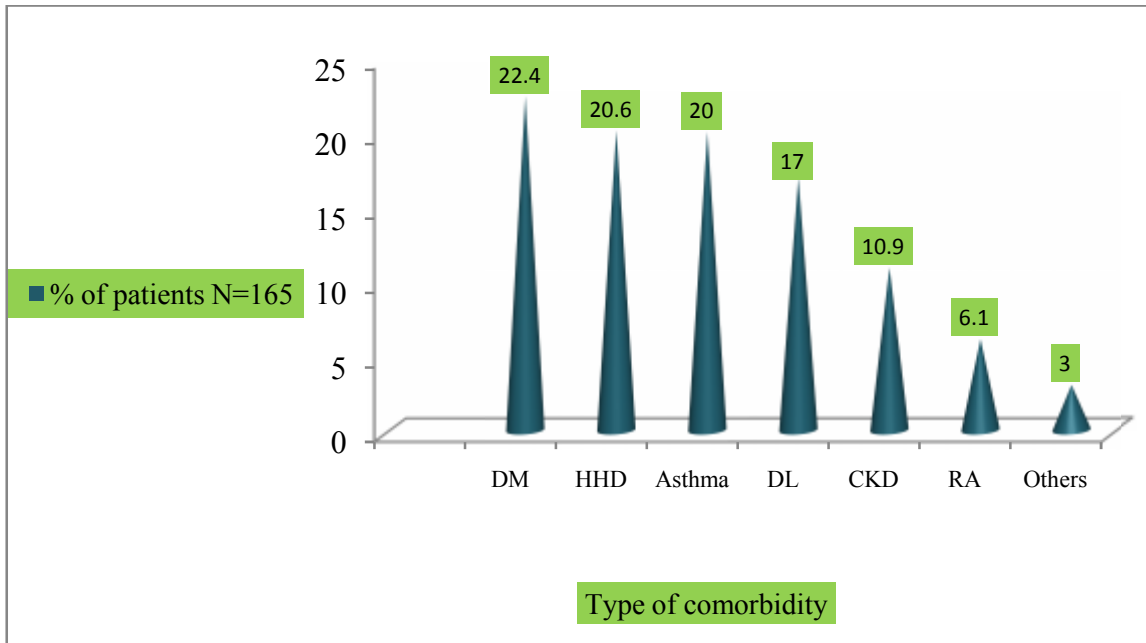


Figure 3 Type of comorbidity of study subjects ARH, Mekelle, northern, Ethiopia 2018, N=165

NB:HHD (hypertensive heart disease), DM (diabetes mellitus) and DL (dyslipidemia) RA (Rheumatoid arthritis) Others: Hepatitis, HIV, schizophrenia

4.5 Drug therapy problems and causes

Drug therapy problems were found in 52.86% of study subjects. A total of 277 drug therapy problems were identified from 203 study subjects in which, 1 DTP was identified from 133(65.5%) patients, 2 in 66 (32.5%) patients and 3 in 4(1.97%) of patients. Average number of DTP per patient was 1.36(Table 4).

Table 4Total number of drug therapy problems per patient, among study subjects ARH, Mekelle, northern Ethiopia, 2018, N=203

s.No	No of patients	No of DTPs	Total No of DTPs	% of patients with DTPs
1	133	1	133	65.5
2	66	2	132	32.5
3	4	3	12	1.97
Total	203		277	100

Unnecessary drug therapy was the top leading drug related problem (32.5% of all DTPs) followed by needs additional drug therapy (24.9%), dose too high (22.74%), ineffective drug therapy (11.9%), and dose too low (7.94%) of study subjects. Of the 90 DTPs classified as unnecessary drug therapy 32(35.5%) were due to no medical indication, 40(44.4%) were due to duplicate therapy and 18(20%) were due to non drug therapy indicated. According to the modified Morisky medication adherence scale 259(67.4%) of the study subjects had good adherence to their medication, 72(18.8%) had medium adherence and 53(13.8%) had low adherence and only 64(16.7%) of study subjects had possible ADR. The type and number of drug related problems identified were listed as shown in the following table (Table 5).

Table 5 Types of drug therapy Problems identified and causes among the study subjects, ARH, Mekelle, northern Ethiopia, 2018, N=277

S. No	DTPs	Class of DTPs	Cause of DTPs	No of DTPs	Total No of DTPs	%
1	Indication	Unnecessary drug therapy	No medical indication	32	90	32.5
			Duplicate therapy	40		
		Needs additional drug therapy	Non drug therapy indicated	18	69	24.9
			Untreated medical condition	69		
2	Effectiveness	Ineffective drug therapy	More effective alternative is available	33	33	11.9
		Dose too low	Wrong dose	22	22	7.94
3	Safety	Dose too high	Wrong dose	47	63	22.74
			Frequency inappropriate	13		
			Drug interaction	3		

4.5.1 Drugs involved in drug therapy problems

A total of 67 drugs were involved in different types of DTPs. As shown in table 6 the most frequent drug classes involved in drug therapy problems were ACEI (36.94%) followed by CCB (23.15%) and diuretics (18.7%).

Table 6 Drugs & classes of drugs involved in DTPs among the study subjects in ARH, Mekelle, northern, Ethiopia 2018, N=203

Drug classes involved in DTPs	Nº of patients % (N=203)
ACEI	75 (36.94)
Diuretics	38(18.7)
CCB	47(23.15)
Metoprolol	1(0.49)
Simvastatin	1(0.49)
Asprin	6(2.95)
Warfarin	14 (6.89)
PPIs	12(5.9)
Others*	9(4.33)

Others* (Antibiotics, Analgesics, minerals and vitamins)

Anemia, persistent head ache, uncontrolled BP, peptic ulcer disease, and amebiasis were among the untreated medical conditions. Patients in need of additional drug therapy are those with urinary tract infection, hypo kalmia, H .pylori antigen positive peptic ulcer disease, moderate to severe head ache and anemia. Drugs involved in ADR were those used for deep venous thrombosis prophylaxis, for the treatment of migraine head ache, lipid lowering agents and anti-hypertensive agents (ACEI, CCB and diuretics). The frequencies of classes of drugs with each particular DTP indicated that the most leading drug categories were ACEIs in ‘unnecessary drug therapy, dose too high, drug interaction and ineffective drug therapy. Table 7 shows drug classes involved in specific type of DTPs.

Table 7 Drugs and classes of drugs involved in each type of drug therapy problems, among the study subjects in ARH, Mekelle, northern Ethiopia, 2018.

S.No	Drugs (class of drugs) involved in DTPs	Types of DTP					
		UDT	NADT	IEDT	DTH	DTL	MDI
1	ACEIs (enalapril)	37	0	3	34	0	1
2	Diuretics (HCT)	21	2	7	6	2	0
3	CCB (amlodipine,nifedipine)	18	11	10	5	2	1
4	Metoprolol	1	0	0	0	0	0
5	Simvastatin	0	0	0	0	0	1
6	Asprin	0	5	0	0	0	1
7	Warfarin	6	4	0	4	0	0
8	PPIs	4	5	3	0	0	0
9	Others*	3	5	0	0	0	1

Others*: (Antibiotics, analgesics, Allopurinol minerals and vitamins)

NB: UDT (unnecessary drug therapy), NADT (needs additional drug therapy), IEDT (ineffective drug therapy), DTH (dose too high), DTL (dose too low), MDI (Major drug interaction), ASA (Asprin), BB (Beta blockers), HCT (Hydrochlothiazide), CCB (Calcium channel blockers) and ACEIs (Angiotensin converting enzyme inhibitors)

4.5.2 Factors contributing to drug therapy problems

The detection of risk factors for DTPs could help in finding patients who are at high risk for the development of DTPs. This could lead health care providers to give special attention for patients in the implementation of Pharmacotherapeutic plan with the hope of minimizing overt DTPs. Sex, age, marital status, occupation, educational status, chat chewing, coffee drinking, smoking, use of traditional medicine, history of hospitalization, number of medication and presence of comorbidity were analyzed to determine whether they could predict the occurrence or not. Of all factors considered only the total number of drugs taken by the patient was shown to be a risk factor for the occurrence of DTPs as shown in table 8. AOR = 2.572 95% CI (1.062-6.229)(Table 8).

Table 8 Associations between sociodemographic disease and treatment related characteristics with DTPs among the study subjects in Ayder referral hospital Mekelle, northern, Ethiopia 2018.

Predictors		No of patients %	COR(95%CI)	AOR (95%CI)	P value
Age cat	18-35	16(4.2)	(1)	(1)	(1)
	36-59	204(53.1)	0.429(1.44-1.277,)	0.375 (0.119-1.176)	0.093
	>60	164(42.7)	0.595(1.98-1.791)	0.475(0.148-1.524)	0.211
Residence	Urban	311(81)	(1)	(1)	(1)
	Rural	73(19.0)	1.556 (0.924-2.622)	1.377(0.800-2.368)	0.248
Smoking	Yes	5(1.3)	0.215 (0.45-1.027)	0.248 (0.05-1.236)	0.089
	No	379(98.7)	(1)	(1)	(1)
Total number of medication	<=2	167(43.5)	(1)	(1)	(1)
	3-4	122(31.8)	2.601(1.317-5.138)	2.572(1.062-6.229)	0.01*
	>4	95(24.7)	2.598 (1.419-4.756)	2.365(1.394-4.012)	0.001*
Presence of co morbidity	Yes	165(42.96)	(1)	(1)	(1)
	No	219 (57.04)	0.887 (0.594-1.325)	0.621 (0.377-1.023)	0.61

Patients were assessed for adherence to their medication according to Morisky's 8 items assessment scale, the cut-off for adherence. Patients who score 8 were considered to have high adherence, those with a score of <8-6 medium adherence and <6 were considered to have low adherence. In the current study 259(67.4%) of the study subjects had high adherence to their medication, 72(18.8%) had medium adherence and 53(13.8%) had low adherence. Among the reasons for non adherence forgetfulness was the most prevalent 85(68%), difficulty in remembering (sometimes) to take their medication 30(24%) and none affordability 10 (8%). According to the Naranjo adverse drug reaction probability scale only 64(16.7%) of study subjects had possible ADR and the common ADR experienced by the patient were side effects of drugs.

4.5.3 Examples of drug therapy problems identified among patients with hypertension

Many of the drug therapy problems listed below occurred because of lack of medication dosage adjustment or tapering, ignorance of medical conditions that required drug therapy, not following the treatment guideline and major drug - drug interaction.

Table 9 Examples of DTPs identified among ambulatory hypertensive in ARH, Mekelle, northern, Ethiopia 2018.

S.No	Brief Patient case	Drugs prescribed	DTPs identified	Justification
1	Age=50,sex=female , BP=120/70, investigations, all normal except serum electrolytes (K ⁺) = 2.5	HCT 25mg po daily, nifedipine 20mg po bid	needs additional drug therapy	Serum K ⁺ <3 requires K ⁺ replacement therapy
2	Age=69, Sex= Male Type 2 DM + HTN history of ischemic stroke , FBG=118,BP= 150/70	Metformin 500mg bid Enalapril 10mg po bid Aspirin 81mg po daily	Needs additional drug therapy	Prevention of CVDs with lipid lowering agents required since the patient had established CVDs (IS) and he had also HTN & T2D Mand age 40-75 yrs old.

3	Age=47,sex=female,HTN,thyrotoxicosis BP=120/80,with normallab investigation	Enalapril 5mg po daily,PTU 100mgpotid ,allopurinol100mgp otid and propranolo 20mg po daily.	Adverse drug reaction	Due to major drug interaction between Enalapril & allopurinol (severe allergic reaction)
4	Age=58,sex=male BP=150/100,HTN,H HD,T2DM,CKD	Lasix 80mgpoqid,simvast atin 40mgpodaily,N PH6/12,amlodipin 5mgpodaily	Major drug- drug interaction	Major drug interaction b/n amlodipin& simvastatin
5	Age=48,sex=female, HTN, intermittent cough with normal lab investigations	Enalapril 10mg podaily,almentamin 2.25mgpodaily	Adverse drug reaction	While the patient had ADR due to enalapril(ACEI induced cough)was prescribed with enalapril diuretic /CCB is better

NB:DVT (deep venous thrombosis), OIS (old ischemic stroke), BP(Blood pressure), DL (dyslipidemia), HCT (hydrochlorothiazide), HHD (hemorrhagic heart disease), HTN (hypertension), PTU (propylthiouracil), CKD (chronic kidney disease), ADR (adverse drug reaction), ACEI (angiotensin converting enzyme inhibitor), CBC (complete blood count),T2DM (type 2 diabetes mellitus), BA (bronchial asthma), IS (ischemic stroke), yrs (years) and Hgb (hemoglobin).

5. Discussion

Improper use of drugs during disease management may lead to drug therapy problems. Identification of common types of DTPs and factors associated with DTP was important in reduction of drug related morbidity and mortality (Al-Azzam *et al.*, 2016). Such studies help to achieve therapeutic outcomes and get better patient's quality of life in addition to minimize risk factors. Therefore, this study was aimed to assess the magnitude and factors associated with developing DTPs among ambulatory patients with hypertension.

This study revealed that greater than half of the adult ambulatory hypertensive patients treated at Ayder referral hospital (52.8%) had at least one drug therapy problem. The average number of drug therapy problems per patient was 1.36 this result was almost similar with the study done in Ambo general hospital which indicated the mean DTP found among ambulatory hypertensive was 1.32 ± 0.47 (Tegegne *et al.*, 2015).

The main type of DTPs identified were indication problems (unnecessary drug therapy and needs additional drug therapy) with the highest frequency followed by safety problem (dose too high) and effectiveness problems (ineffective drug therapy and dose too low). These problems were caused by therapeutic duplication, use of ineffective drug, use of drug without indication, drug interaction, wrong dose and inappropriate frequency. The findings of this study were in agreement with some the previously done studies in Minocita and South Australia (Rao *et al.*, 2007), Bonga (Gizaw, 2017) and Harar (Ayele *et al.*, 2018).

On the type of DTP identified (indication problem) the current study also agreed with the study done in Felege Hiwot Referral hospital and Indonesia. (Tegegne *et al.*, 2014, Nasution & Tanjung, 2016). But the average number of DTPs per patient in this study was lower than the result found in Felege Hiwot referral hospital (1.69 ± 0.993). This difference could be the study in Felege Hiwot referral hospital includes patients with cardiovascular disease that were expected to take more drugs because of their associated co morbidity conditions.

Unlike our findings the study done in India tertiary care teaching hospitals on cardiovascular patients showed the main types of DTPs were drug interactions (49.05%) followed by Adverse drug Reaction (18.86%) and failure to receive drugs (9.43%) (Shareef *et al.*, 2015), this difference could be the variation in the underlying co morbid conditions and study setting in which the study in India was on admitted cardiovascular patients who are exposed to more medications which leads to increased risk of developing adverse drug reactions and drug-drug interaction.

More over our findings varied with the findings in Malaysia among hypertensive patients with multiple co morbidity that indicated the most frequent category of DTPs were interactions (33.7%), followed by adverse reactions (23.9%), drug choice problems (14.5%), dosing problems (13.4%), others (8.1%) and drug use problems (6.4%) (Redzuan *et al.*, 2017), these discrepancies might be explained due to dissimilarity in study setting, disease condition of study subjects and study period.

The findings of the present study also varied from the findings in Adama hospital among hypertensive patients which showed the most common DTPs were drug interaction (58.7%), followed by non-adherence and adverse drug reactions constituting 19.5% and 18.6% respectively. This variation might be due to the difference in study setting, study period, sample size (the study in Adama was among 192 patients) and clinical characteristics of patients included in the study (patients with multiple co morbidity) (Hussein *et al.*, 2014).

In this study the average number of DTPs per patient was 1.36 which was higher from the study done in medical wards of Tikur Anbessa specialized hospital (Ayalew *et al.*, 2015) this small difference might be explained by the study in Tikur Anbessa Specialized Hospital includes patients admitted in medical wards which could receive close monitoring and follow up than the ambulatory patient with less frequent monitoring. In addition the average number of drug therapy problems was lower as compared to study done in India (1.9 ± 1.2 problems per patient.). This difference could be the study in India was for longer period and includes patients with diabetes and hypertension as patients with additional co morbid condition are expected to take more medications that could increasing the likelihood of drug relate problems (Huri & Wee, 2013).

In the current study a total of 67 drugs were involved in different types of DTPs. ACEIs was the most frequent drug classes involved in drug therapy problems. ACEIs account 75 (27.1%) followed by CCB 47(16.67%), diuretics 38(13.7%) and other drug classes 59 (13.56%). The findings of the current study was in line with the findings of the study done in United Kingdom and Saudi Arabia among cardiovascular and diabetic patients that showed the main medicine classes associated with MRPs were insulin and anti- hypertensive drugs (Al Hamid *et al.*, 2016), in addition to this the study done in India found that anti-hypertensive drugs were presented with the highest drug risk ratio for drug related problems (Abraham & Devi, 2013).

In the present study the most common classes of drugs involved in drug therapy problems were ACEIs, CCBs, diuretics, antibiotics, analgesics, anticoagulants, and Proton pump inhibitors (others class of drugs), this finding was supported by the study done in Taiwan among heart failure patients which showed the drugs most frequently involved in DTPs were angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers, diuretics, warfarin, spironolactone and b-blockers (Hsu *et al.*, 2016). Additionally study done in Taiwan among geriatric patients also supported the result that the most common offending drug category involved in DTPs were cardiovascular agents (33%) (Chan *et al.*, 2012).

However, the result of the this study in the types of drugs involved in drug therapy problems was somewhat differ from the findings of the study done in University of Malaysia among diabetic patients with hypertension that indicated the most common drugs associated with drug therapy problems were aspirin, clopidogrel, simvastatin, amlodipine and metformin. This slight different could probably be due to the variation in study design, sample size and study subjects (the study in Malaysia includes hypertensive patients with diabetes), that could bring the choice of antihypertensive differ in addition to difference in coo morbid conditions and number of medications (Huri & Wee, 2013).

In case of the causes for each specific types of drug therapy problems the present study found that the causes of drug therapy problems were indication problems (no medical indication, duplicate therapy, non-drug therapy indicated and untreated medical condition), and also effectiveness and safety problems (dose too low, dose too high and drug interaction). This result was in line with the study done in southern Brazil (Andreazza *et al.*, 2011).

Despite the overall causes of drug therapy problems which were similar with the current study one study done in Amsterdam among geriatric patients >60 years old and taking 5 or more chronic drugs and discharged from hospitals found that among the DTPs identified about 10% were due to drug interaction. This finding greatly differs with present study where only 1.1% of DTPs was due to drug interaction. This great difference might be due to the variation in study design, patient demographic and clinical characteristics and study setting (Ahmad *et al.*, 2014).

Detection of risk factors for DTPs is important in finding patients who are at high risk for the development of DTPs and helps health care providers to give due attention for patients in the implementation of Pharmacotherapeutic plan with the hope of minimizing overt DTPs (Urbina *et al.*, 2015). In the way to assess the major risk factors that contribute for the development of drug therapy problems, sex, age, marital status, occupation, educational status, chat chewing, coffee drinking, smoking, use of traditional medicine, hospitalization, duration of therapy, number of medication and presence of co morbidity were analyzed whether they could predict the occurrence of DTPs or not using bi variate and multi variate regression analysis and found that only the total number of medications taken by the patient to be predictor for the occurrence of DTPs, AOR = 2.572 95% CI (1.062-6.229), P=0.01.

The result of the current study was found to be in agreement with the study done in Adama hospital medical college among hypertensive ambulatory patients that showed the number of complications that patients experience and number of drugs patients took had significant effect on drug therapy problems (Hussein *et al.*, 2014). More over the finding of the current study was also similar with the literature review done in Pakistan that showed the number of drugs taken by the patient was an important predictor of drug therapy problems (Bhatti *et al.*, 2017). Additionally the findings of our study was also supported by study done in Oslo Norway that indicated the association between the increased number of drugs used and occurrence of DTPs was strong (Viktil *et al.*, 2006).

On the other hand the study done in Jimma university specialized hospital among heart failure patients indicated that the factors contributing to DTPs were age >50 years, negative medication belief, poor involvement of patients in the therapeutic decision makings, number of co-morbidity, and number of medications. Except the number of medications the results of the current study were quite different and the variation could be due to the differences in study methods, where the study in Jimma University specialized hospital was prospective observational study unlike the current study which was institution based cross sectional study. The other factor could be differences in study period (study in Jimma was for one month), patient clinical characteristics (study in Jima was among heart failure patients) that were expected to take more medications unlike that of hypertensive patients (Niriayo *et al.*, 2018)

Additionally the result of the study done in Jimma University specialized hospital among medical ward patients found that the factors that predict the occurrence of medication related problems were sex, age, polypharmacy, and clinically significant potential drug-drug interactions (Tigabu *et al.*, 2014) most likely this disagreement could be due to variation in study subject clinical conditions (where the study in Jimma includes all medical patients), number of medications taken by the patient, type of medications, co morbidity conditions, clinical stage and severity of the disease, study setting and study period. Similarly the study done in USA indicated that patients who took > 10 medications and saw at least 7 providers have significantly increased risk of MRPs (Jacquez *et al.*, 2015). The variation might be the difference in study setting, and patient clinical characteristics.

Unlike our findings the study done in Kansas city clinics showed that as the number of co morbidity increases the number of drug related problems increases (Manley *et al.*, 2003). in addition to this the study done in south west Ethiopia also indicated independent predictors of drug related problems were age and the presence of co morbidity(Yimama *et al.*, 2018). This difference could be explained by the variation in study setting, sample size, patient medication status, duration of disease, duration of therapy and study period. However, the result of the study conducted in Gondar university hospital among both ambulatory and inpatient cardiovascular patients showed the most identified risk factors for DTPs were need of additional drug therapy and lack of therapeutic monitoring (Abdela *et al.*, 2016).This variation might be because of the difference in study setting and co morbidity conditions, where the current study includes only ambulatory patients with hypertension only or hypertension plus other coo morbid conditions.

In the current study 67.4% of the study subjects had high adherence to their medication which was lower than the finding of the study done in Spain that indicated 77.4% of the study subjects had adherence to their medication(Marquez-contreras *et al.*, 2018).In addition the result was also lower than the study done in India among urban hypertensive patients that indicated 39% of the study patients had high adherence to their medication(Jhaj *et al.*, 2018).This variation might be due to the difference in study design (the study in Spain was prospective), small sample size and residence (study in India was among Urban hypertensive patients) as compared to the current study (urban and rural).

On the reasons for non adherence the result of the current study was similar to the qualitative study done among hypertensive patients in Iran which showed medication forgetfulness was one of the reasons for non adherence in addition to other factors (Najimi *et al.*, 2018).Generally the overall adherence among study subjects was also almost similar to the study done in University of Michigan Medical Centers which founds that majority of patients (67.7%) were adherent with their hypertensive medications (Patel& Taylor, 2002).

In the current study the reasons for the medium and low adherence were assessed and found that forgetfulness to take their medicine was the most prevalent cause 85 (68%) followed by difficulty in remembering to take their medicine now and then 30 (24%) and none affordability 10(8%) these results were in line with the study done in Sunderland among ambulatory hypertensive patients which indicated the major reasons for non-adherence were side effects and forgetfulness to take medicines (Khan *et al.*, 2014).In addition to this the result of the present study was somewhat similar with the study done to assess anti hypertension medication adherence and associated factors at Dessie hospital, north east Ethiopia, that showed the factors associated with non-adherence were health system and health care provider poor interaction with patient and therapy factors like frustration and unwanted effect of the medication in the long run (Chelkeba & Dessie, 2017).

But the findings of the present study was narrow and patient specific in case of the reasons for medication non adherence based on the result of the systematic review done from 42 studies across 19 developing countries that revealed a range of factors can influence medication none adherence including low household income, socioeconomic status, knowledge and beliefs of hypertension and its management, avoiding side effects of medications, cost of medication; use of herbal preparations, absence of symptoms, irregular follow-up; and dissatisfaction with the treatment and health services provided (Dhar *et al.*, 2017).

As reported by the WHO, the risk of non-adherence for patients was dependent on several factors; this includes those linked to the patient, to the health care providers, to the health care system, and the therapy itself (Burnier, 2017). So, the variation of the results of this study from the systematic review might be due to the reason that the present study focus only on specific patient response to their non adherence based on the MMAS-8 measurement unlike that of the studies in the systematic review that includes patient knowledge and beliefs of hypertension and its management and difference in study period and design.

6. Limitations of the study

Despite the fact that the study was conducted on relatively large sample size, and covers the outpatient settings, which is an area that has limited literature compared to inpatient settings the following limitations could be considered;

- Conducted on single public hospital
- Used retrospective study design
- Did not consider the effect of white coat hypertension (retrospective data)
- BP measurement trends in the three visit was not considered

7. Conclusion

The magnitude of DTPs among ambulatory hypertensive patients was high. The most commonly identified DTPs were indication type problem (Dosage too high, ineffective drug therapy and need additional drug therapy). Majority of those drug therapy problems were caused by using high initial dose of the medication than it was recommended in the guide line, use of medication where more effective alternative was available, and presence of untreated medical condition. The maximum number of DTPs identified was three. Greater than half of the study subjects had good adherence and only a small quantity had possible ADR. ACEIs were the most frequent drugs involved in DTPs. From the overall findings of the current study it can be concluded that the total number of drugs taken by the patient per day was an important predictor of drug therapy problem AOR = 2.572 95% CI (1.062-6.229), P=0.01.

8. Recommendations

Based on findings of this study, the following recommendations were placed under

- Health care providers should pay more attention to patients at high risk of DTPs like patients with poly pharmacy
- Health care providers should stick with the guideline when they prescribe the medications.
- Health care providers should also pay due attention on the negative impact of DTPs and the factors associated with them that influence the goal of therapy.
- The hospital should establish policies and strategies like pharmaceutical care services in a way that could help minimize preventable DTPs so as to increase patient quality of life and achieve therapeutic goal.
- Conducting additional studies like interventional studies.

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Annexes

Annex I Participants' information sheet

Name of principal investigator: Werkya Mahammedsied

Name of study area: medical referral clinics of Ayder referral Hospital

Research budget covered by: Addis Ababa University

Research objective: To assess the prevalence and factors associated with drug therapy problems among adult ambulatory patients with hypertension at Ayder referral Hospital.

Significance of the study: The occurrence of DTPs potentially interferes with desired health outcomes it may also result in reduced quality of life, and increased morbidity and mortality. More attention should be aimed at developing solutions that could reduce preventable morbidity, mortality, and costs associated with DTPs.

Risks: The risk could be minimal to the patient during the study. Only 15-20 minutes will be spent for the interview

Participant right: The right of participants to withdraw at any time from the interview or not to participate was reserved.

Beneficial: The study could be helpful for patients to obtain quality service delivery system and to promote an intervention for the future perspective.

Confidentialities: The study result did not include patient's name and address. Hence confidentiality was kept as data was accessed only by ethically conducted, well trained and experienced health professionals of the study as well as interviewed and analyzed by the principal investigator.

Agreement: participants were fully voluntary to participate in the study.

Annex II; Informed Consent

Name of principal investigator; Werkyah Mahammedi

Research title: Assessment of drug therapy problems and contributing factors among adult ambulatory hypertensive patients in Ayder referral hospital, Mekelle, northern Ethiopia, a cross sectional study.

Card number _____ Code number _____

1. I confirm that I understand the information sheet for the above study and have had the opportunity to ask questions.
2. I understand that my participation is completely voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
3. I understand that my medical notes will be looked at by data collectors of this study and necessary information will be extracted. I give permission for these individuals to have access to my records.
4. I agree to take part in the above study. I would like to confirm my agreement by signing.

Participant's name _____ Signature _____ date _____

Name of the data collector: _____ Signature: _____ date _____

Name of the principal investigator: _____ Signature: _____ date _____

Thank you for your participation and cooperation

Greetings!

My name is Sr. / Ato -----

I am data collector for master student werkya mahammedsied currently working his research work for graduation in Clinical Pharmacy in Addis Ababa University, College of Health Sciences, and Department of Pharmacy.

I would like to assure you that the study is confidential and secure I will not keep a record of your name and address. You have a right to stop the interview at any time, or to skip any question that you do not want to answer. Your correct answer to the questions can make the study achieve its goals. Therefore, you are kindly requested to respond genuinely and voluntary with patience. The interview may take only 15-20 minutes. I would greatly appreciate your help in responding to this study.

Result of the interview:

1. Completed
2. Partially completed
3. The interviewee refused
4. Others _____

Annex III

Data abstraction tool

Addis Ababa University
College of Health Sciences
School of Pharmacy

Department of pharmacology and clinical pharmacy

A. Questionnaire English Version

Part I patient socio demographic information

Variable	1. Socio demography		variable		
1	Card #				
2	Age group	_____	8	Coffee drinking	1. Yes 2. No
			9	Alcoholic status	1. Yes 2. No
3	Sex	1. Male 2. female	10	Chat chewing	1. Yes 2. No
4	Marital status	1. Single 2. Married 3. Widowed 4. Divorced	11	Smoking status	1. Yes 2. No
5	Educationa l status	1. No formal educated 2. Primary school 3. Secondary 4. College	12	Physical activity	1. Yes 2. No

		&above	13	Use of traditional medicine	1. Yes 2. No
6	Religion	1. Muslim 2. Orthodox 3. Catholic 4. Protestant 5. Others	14	Occupation	1. Employed 2. Unemployed
			15	Hospitalization	1. Yes 2. No
7	Residence	1. Urban 2. Rural	16	If yes number of Hospitalization	1. One 2. Two 3. Three 4. >three

Var2. Clinical characteristics

Duration of HTN				
1. 1-2 year	2. 2-5 years	3. 6-10years	4. 11-15years	5. >15
Duration of Therapy				
1. 1-2 year	2. 2-5 years	3. 6-10years	4. 11 -15years	5. >15

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

S.No	Items(Y/N for each items and use reversion sentence for the value of item 5)	No	Yes
1	Do you sometimes forget to take your pills?		
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? If yes why?		
3	Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it?		
4	When you travel or leave home, do you sometimes forget to bring along your medicine?		
5	Did you take all your medicine yesterday? If no why?		
6	When you feel like your symptoms are under control, do you sometimes stop taking your medicine?		
7	Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?		
8	How often do you have difficulty remembering to take all your medicine?		
	1. Never/Rarely 3. Sometimes 4. Usually 5. All the time		
	2. Once in a while		
	Total score		

Part III: Assessment of adverse drug reaction/allergic reaction

1. Have you experienced any undesirable, unusual adverse drug events /allergic reaction to the prescribed medicines for you since the last 1 year? 1. Yes 2. No:

If yes, describe the manifestation of the

events _____

2. If your answer is “yes” for question number-1, answer the following questions:

- 2.1.Did the adverse event occur after the suspected drug was administered? 1. Yes 2. No 3.

Don't know

- 2.2.Did the adverse reaction improve when the drug was discontinued or a specific antagonist/antidote was administered? 1. Yes 2. No 3. Don't know

- 2.3.Did the adverse reaction reappear when the drug was re-administered? 1. Yes 2. No 3.

Don't know

- 2.4.Are there alternative causes (other than the drug) that could have on their own caused the reaction? 1. Yes: 2. No 3. Don't know

- 2.5.Was the reaction more severe when the dose was increased or less severe when the dose was decreased? 1. Yes: 2. No 3. Don't know

- 2.6.Did you have a similar reaction to the same or similar drugs in *any* previous exposure?

1. Yes: 2. No: 3. Don't know

Part V: Data abstraction format [Patients' Medical and Medication Record Chart Review]

Card # _____ Age ____ Weight (kg) ____ Height (cm) ____ Body mass index (BMI)[kg/m2] _____

1. Current medical conditions and medications

S. No	Date of visit	Medical condition	Medication Regimen/ type, dose frequency and duration	BP
1				
2				
3				

2. Relevant laboratory series results and diagnostic investigations

S. No	Parameter		Date of Visit 1	Date of Visit 2	Date of Visit 3
1	CBC	Hb			
		Hct			
		Mcv			
2	Electrolyte	Na ⁺			
		K ⁺			
		CL			
3	RFT	SrCr			
		BUN			
4	BG	RBS			
		FBS			
		HBA1C			
		LDL			

5	LP	HDL			
		Total cholesterol			
6	DEs	Echo			
		ECG			
		US			
7	Others				

NB. CBC, complete blood count, RFT = renal function test, BG = blood glucose, LP = lipid profile, DES = diagnostic examinations, US= ultra sound, ECG =echocardiogram

3. Adverse Drug Events (documented)

<u>S.No</u>	Drug Regimen	Adverse drug reaction /Drug allergies /Other alerts	Event date
1			
2			
3			

A. Logical questions to identify whether or not the patient is experiencing a drug therapy problem

1. Is the medication (indication) appropriate?

1.1. Unnecessary drug therapy

- a. Is there no valid medical indication for the drug therapy at this time?
- b. Do multiple drug products are being used for a condition that requires single drug therapy?
- c. Is the medical condition more appropriately treated with nondrug therapy?
- d. Does drug therapy is being taken to treat an avoidable adverse reaction associated with another medication?
- e. Is drug abuse, alcohol use, or smoking causing the problem?

1.2 Need for additional drug therapy

- a. Does a medical condition require the initiation of drug therapy?
- b. Does Preventive drug therapy required to reduce the risk of developing a new condition?
- c. Does a medical condition require additional pharmacotherapy to attain synergistic or additive effects?

2. Is the drug therapy effective for the disease condition?

2.1 Ineffective drug therapy

- a. Is the drug not the most effective for the medical problem?
- b. Is the medical condition refractory to the drug product?
- c. Is the dosage form of the drug product inappropriate?
- d. Is the drug product not an effective product for the indication being treated?

2.2 Dosage too low

- a. Is the dose too low to produce the desired response?
- b. Is the dosage interval too infrequent to produce the desired response?
- c. Does a drug interaction reduce the amount of active drug available?
- d. Is the duration of drug therapy too short to produce the desired response?

3. Is the drug therapy as safe as possible?

3.1 Adverse drug reaction

- a. Does the drug product cause an undesirable reaction that is not dose-related?

- b. Is a safer drug product required due to risk factors?
- c. Does a drug interaction cause an undesirable reaction that is not dose-related?
- d. Was the dosage regimen administered or changed too rapidly?
- e. Does the drug product cause an allergic reaction?
- f. Is the drug product contraindicated due to risk factors?
- g. Is there any history of allergy of the prescribed drug

3.2 Dosage too high

- a. Is dose too high?
- b. Is the dosing frequency too short?
- c. Is the duration of drug therapy too long?
- d. Does a drug interaction occur resulting in a toxic reaction to the drug product?
- e. Was the dose of the drug administered too rapidly?

B.Tigrigna version questionnaire

ናይ ተሓከምቲ መረዳኢታ ቅጥዒ

1. ናይ ተመራማሪይ ሽም፡ ወርቅያማሐመድሲዒድ
2. ፅንዓት ዝካየድሉ ቦታ፡ዓይደር ሪፈራል ሆስፒታል
3. ናይ ፅንዓት ከፋሊት ዝሸፈን፣አዲስ አበባ ዩኒቨርሲቲ
4. ናይ ፅንዓት ዓላማ፣ብተመላለስቲናይ ደምፀቅጢ ሕሙማት መድሓኒት ዙርያ ዘለዉ ፀገማት ን መንቀሊኡምንምምርማርንምፍላይ ንእዩ።
5. ናይ ፅንዓት ጥቅሚ፣ እዚ ፅንዓት ባዓልሞያታትን፣ አውባእቲ ፖሊሲ ስለ መድሓኒት አጠቃቅ ማ ዘለዉ ፀገማት ዘለዎም ትኩረት ንክውስክይገብር። ብተወሳኪ ነዚ ተመሳሳሊ ንዝስራሕ ፅንዓት መሰረታዊ መረዳኢታይ ህብ።

ከይዲ ፅንዓት

መረዳኢታ ሰብሰብቲ ናይ ተሳፍቲ ፍቃደኝነት ምስ አረጋገፁ ብመጠየቂ ወረቀት ቃለ መጠይቅ ይገብሩ።

ካብዚ ብምቅፃል አብ ናይ ሕክምናካርዲ ዝተመዝገበ መረዳኢታ ይወስዱ።

ጉድኣት፡እዚ ፅንዓት ምንም ዓይነት ጉድኣት የብሉን።

ናይ ተሳተፍቲ መሰል፡ተሳታፊ ነዚ ቃለመጠይቅ ብማንኛዉም ሳዓትምቁራፅ ወይ ድማ ዘይደለይዎ ሕ ቶ ዘይምምላስይኽኡሉእዮም።

ጥቅሚ፡እዚ ፅንዓት ንቀፃሊ ግዜ ፅርየት ዘለዎግልጋሎት ንክዋሃብይጠቅም።

መበረታተዒ፡አብዚ ፅንዓት ዝተሳተፉ ምንም ዓይነት መበረታተዒ የብሉምን።

ምሽጥርሓላውነት፡ናይ ፅንዓት ተሳታፊ ሽም፣ አድራሻክም እውን ካልኣት ዘማሓልፍዎ መልእክቲ ብግቡእ ይሕሉ።

ስምምዕነት፡ተሳታፊ ሙሉእ ብሙሉእ ተሳታፊ ከምዝከውንይግመት።

ንተወሳኪ ሓበሬታ ናይዚ ፅንዓት መተሓባበሪ ከነጋግሩ ይክእሉእዮም።

ወርቅያማሐመድሲዒድ

ስልክ.ቁፅሪ 0920026123

ኢሜል አድረስ: wmahammedsied@gmail.com

አብ ፅንዓት ንዝሳተፉ ናይ ፍቃደኝነት መረጋገጫ ቅጥፂ

አነ ነዚ ፅንዓት ሙሉእ ብሙሉእ ተነገሩኒ ተረዲአዮ አለኩ ዓላምኡ ብተመላለስቲ ናይ ደምፀቅጢ ሕሙት ዝተመስረተ ምዃኑ ተረዲአ አለኩ። ብተወሳኺ በዚ ተሳትፎ ምክንያት ምንምዓይነት አገልግሎት፣ ክፍሊት፣ ወይድማ ወ.ህብቶክምዘይህልወኒ ተረዲኤአለኩ። እዚ ውዕልዘገልግል ነዚ ፅንዓት ጥራሕ እዩ። ከብዚ ቀዲሉ ዝተገለፀኸመይ በዚ ፅንዓት ንክሳተፍ ተስማሕሪኦለኹ።

- | | ሽም | ፊርማ | ዕለት |
|----|--|-----|-----|
| 1. | ተሳታፊ፡ _____ ፣ _____ ፣ _____ | | |
| 2. | መረዳኻታ ሰብሳቢ፡ _____ ፣ _____ ፣ _____ | | |
| 3. | ናይ ፅንዓት ተመራማሪ ወርቅያ መሓመድ ሲዒድ፡ _____ ፣ _____ | | |

ንተወሳኺ ሓበሬታ ናይ ፅንዓት መተሓባበሪ ምንግጋር ይክእሉ እዮም። ንተሳትፎኹም የመስግን።

ሽመይ _____

አነ ናይ ወርቅያ መሓመድ ሲዒድ ዝተባሃለት በዚ ሰዓት ብክሊኒካል ፋርማሲማስተርስ ንትሠርሖ ፅንዓት መረዳኻታ ሰብሳቢ እዩ። ናይቲ ፅንዓት ዋና ዓላማ ብተመላለስቲ ናይ ደም ፀቅጢ ሕሙማት መድሓኒት ዙሩያ ዝተተሓሓዙ ፀገማት ምግምጋምን ምፍላይን እዩ። ናይዚ ፅንዓት ምሽጥር ዝሕሉው ምዃነይ ከረጋግፀልኩም ይፈቱ። እዚ ቃለ ምልልስማት መድሓኒት ዙሩያ ዝተተሓሓዙ ፀገማት ምግምጋምን ምፍላይን እዩ። እዚ ተሳትፎ ብፍቃደኝነት አብ ዝደለይዎ ሳዓት ምቁራፅወይ ድማ ዘይደልይዎ ሕቶ ዘይምህላስ ይክእሉ እዮም። ነዚ ፅንዓት መልሲ ብምሃብ ስለዝተሓባበሩኒ የመስግን።

ናይዚ ቃለ መልልስ ውፅኢት

1. ሙሉእ ብሙሉእ ተፈጻሙ
2. ብክፍል ተፈፀሙ
3. ተነፊጉ
4. ወይ ድማ ካልኦት ፀገማት

ሀ.ናይ ተሐከምቲ ማሕበረሰባዊ ባህርያት መረዳኝታ መሰብሰቢ ቅጥዒ

አብቲዝተዘጋጀዎሉምክፍቲቦታ—ምልክትይግብሩ

1. ካርዲቁፅሪ_____

2. ዕድመ_____

3. ፆታ 1.አነስታይ _____ 2. ተባኝታይ _____

4. ኩነታትመርዓ

1. ዘይተመርዐወ _____ 2. ዝተመርዐዎ _____ 3. ዝሞታ/ዝሞቶቶ _____ 4
ዝፈትሐ/ዝፈትሐት _____

5. ኩነታት ትምህርቲ

1. ዘይተማሃረ_____ 2. ቀዳማይደረጃ_____ 3. ካልአይደረጃ_____ 4. ኮልጅን ልዕሊኡ
ዘጠናቐቐ_____

6. ሃይማኖት

1. ሙስሊም _____ 2.ኦርቶዶክስ _____ 3.ፕሮቴስታንት _____ 4.ካቶሊክ _____ 5.ካልኦት

7. ቡናይስትዩዶ ? 1. እዎ _____ 2. አይፋሉን _____

8. መስተይስትዩዶ ? 1. እዎ _____ 2. አይፋሉን _____

9. ጫትይቅሕሙዶ ? 1. እዎ _____ 2. አይፋሉን _____

10. ሲጋራዮጭሱዶ ? 1. እዎ _____ 2. አይፋሉን _____

11. ኣካላዊእንቅስቃሴይግብሩዶ ? 1. እዎ _____ 2. አይፋሉን _____

12. ባህላዊመድሃኒትይትቀሙዶ ? 1. እዎ _____ 2. አይፋሉን _____

13. ኩነታትስራሕ 1. ስራሕዘይብሉ _____ 2.ቁፁርስራሕተኛ _____

14. ብደምፀቅጢምኽንያትሆስፒታልሃሪሶምይፈልጡዶ? 1. እዎ _____ 2. አይፋሉን

15. ንሕቶ 14 መልሶምእዎእተኮይኑክንደይጊዜ

1. ሓደጊዜ _____ 2.ክልተጊዜ _____ 3. ሰለስተጊዜ _____ 4. ሊዕሊሰለስተጊዜ _____

ለሕመም ደም ፀቅቲ ዝምልከት

1.ሕመም ደም ፀቅቲ ካብ ዝጅምሮም ክንደይ ገይሮም?

- | | |
|-------------------|----------------|
| 1. ካብ 1-2ዓመት | 4. ካብ 11-15ዓመት |
| 2. ካብ 2 ዓመት-5 ዓመት | 5. ልዕሊ 15 ዓመት |
| 3. ካብ 6-10ዓመት | |

2.ናይ ደም ፀቅቲ መድሓኒት ምውሳድ ካብ ዝጅምሮም ክንደይ ገይሮም?

1. ካብ 1-2ዓመት
2. ካብ 2 ዓመት-5 ዓመት
3. ካብ 6-10ዓመት
4. ካብ 11-15ዓመት
5. ልዕሊ 15 ዓመት

ሐ. ናይ ተሓክምቲ ናይ መድሃኒት ኣዎሳስዳ ዝምልክት

1. ሓደ ሓደ ጊዜ መድሃኒት ምውሳድ ረሲዖም ይፈልጡዎ ? 1. እዎ _____ 2. ኣይፋሉን _____
2. ሓደ ሓደ ጊዜ ካብ ምርሳዕ ወጪ መድሃኒቶም ከይዎስዱ ዝገበሮም ፀገም ኣሎ ዶ? 1. እዎ _____ 2. ኣይፋሉን _____
3. ንሕቶ ቁፅሪ 2 መልሶም እዎ እተኮይኑ ንምታይ ? _____
4. ሕማሞም ስለ ዝተባኣኣሰ ሓኪሞም ከየማኸሩ መድሃኒቶም ዎሲዶም ዶ ይፈልጡ ? 1. እዎ _____ 2. ኣይፋሉን _____
5. ኣብ መንገሻ ጊዜ መድሃኒቶም ብትክክል ዶ ይዎስዱ ? 1. እዎ _____ 2. ኣይፋሉን _____
6. ትማሊ ኩሉ መድሃኒቶም ዎሲዶም ዶ ? 1. እዎ _____ 2. ኣይፋሉን _____
7. ሕማመይ ቀኒሱ/ሕሹኒ ኢሉም መድሃኒቶም ጠጠው ኣቢሉም ዶ ይፈልጡ ? 1. እዎ _____ 2. ኣይፋሉን _____
8. መድሃኒት ብምውሳድ ለዉጢ ኣይረኽብኩን ኢሉም መድሃኒቶም ጠጠው ኣቢሉም ዶ ይፈልጡ ? 1. እዎ _____ 2. ኣይፋሉን _____
9. መድሃኒት ዘይምውሳድ ናይ ሓደ ሓደ ሰባት ፀገም እዩ መድሃኒቶም ብትእዛዝ መሰረት ንምውሳድ ይሰላቸው ዶ ? 1. እዎ _____ 2. ኣይፋሉን _____
10. ኩሉ መድሃኒቶም ንምውሳድ ዝኸበደኩም ክንደይ ጊዜ እዩ ?

1 ፈጻሚ

2 ብዝኾነ ጊዜ ሓደ ጊዜ

3 ሓደ ሓደ ጊዜ

4 ኩሉ ጊዜ

መ. ምስ መድሓኒት ዝተታሓሓዘ ኣብሰዉነት ዝረከዩ ዘይተለመዱ ምልክታት ዝምልከት

1. ካብ ዓሚ ጀሚሩ ናብዚ ዘሎ ጊዜ ምስ ዝትዕዘድዎ መድሓኒት ዝተታሓሓዘ ዘይተለመደ ኩነታት ኣብ ሰዎነትኩም ተራእዮዶ ይፈልጥ? 1 እዎ _____ 2 ኣፋሉን _____ 3 ኣይፍለጥን _____

2 ንሕቶ ቁፅሪ 1 መልሶም እዎ እንተኾይኑ ምልክቱ ይግለፁ _____

2.1 እዚ ግዳማዊ ጉድኣት ድሕሪ መድሓኒት ምወሳዶም ድዩ ተኸሲቱ?

1 እዎ _____ 2 ኣፋሉን _____ 3 ኣይፍለጥን _____

2.2 ድሕሪ መድሓኒት ምቁራፅ እዚ ግዳማዊ ጉድኣት ተመሓይሹ ዶ?

1 እዎ _____ 2 ኣፋሉን _____ 3 ኣይፍለጥን _____

2.3 መድሓኒቶም እንደገና እንትዕዘዱ ወይ ድማ መጠኑ እንትወስኽ እዚ ግዳማዊ ጉድኣት ዎሲኹ ተራከዩ ዶ ?

1 እዎ _____ 2 ኣፋሉን _____ 3 ኣይፍለጥን _____

2.4 ካብ መድሓኒት ወጪካልኻ ከምዚ ዓይነት ግዳማዊ ፀገም ከምጽኡሎም ዝኽእል ነገር ኣሎ ዶ?

1 እዎ _____ 2 ኣፋሉን _____ 3 ኣይፍለጥን _____

2.5. እዚ ጉድኣትናይ መድሓኒት መጠን እንተወስኽዎ ወስኽዎ ይስእንትቅንስይቅንስ?

1 እዎ _____ 2 ኣፋሉን _____ 3 ኣይፍለጥን _____

2.6 ቅድሚ ሕዚ ከምዚ ዓይነት ተመሳሳሊ ግዳማዊ ፀገም ኣጋጢምዎም ዶ ይፈልጥ?

1 እዎ _____ 2 ኣፋሉን _____ 3 ኣይፍለጥን _____

