

Assessment of Drug Related Problems among Elderly Patients Visiting Menelik II Referral Hospital, Addis Ababa, Ethiopia

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This is to certify that the thesis prepared by Bedilu Linger entitled with “Assessment of drug related problems among elderly patients visiting Menelik II Referral Hospital, Addis Ababa, Ethiopia” 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

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Drug therapy in the elderly needs an emphasis on the age related changes in drug pharmacokinetics and pharmacodynamics profile. As the age increase, people usually have more health problems that lead to the use of more medications than younger people do. Identification and prevention of drug related problems (DRPs) in geriatric outpatients will be an important step towards reducing hospital admissions. There are different studies regarding to DRPs in general population but studies regarding DRPs in elderly patients are scarce specifically in MIIRH there is no previous studies. This study aimed to assess DRPs among chronic elderly patients. A hospital based cross-sectional study was conducted on 236 chronic elder patients who were on follow up-care at MIIRH. Data collection was done through patient interview and medical charts review. Epi data version 4.2 and IBM SPSS version 23 were used for data entry and analysis respectively. Descriptive statistics, cross-tabulation, univariable and multivariable binary logistic regressions were used and $P < 0.05$ was used to declare association. More than two-thirds of patients had two or more comorbid disease. The most common diseases encountered were hypertension (72.0%) and diabetes mellitus (56.7%). In this study, 740 medications were used with the mean number of drugs per day was 3.14 ± 1.658 per patient. ACEIs 121(50.8%), antidiabetic agents 94(39.5%) and CCBs 75(31.5%) were commonly prescribed class of drugs. Forty nine percent of patients encountered at least one DRP and 118 drug related problems were identified. The average number of drug related problems per patient was 0.5. Non-compliance (45.8%) and needs additional drug therapy (24.6%) were major DRPs identified. antidiabetic agents were the most frequent drug class involved in DRPs. From 740 medications, 122(16.5%) drugs were from beers medication list, where (44.1%) of participants were exposed at least to one potentially inappropriate medications. To conclude, there is high prevalence of DRPs and PIMs. Marital status, number of comorbidity and number of drug prescribed have significant association with the occurrence of DRPs.

Keywords: Potentially Inappropriate Medication, Drug Related Problems, Elders

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List of Abbreviations/Acronyms

ACEIs	- Angiotensin-converting Enzyme Inhibitors
ADR	- Adverse Drug Reaction
AGS	- American Geriatrics Society
ASA	- Acetylsalicylic Acid
CNS	- Central Nervous System
CVD	- Cardio Vascular Disease
COR	- Crude Odds Ratio
DI	- Drug Interaction
DRP	- Drug-Related Problems
MIRH	-Menelik II Referral Hospital
MTF	- Metformin
NSAIDs	- Non-Steroidal Anti Inflammatory Drugs
PK	-Pharmacokinetics
PIM	- Potentially Inappropriate Medication

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1 Introduction

1.1 Background

Drug related problem (DRP) is an event or circumstance involving drug treatment that actually or potentially interferes with desired health outcomes (Mil, 2019) or any undesirable occasion experienced by the patient that includes, or suspected to include drug treatment, that interferes with achieving the specified goals of treatment. DRPs are clinical space of pharmaceutical care professional which require professional judgment to resolve. If not resolved, DRPs have poor clinical outcomes (Cipolle, Strand, & Morley, 2012) and may happen during prescribing, transcribing, dispensing, and patient use of medication therapy (Vogenberg & Benjamin, 2011).

Age related physiologic changes may lead to a diminished capacity to respond to stresses and the ability to preserve homeostasis, making older adults vulnerable to decomposition in stressful circumstances. In older adults, pharmacokinetics (PK) and pharmacodynamics profiles such as drug metabolism and excretion decrease, body tissue composition and drug volume of distribution change and drug-receptor sensitivity may be altered (Bazargan, Smith, & King, 2018; Blanda, 2006) which lead to exaggerated response of drugs in elderly. Old age is the major independent risk factors for chronic diseases that are most prevalent in developed countries such as cardiovascular disease, cancers, and neurodegenerative disorders. Consequently, older people have multiple comorbidities, usually in the range of 5 to 10 illnesses (Jaspinder, Sargun, & Kawaljit, 2014).

Drug therapy within the elderly needs an emphasis on the age related changes in drug PK and sensitivity profile (Olsen & Tindall, 2007). Due to a decline in renal function; decrease in metabolic clearance, decrease in water content of the body, increase fat content; the distribution volume of hydrophilic drugs may reduce in the elderly, resulting in increased plasma concentrations. Whereas the distribution volume of lipophilic drugs is increased, their plasma concentrations may decrease (Turnheim, 2004). As the age increase, people usually have more health problems that lead to more medications than younger people do. Because of this, elders are more likely to develop serious drug-drug interactions. One from three elders 65 or older develops at least one or more adverse drug reactions (ADR)(AGS, 2012).

Studies indicated that prevalence of DRPs in Ethiopia is high (60.65%) (Gelchu & Abdela, 2019), (71%) (Hussen & Daba, 2017), (72%) (Gizaw & Dubale, 2017) in different health care institution. Another study from Dessie referral Hospital reported that the prevalence of patients with at least one potentially inappropriate medication (PIM) was 23% (Sada, 2017); a similar study from Ayder Referral Hospital (28.6%) of patients received at least one PIM (Dinkashe, Ayalew, & Kassa, 2016). Adults 65 years and older have a history of being prescribed PIM. These medications contribute to adverse drug events, falls, delirium, and gastrointestinal bleeding (Beyer, 2015). The purpose of identifying DRPs is to achieve the desired goals of therapy and realize the best possible outcomes. In Ethiopia, there are no specific guidelines for geriatrics disease management and medications used in elders and no specialized health institution to give separate services for elders.

1.2 Statement of the Problem

According to the U.S. Census Bureau report, the world's 65 years and-older population will twofold by the year 2050, and the 85 and older population will have an increment of five folds (Hutchison, 2015). Increases in life expectancy resulting in higher healthcare costs and substantial changes in cause of death. Having more than one disease and polypharmacy is a major problem for elder patients (Beard, Margrit, Jordan, & Jotheeswaran, 2017). Older adults are at high risk for inappropriate use of medication given their large number of medical conditions and drugs (Zullo, Gray, Holmes, & Marcum, 2017). Certain drugs may lead to an increased risk of adverse outcomes in older adults (Holt, Schmiedl, & Thürmann, 2010). Cardiovascular disease, osteoporosis, dementia, osteoarthritis, diabetes, and related mobility disability will increase as people age increases (Jaul, 2017).

In USA elders 65 years and above expend for one-third of all drugs endorsed, which represent around 13% of the population. Besides, the number of individuals over 65 age taking three or more drugs expanded from one-third in 1988 to nearly one-half in 2000 (Basca, 2008). Studies done in Saudi Arabia elders reported that the average number of illnesses per person is five and the average number of drugs was eight (Sultan et al., 2015). Around two-thirds of Australians over the age of 60 years utilize four or more drugs (Elliott, 2006). In China, the curative care consumption for the aged was 233.18 billion RMB. Most of the curative care consumption for the old individuals were within the hospital accounting for 92.96%, (Duan et al., 2017). In tertiary care hospital Indian cardiac patients, the whole one-day cost of treatment is 10,029.2 Indian rube for elders (Kartik, Nitinbhai, Joshi, Christian, Patel, & Malhotra, 2016).

The prevalence of PIM has differed significantly from country to country, in India 29.3% (Kartik, Nitinbhai et al., 2016), in Netherland, 34.7% (Bruin-Huisman, Abu-Hanna, Weert, & Beers, 2017), 11% in USA (Lichtman & Boparai, 2008), 66% in Indian (Narvekar, Bhandare, Gouveia, & Bhandare, 2017) and 88% in Germany (Anne, 2016) received at least one PIMs in geriatrics age group. Another retrospective study in USA cardiovascular patients declared a high prevalence of PIMs in geriatrics observed (Sheikh-taha, 2017).

The utilization of PIMs listed in Beers criteria among the geriatric population can cause unplanned hospitalization (Sarwar et al., 2018). PIM carries the risk of causing ADRs in the elderly (Holt et

al., 2010). Diminished utilization of PIMs will decrease the event of adverse drug reactions, cost of treatment, and compliance in elderly patients (Pradhan, Panda, Mohanty, J. P. Behera, & Pradhan, 2015). Identification and prevention of DRPs in geriatric outpatients will be an important step towards reducing hospital admissions (Courtman&Stallings, 1995).

In India, the frequency of DRP was 1.54 per patient with drug interactions (25.0%), drug use without indication (15.0%) and ADRs (15.0%) (Celin, Seuma, & Ramesh, 2012). In Sweden, 66% of participants had at least one DRP (Pfister, Jonsson, & Gustafsson, 2017) and in Nagara, (83.4%) (Kv & Nedumballi, 1991) patients had medication related problems.

In Felege Hiwot Referral Hospital, Bahir Dare, most of the patients had DRPs, of which indication related problems constituted the highest part (Tegegne, Yimam, Yesuf, Gelaw, & Defersha, 2014). A retrospective study done in Gondar indicated that 27.72% of patients were utilized at least one PIM and immediate-release nifedipine (53.89%) was exceedingly prescribed inappropriately taken after by diclofenac (22.19%), ibuprofen (7.78%) and indomethacin (5.19) (Mekonnen & Bhagavathula, 2014). Another study in similar institutions reported that two-thirds of the elderly encountered inappropriate prescriptions. In this study, ACEIs were the most common inappropriately prescribed medication (Abegaz, Birru, & Mekonnen, 2018). Older people are prone to age related disease comorbidity, which leads to an increased number of inappropriate medications (Fialová & Onder, 2009). Inappropriate prescribing to older patients influenced by the total number of drugs prescribed (Lim et al., 2016).

Polypharmacy has a negative impact on the elderly health through predisposing to ADRs and leading to noncompliance so, prescribing in the elderly is an important issue, which needs more attention by healthcare professionals (Fitzgerald, 2007). Even if polypharmacy is a known risk factor for ADRs, the use of polypharmacy may be unavoidable in the elder patients since they have more disease comorbidities (Elliott, 2006). Inappropriate prescribing is a major health problem affecting elders (Fialová & Onder, 2009), therefore; medication appropriateness is concerning issues in older adults as if they exposed to multiple medications and are more vulnerable to medication related problems (Zullo et al., 2017). Effective interventions to optimize drug prescribing is needed to minimize PIM (Morin, Laroche, Texier, & Mscpharm, 2016). Improving the prescribing pattern in the elderly reduces the occurrence of ADRs, cost of treatment, and

increase compliance in elderly patients (Pradhan, Panda, Mohanty, J. P. Behera, & Pradhan, 2015). The prevalence of PIM had a significant association with adverse outcomes in terms of hospitalizations. So further development of interventions is needed to decrease DRPs and manage patients with multiple chronic conditions (Osei, Berry-cabán, Haley, & Rhodes-pope, 2016; Rawat, 2018)

The occurrence of DRPs might delay achieving of desired therapeutics out comes specifically this is serious in elderly patients in addition elders re not candidate for clinical trials during drug development so they might be high risk group of developing undesired effects of drugs. This might leads to unnecessary cost of treatment, hospitalization and risk of dying. All pharmacists need to be prepared to provide appropriate pharmaceutical care to the elder population and, more importantly, be able to implement it. In Ethiopia, there are different studies regarding to DRPs in general population (Gelchu & Abdela, 2019; Hussen & Daba, 2017; Tegegne et al., 2014) but studies regarding DRPs in elderly patients are scarce specifically in MIIRH there is no previous studies, Thus, this study aimed to assess DRPs among chronic elderly patients.

1.3 Significance of the Study

Identifying the use of drugs that are associated with more risks than benefits in older people is important. Optimal drug therapy is necessary for caring for elders since; they are vulnerable population groups because of the increased prevalence of chronic diseases and drug consumption. In Ethiopia, there are no specific guidelines for the management of medications used in geriatrics and no specialized health institution give separate service for elders, in addition, no specialized physicians in geriatrics so, this study may use as an impute for the appropriateness of medications used in geriatrics medication and to develop special guideline. This study mainly helps the Federal Ministry of Health, different health institutions and health care providers in this institution and other health institutions to have knowledge on the prevalence and factors associated with drug related problems in elders. It can be also used as baseline data to integrate programs, which are interested to work in this area. The data can also serve as a base for researchers and academic institutions to do research on geriatrics medication appropriateness. Finally, it may help different government stakeholders to minimize the burden of DRPs and its consequences, to have strategies for effective implementation of appropriate medication use in geriatrics.

2 Literature Review

The prevalence of DRPs among elderly chronic patients were differ from country to country.in An Scotland the incidence of DRPs was 14.2% with (5.3%) admissions identified as being definitely or probably drug-related (Cunningham, Dodd, Grant, Marion, & Richards, 1997) and in Netherland, 992 potential DRPs (Ahmad et al., 2014), in Portuguese 2109 DRPs were identified (Costa et al., 2016). A randomized controlled clinical trial in Sweden revealed that at least one DRP were identified in 66% of participants (Pfister, Jonsson, & Gustafsson, 2017). Another study in Norway stated that a total of 6158 DRPs were identified (Fog, Kvalvaag, Engedal, & Straand, 2017). In Nigerian elderly patient's prevalence of DRPs was 83.4% (Kv & Nedumballi, 1991). A studies done in Ethiopia, 105 with 1.38 ± 0.8 mean number of DTPs were reported (Tegegne et al., 2014) and in another Ethiopia hospital 72% of patients had DRPs, (Gizaw & Dubale, 2017).

A retrospective study conducted at the Singapore oncology center showed that elderly patients encountered three comorbid disease and six medications per patient with potential drug interactions (36.4%), adverse drug events (31.7%), and non-adherence (8.9%) are common DRPs (Ting, Yin, Si, & Chew, 2015) where as in Netherlands, needs additional drug therapy, dose too high, dose too low and wrong drug selection were the most commonly identified DRPs (Ahmad et al., 2014). In addition in India drug interaction is the most common DRPs followed by duplication of drugs and long duration of therapy with patient counseling problem is the cause of many DRPs (Inamdar & Kulkarni, 2016). In Oslo, use of unnecessary drugs (43.5%), excess dosing (12.5%) and lack of monitoring of the drug use (11%) was the most frequent DRPs with opioids and psychotropic drugs were involved in 34.4% of all DRPs (Fog et al., 2017) where as 90.2% patients needed medication counseling, 8% prescriptions had drug-drug interaction, 19% patients were using medication inappropriately and 24.5% of patients had risk factors for DRPs (Kv & Nedumballi, 1991) and drug indication related problems 39.26% which is the highest prevalent in Ethiopia (Gizaw & Dubale, 2017). A systematic review indicated that the most common DRP was the patient's nonadherence on the prescribed drugs, 35.2 % of patients not take the medication based on correct instruction (Lau & Dolovich, 2005).

A retrospective study in the USA concluded that 87.4% of patients (Sheikh-taha, 2017) and 45.5% in Texas USA geriatrics hospital had at least one PIM (Elghol, Charles, Dobbs, & Tian, 2012). In

African-American elders, about 50% develop PIM, 23% of PIMs due to drugs with potential drug-drug interactions. In European countries, the prevalence of PIM was, in Irish 8.7%, Swiss 16.7%, and Dutch 12.5%. Z-drugs (zolpidem, zopiclone, and zaleplon) were the most frequent PIM in Irish 3.5%, while NSAIDs, oral anticoagulant combination, sulfonylurea, and benzodiazepines 4.3% in Swiss, and benzodiazepines 7.1% in Dutch (Riordan et al., 2018). However, higher in Germany, 88% received at least one PIM (Anne, 2016). Another systematic review of seventeen studies analyzed by two versions of Beers criteria stated that prevalence PIMs were 18.5% and 82.6% (Storms et al., 2017). A retrospective cross-sectional study done in Gondar University Hospital elder patients stated that 27.72% received at least one PIM. Immediate-release nifedipine 53.89%, diclofenac 22.19%, ibuprofen 7.78% and indomethacin 5.19% (Mekonnen & Bhagavathula, 2014). In Dessie referral Hospital and Ayder Referral Hospital, 23% (Sada, 2017), 28.6% (Dinkashe et al., 2016) of patients received at least one potentially inappropriate medication respectively.

The prevalence of polypharmacy and PIMs use can lead to a higher number of DRPs and increased hospital stay (Subeesh, Gouri, Beulah, & Shivashankar, 2017). A study in India showed that the highest frequency of geriatric patients with polypharmacy was from the age group of 65-70 years (65%), (43%) were taking 5-10 drugs, 83% patients had comorbidities (Tamilselvan et al., 2018). In Switzerland, using PIM increased the risk of hospitalization (Reich, Rosemann, Rapold, Blozik, & Senn, 2014). The number of home medications, sex (female gender), and number and types of comorbidities were significantly associated with PIMs (Sheikh-taha, 2017). Female gender, number of diagnostic diseases or having more comorbid conditions and the number of prescribed medications were significantly associated with PIM exposure (Mo et al., 2016) and polypharmacy and PIM had a significant association (Rizky et al., 2018). As the number of comorbid chronic conditions increased, the prevalence of PIM was significantly increased among elders (Bazargan et al., 2018)

Elders have usually a large number of health problems and take more medications. As a result, they are more likely to develop serious drug-drug interactions (AGS, 2012). Polypharmacy, aging, quality of diabetes treatment and comorbidity were potential risk factors for developing DRPs (Inamdar & Kulkarni, 2016). A study conducted in Ethiopian referral hospital concluded that taking ≥ 3 medications per day, having comorbidity, and uncontrolled blood pressure (BP) were

factors associated with DTPs (Hussen & Daba, 2017). The use of PIM significantly increased among participants with a higher number of comorbid chronic conditions (Bazargan et al., 2018).

Potentially inappropriate medication is highly associated with a 16% increased risk of hospitalization (Varga et al., 2017). Hospitalized elderly patients in India about (87.3%) patients receive at least one inappropriate medicine. Metoclopramide, alprazolam, diazepam, digoxin, and diclofenac commonly used inappropriately (Tripathi, Jhaveri, Patel, & Barvaliya, 2014). Among inappropriately prescribed medications, clonidine, clonazepam and sliding scale use of insulin were common drugs (Rawat, 2018). From 44% of PIMs in India, ranitidine and prazosin are the most commonly prescribed drug (Narvekar et al., 2017). A prospective, cross-sectional study in Saudi Arabian hospitalized elderly patients showed that the prevalence of PIM is 15.6% (Sultan et al., 2015). In Indonesia, the prevalence was 52.2%, Chlorpheniramine, ibuprofen, and nifedipine was the most commonly prescribed PIM (Rizky et al., 2018). Prevalence of PIM in China 58.2% with age 80 years or older (Mo et al., 2016), in Taiwan's 63.7% by 2015 version of the Beers Criteria. Ketorolac is the most inappropriately prescribed (Goyal et al., 2018). In Brasil, 44.2%, NSAIDs, cardiovascular agents, benzodiazepines and antidepressants were commonly prescribed PIMs (Dinkashe, Ayalew, & Kassa, 2016; Lopes, 2016)

2.1 Conceptual Frame Work

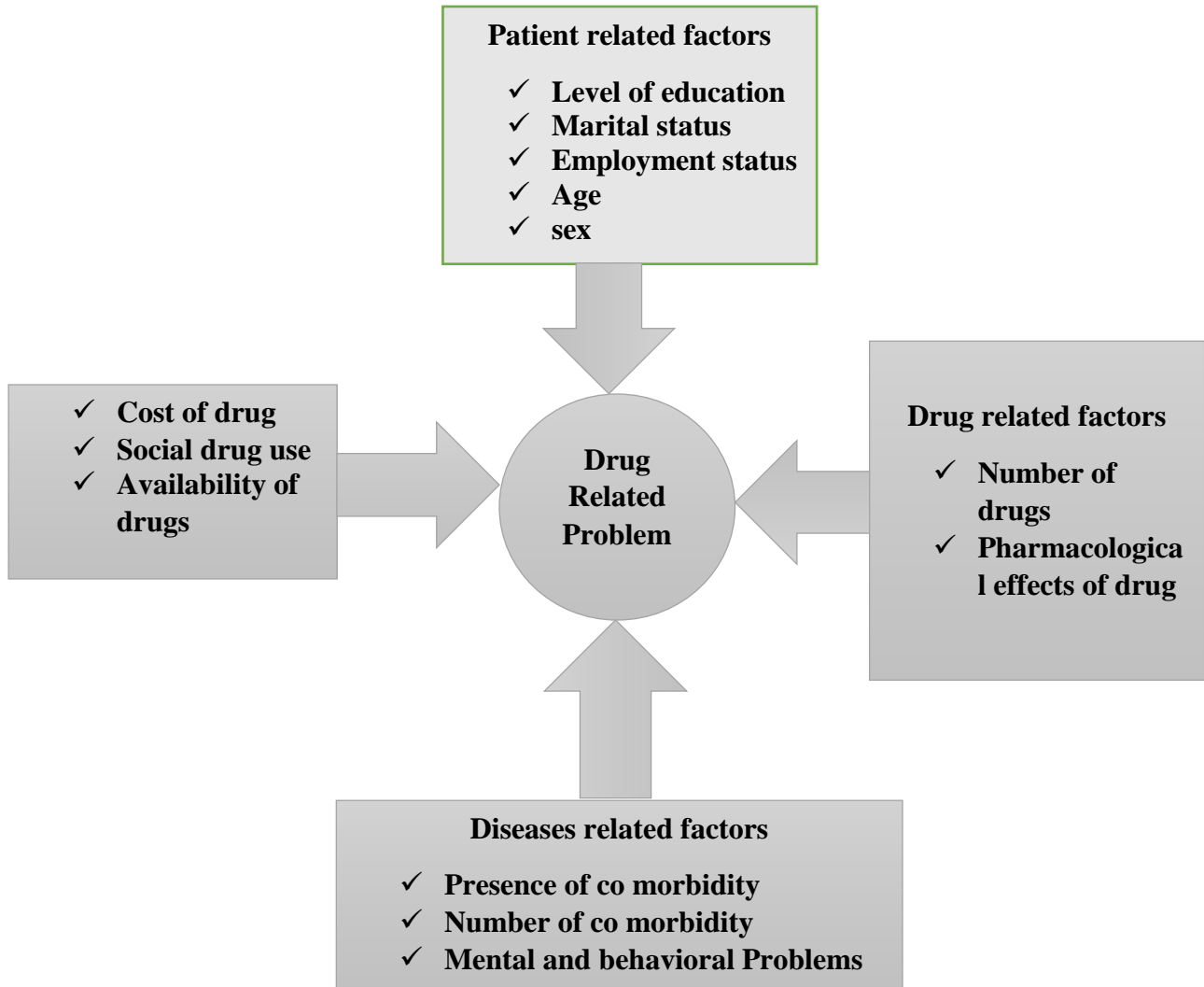


Figure 1: Conceptual framework showing factors involved in drug related problems

3 Objective

3.1 General Objective

The general objective of this study was to determine drug related problems in elder patients attending at Menelik II Referral Hospital Medical Referral Clinic.

3.2 Specific Objectives

- ✓ To determine the prevalence of drug related problems.
- ✓ To identify the most commonly encountered drugs or classes of drugs for drug related problems.
- ✓ To identify predictors of the occurrence of drug related problems.
- ✓ To determine the prevalence of potentially inappropriate medications.
- ✓ To determine the prevalence of drug interactions.

4 Materials and methodology

4.1 Study Area

The study was conducted at Menelik II Referral Hospital (MIIRH), which is located in the center of Addis Ababa, the capital of Ethiopia. MIIRH is one of the hospitals under the Addis Ababa city Administration Health Bureau established in 1902 E.C and it has been giving routine health care services for the city community and other referral cases from different regional states of Ethiopia. Menelik II Referral Hospital has various services, which include clinical, laboratory, diagnostic, forensic, pathology and optometry services are given. Among the clinics in MIIRH, a medical referral clinic is one of them serving for chronic patients 'follow up. Menelik II Hospital has various professionals that included 112 physicians, 34 pharmacists, 353 nurses, 125 other health professionals, and 354 administrative staff (MIIRH, 2019).

4.2 Study Design and Study Period

A facility based cross-sectional study design was employed and data collection was done from June 25 to September 25, 2019.

4.3 Source of Population

All patients attending the medical referral clinic of Menelik II Referral Hospital from June 25 to September 25, 2019.

4.3.1 Study Population

All patients aged 65 years and above attending the medical referral clinic of Menelik II Referral Hospital June 25 to September 25, 2019.

4.4 Eligibility Criteria

4.4.1 Inclusion Criteria

- Patients who were willing to participate in the study.
- Patients with age greater than or equal to 65 years.
- Patients having at least one medication.

4.4.2 Exclusion Criteria

- Patients with incomplete medical and medication information
- Patients with their first visit.
- Patients with having hearing and speaking problem

4.5 Sample Size Determination and Sampling Technique

4.5.1 Sample Size Determination.

All elderly patients with 65 and above years, visited the medical referral clinic in MIIRH from June 25 to September 25, 2019, who fulfill the inclusion criteria were enrolled and 236 patients were selected.

4.5.2 Sampling Technique

A convenient sampling technique was used as per the data collection period and inclusion criteria.

4.6 Variables of the Study

4.6.1 Dependent Variable

- Drug related problems

4.6.2 Independent Variables

- Demographic variables (age, sex, educational status, marital status, occupation, source of medication, social drug use).
- Class and number of prescribed drugs,
- Number of comorbidities.

4.7 Data Collection, Procedure, and Instrument

Information was collected through medical records and interviews of patients using a prepared standard checklist and structured questionnaire (annex II). The structured questionnaire was translated into the Amharic language. The content of the checklist includes patient details, investigations, current and past medication and disease conditions. Others like biochemistry and hematology results also collected. The contents of the standard questionnaire include social drug

use, drug and diseases related questions, and allergies. DRPs were identified based on a review of patients' medical and medication records, assessment of laboratory investigations, and patient's interview about medication experience. Specific information about medication therapies, such as the recommended drug of choice, recommended dosages, frequency of administration, duration of therapy, drug interactions, and ADRs were compared from the standard books and guidelines such as UpToDate2018, American Diabetes Association. 2019 and guideline 2017 Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. The appropriateness medications were assessed by using updated 2019 AGS beers criteria.

Adverse drug reactions identified from the patient reports (experiencing undesired effects) and from Medical charts, which already recorded by the physician. Micromedex® drug interaction checker was used to identify drug-drug interactions. Only major drug interactions by Micromedex® were considered as significant drug interactions. The identified DRPs were recorded and classified by using the DRP registration format, which taken from Cipolle et al, (2012) (annex II).

The AGS Beers Criteria® is an explicit list of PIMs that are typically best avoided by older adults in most circumstances or under specific situations, such as in certain diseases or conditions, drugs that should be prescribed at reduced dosage or with caution or careful monitoring, and selected drug–drug interactions documented to be associated with harms in older adults. The term PIMs encompasses the use of such therapeutic agents whose risk may outweigh their potential benefits(AGS, 2019). The updated 2019 AGS Beers Criteria was used to identify PIM. In this study, PIM was defined as the number of medications that must be avoided but were prescribed for an older adult.

4.7.1 Data Collectors

One trained clinical pharmacist as a supervisor and two nurse professionals as a data collector participated in data collection. One day training was given to the data collectors to familiarize them with the data collection instrument as well as how to collect the necessary data from charts and how to conduct patient interviews. Daily supervision and routine follow up were done by the principal investigator and drug-related problems were identified by the principal investigator.

4.8 Data Quality Assurance

The selection of data collectors was based on the educational level and with possible familiarity in medical and health research. The training was given for two data collectors and one supervisor about the objectives of the study and the process of the data collection. Strict supervision by the principal investigator assumed; meanwhile, any doubts in the questionnaire/ checklist were clarified. The pretest was also done and the correction was done accordingly.

4.9 Data Entry and Analysis

The data was entered into EPI-data version 4.2 and analyzed using Statistical Package for IBM social sciences (SPSS) version 23. Descriptive statistics were used for analyses of socio-demographic variables and to characterize DRPs. Categorical variables were described by frequencies and percentages, and continuous variables were described by means and standard deviations. Univariable binary logistic regression analysis was performed to relate each independent variable to DRPs. Those variables with a p-value <0.25 in univariable analysis were introduced to multivariate analysis and those variables with a p-value <0.05 were considered as significant in multivariate analysis. Odds ratio (OR) with a 95% confidence interval was also computed for each variable for the corresponding P-value to see the strength of association.

4.10 Ethical Consideration

Ethical approval was obtained from the research and ethics review committee of the School of Pharmacy, Addis Ababa University (Annex IV). After getting the official letter for permission from the Department of Pharmacology and Clinical Pharmacy, permission obtained from the Addis Ababa health office ethical review committee to conduct this research in MIIRH. Verbal consent from each patient was requested to participate in the interview and to extract data from their medical charts (Annex I). Patients were informed about the objective of the study and they were told that they have full right to refuse their participation at any time, and this by no means affects the service they get from the institution. Privacy and confidentiality were ensured during patient interview and review of patient medical charts. Thus, any identification of the patient participants in the data abstraction format.

4.11 Operational Definition

DRP: An event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes (Cipolle et al., 2012).

ADRs: Any noxious, unintended, and undesired effect of a drug, which occurs at doses used in humans for prophylaxis, diagnosis or therapy and bothersome adverse effects complained by the patient, was included (ASHP, 1995).

Elders: The ages of 65 years are arbitrarily used as the definition of elderly persons in developed countries whereas the age of 60 is for developing countries (WHO, 2002). But Beers criteria are intended for use in elders age 65 and above (AGS, 2019).

Non-compliance: The drug used differently as compared to prescribed once because of either patient preference, cost, swallowing or administering problem, difficulty of understanding instructions, unavailability, or forgetfulness (Cipolle et al., 2012)

PIMs: Any medication listed in the updated 2019 Beers criteria® to be avoided in elderly patients (AGS, 2019).

Co-morbid condition: The existence of more than one disorder or disease condition alongside primary diagnosed disease (Valderas, Eld, Sibbald, Salisbury, & Roland, 2009).

Drug interaction. A Change in the effect of the drug when the drugs are taken together with a second drug. The effect may be decreased, increase or leads to toxic effects when it is given with another drug (FDA, 2004).

5 Result

From June 25 to September 25, 2019, 273 chronic elderly patients visited MIIRH, finally 236 patients were selected.

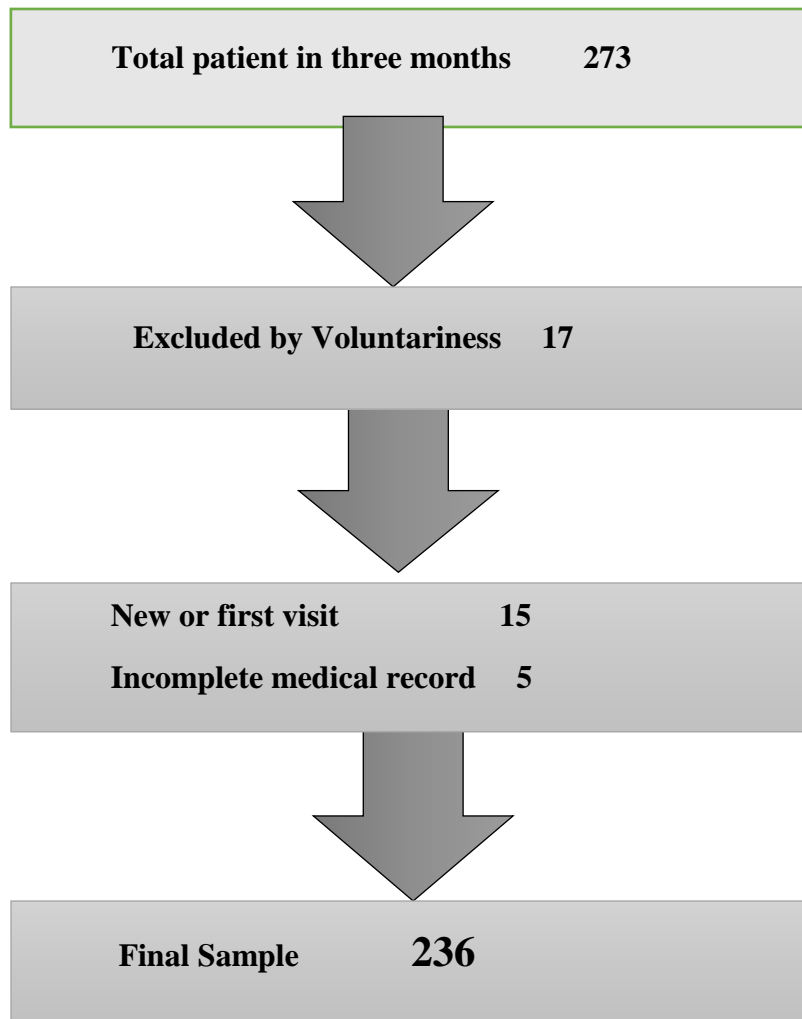


Figure 2: Patient selection procedures

5.1 Socio-Demographic Characteristics

In this study, 236 patients were included with a mean age was 70.51 ± 5.892 and 119(50.4%) of them were males. About half of the patients were married 109(46.2%) and 96(40.7%) patients had no formal education. Most of the patients 202(85.6%) did not use any type of social drugs. The majority of the patients 144(61%) got their medication for free (Table 1).

Table 1: Sociodemographic characteristics of study participants attending the Medical Referral Clinic of Menelik II Referral Hospital, 2019.

Variables		Number	Percent
Sex	Male	119	50.4
	Female	117	49.6
Marital status	Single	26	11
	Married	109	46.2
	Divorced	43	18.2
	Widowed	58	24.6
Educational status	No formal education	96	40.7
	Primary	79	33.5
	Secondary	27	11.4
	College and above	34	14.4
Employment status	Unemployed	97	41.1
	Employed	31	13.1
	Retired	78	33.1
	Other *	30	12.7
Source of medicine	Free	144	61
	Payment	92	39
Social drug use	Yes Cigarette	7	14.4
	Alcohol	23	
	Chat	4	
	No	202	85.6

Others Housewives, merchants*

5.2 Clinical Characteristics

From 236 patients who participated in this study, more than two-thirds of patients have more than one disease, two comorbidities 109(46.2%), three comorbidities 40(17.0%), and four and above comorbidity 18(7.6%).

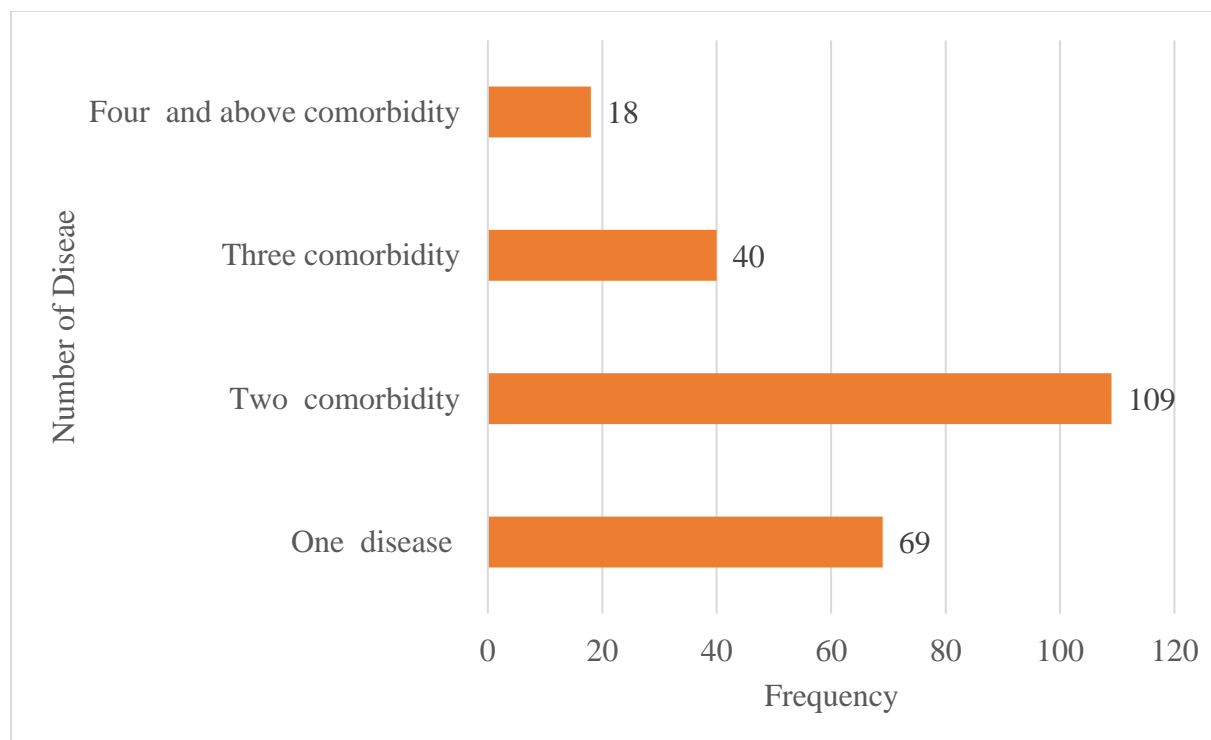


Figure 3: Number of comorbidities among patients attending a Medical Referral Clinic of Menelik II Referral Hospital, 2019.

The most common disease encountered were hypertension 170(72.0%), DM 135(56.7 %), HF 21(8.8%), ischemic heart disease 16(6.7%), primary open-angle glaucoma 15(6.3%) and hyperthyroidism 14(5.9%).

Table 2: Disease pattern among study participants attending the Medical Referral Clinic of Menelik II Referral Hospital, 2019.

Disease	Frequency	Percentage
Hypertension	170	72.0
DM	135	56.7
Ischemic heart disease	23	9.6
HF	21	8.8
Primary open-angle glaucoma	15	6.3

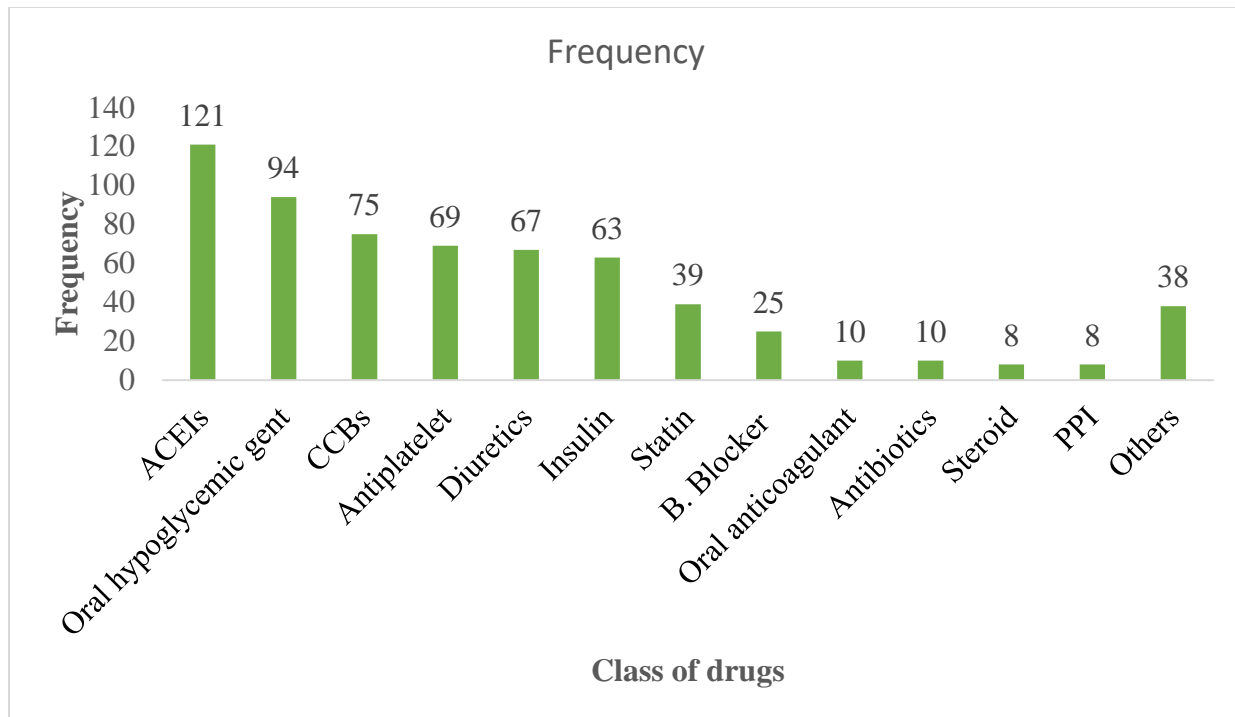
Hypertensive heart disease	12	5.0
Cardiomyopathy	12	5.0
Hyperthyroidism (Goiter)	14	5.9
Bronchial asthma	9	3.8
Dyslipidemia	9	3.8
Atrial fibrillation	6	2.5
Vulvar heart disease	5	2.1
BPH	4	1.7
Other*	21	8.8

Others:* Glomerulonephritis, Arthritis, Chronic Otitis Media, Upper Respiratory Tract Infection, Pulmonary HTN

HTN: hypertension *DM:* diabetes mellitus, *HF:* heart failure *BPH:* Benign prostate hyperplasia
CAP: community-acquired pneumonia,

5.3 Pattern of Drug Uses among the Study Participant

In this study, 740 medications were used with the mean number of drugs per day was 3.14 ± 1.658 per patient. More than, two-third of 187(79.2%) of the patients received less than five drugs per day and a maximum of nine drugs per day. The most common prescribed drug classes were ACEIs 121(50.8%), oral hypoglycemic agents 94(39.5%), CCBs 75(31.5%), antiplatelet 69(29.0%), diuretics 67(28.2%) and insulin 63(26.5%) (Figure 3).



Others: Propylthiouracil, Nonsteroidal Anti-Inflammatory Drugs, Xanthine Oxides Inhibitors, Digoxin. B. Agonists, Amitriptyline, Diphenhydramin, Methyldopa, Dorzolamide/timolol, pilocarpine.

ACEIs: Angiotensin-Converting Enzyme Inhibitors, CCBs: Calcium Channel Blockers, B. Blockers: Beta-Blockers

Figure 4: Pattern of medication use among patients attending a Medical Referral Clinic of Menelik II Referral Hospital, 2019.

5.4 Drug Related Problems

From 236 participants, 116 (49.2%) patients encountered at least one drug-related problem and a total of 118 DRPs were identified. The average number of DRPs per patient was 0.5. Regarding the number of DRP the patient's faced from totals, 71(61.2%) patients suffered one DRP, 30 (26.9%) patients faced to two DRPs, 13(11.6 %) exposed for three DRPs, and 2(1.9%) suffered from four DRPs from 112 patients. Non-compliance 54(45.8%) and needs additional drug 29(24.6%) were major DRPs identified in this study. Needs preventive drug therapy, drugs undesirable effect, drug-drug interaction, and patient's forgetfulness to take the drug as prescribed were common causes of DRPs (Table 3).

Table 3: Types of drug related problems identified from patients attending a medical referral clinic of Menelik II Referral Hospital, 2019.

DRP	Cause of DRP	No of DRP	Total DRP	percent
Needs additional drug	preventive drug therapy is required	15	29	24.6
	Synergism drug therapy required	10		
	Untreated disease condition	4		
Ineffective	More effective drug	2	2	1.7
Dose too low	Ineffective dose/ low dose	17	17	14.3
ADR	Undesirable effect	13	13	11.2
Dose too high	Dose too high	3	3	2.4
Noncompliance	Patient forgets to take	31	54	45.8
	Cannot afford drug product	10		
	Drug product not available	5		
	Patient prefers not to take the drug	4		
	Does not understand instructions	2		
	Cannot swallow/administer the drug	2		
Total		118	118	100

DRPs appeared to be common in patients with hypertension, DM and HF patients. From 205 DRPs, 104, 80, and 19 were identified from patients diagnosed with hypertension, DM and HF respectively (Figure 5).

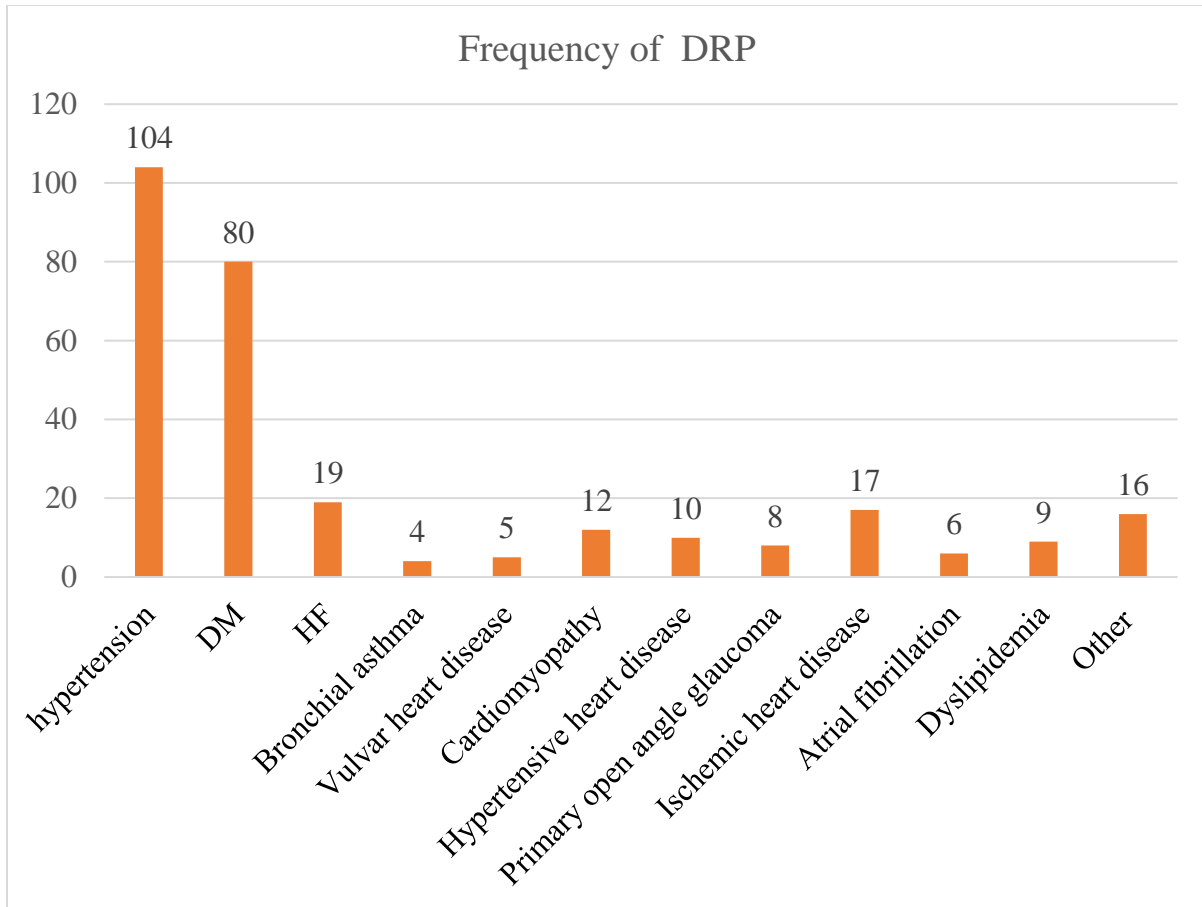
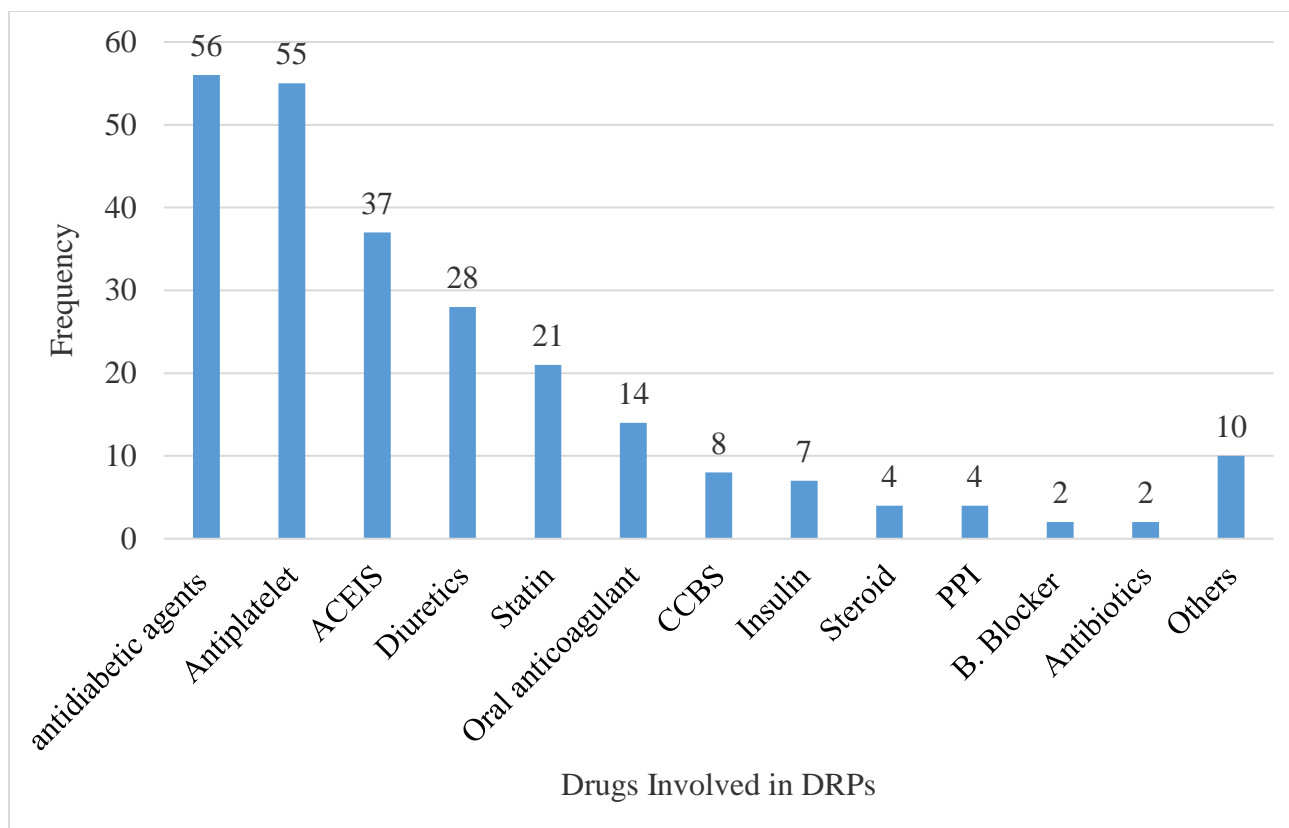


Figure 5: Prevalence of drug related problems by disease condition among patients attending the Medical Referral Clinic of Menelik II Referral Hospital, 2019.

5.5 Drugs involved in Drug-Related Problems

Oral hypoglycemic agents are the most frequent drug class involved in DRPs followed by antiplatelet, ACEIs, diuretics, and statins (Figure 6).



ACEIS: Angiotensin-Converting Enzyme Inhibitors, CCBS: Calcium Channel Blockers, PPI: Proton Pump Inhibitors

Others: Nonsteroidal Anti-Inflammatory Drugs, Digoxin, B. agonists

Figure 6: Drug classes involved in drug related problems among patients attending the Medical Referral Clinic of Menelik II Referral Hospital, 2019.

5.5 Drug Interaction

In this study 87 drug-drug interaction in 51(21.6%) patients, were detected by using Micromedex® drug interaction checker. The most recent drugs were analyzed to identify possible drug interaction. Only major drug interaction by Micromedex® was considered as significant interactions. Aspirin and metformin accounted for the highest frequency (23), aspirin may enhance the hypoglycemic effect of metformin and furosemide and aspirin (13) were the second prevalently faced drug interaction. Aspirin may decrease the diuretic effect of furosemide whereas furosemide may increase the serum concentration of salicylates (table 4).

Table 4: List of drugs involved in drug interaction and their frequency among patients attending at Medical Referral Clinic of Menelik II Referral Hospital, 2019.

Drugs involved in DI	Frequency	Severity	Possible effect
ASA and MTF	23	Major	Increased risk of hypoglycemia
Furosemide and ASA	13	Major	Reduce diuretic effectiveness/nephrotoxicity
Enalapril and spironolactone	10	Major	Hyperkalemia
ASA and glibenclamide	8	Major	Increased risk of hypoglycemia
digoxin and spironolactone	4	Major	Diminish therapeutic effect of digoxin
ASA and diclofenac	4	Major	Increased risk of bleeding
Furosemide and indomethacin,	4	Major	Risk of acute renal failure/ reduce diuretic effectiveness
Diclofenac and furosemide	2	Major	Diminish the diuretic effect of loop diuretics or nephrotoxicity
Diclofenac and HCT,	2	Major	Reduce diuretic effectiveness/nephrotoxicity
ASA and warfarin	7	Major	Increased risk of bleeding
ASA and indomethacin	2	Major	Increased risk of bleeding
ASA and Clopidogrel	2	Major	Increased risk of bleeding
Digoxin and Nifedipine	1	Major	Digoxin toxicity
Ciprofloxacin and indomethacin	1	Major	Enhance the neuroexcitatory and/or seizure-potentiating effect of Quinolones.
Enalapril and cotrimoxazole	1	Major	Increased risk of hyperkalemia
Atorvastatin and digoxin	1	Major	Digoxin toxicity
Diclofenac and dexamethasone	1	Major	Increased risk of gastrointestinal ulcer
Indomethacin and spironolactone	1	Major	Hyperkalemia

5.6 Prevalence of Potentially Inappropriate Medications

From 740 medications, prescribed 122(16.5%) drugs were from the beer's medication list. In this study, 104(44.1%) participants exposed at least one potentially inappropriate medication. From this 90, 10, 4 participants encountered one, two and three PIMS respectively (Figure 6).

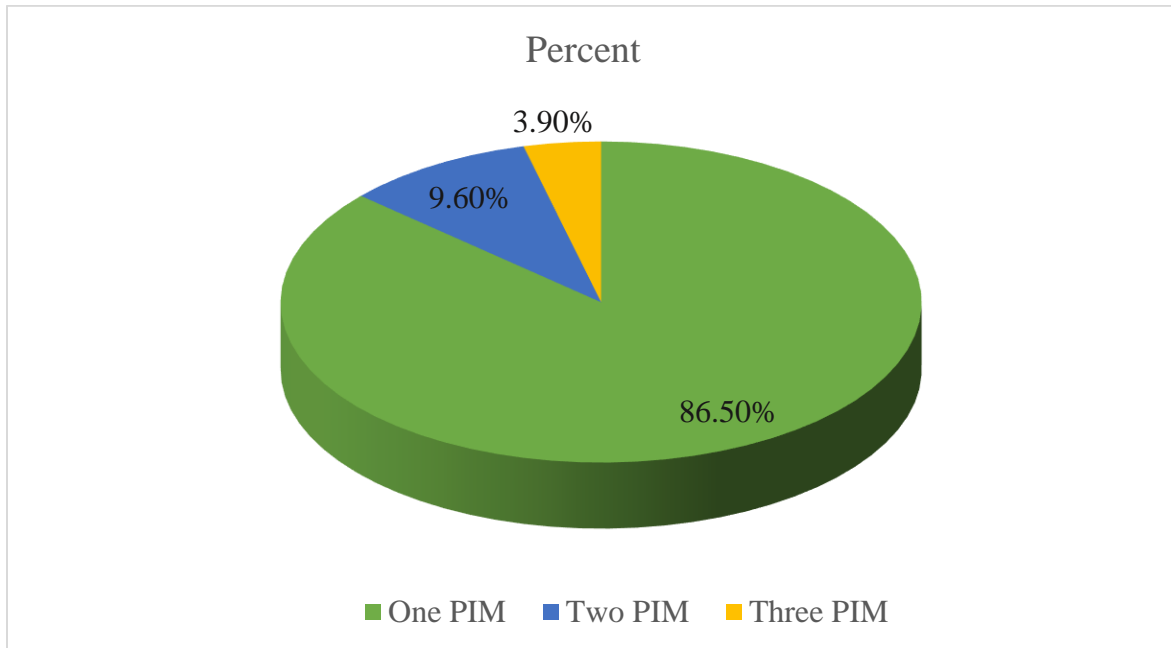


Figure 7: Number of potentially inappropriate medications among elder patients attending a medical referral clinic of Menelik II Referral Hospital, 2019.

From 122 PIMS glibenclamide is the most frequently prescribed drug followed by omeprazole, diclofenac, and Amitriptylin (table 5).

Table 5: List of drugs involved in potentially inappropriate medications among elder patients attending a medical referral clinic of Menelik II Referral Hospital, 2019.

List of Drug	Frequency	Percent
Glibenclamide	75	61.5
Omeprazole	14	11.5
Diclofenac	13	10.7
Amitriptyline	9	7.4
Methyldopa	4	3.3
Indomethacin	3	2.4

Diphenhydramine	2	1.6
Ibuprofen	2	1.6
Total	122	100

5.7 Factors Associated with the Occurrence of Drug Related Problems

Age, marital status, employment status, number of drug and comorbidity fulfills criteria for multivariable analysis. Those variables with a p-value of <0.25 in univariable analysis, further analyzed by multivariable binary logistic regression. Marital status, number of drugs and having comorbid conditions were the only factors associated with the occurrence of DRP. Those patients who took five and above drugs were 3.01 times more likely to develop DRPs as compared to patients who took less than five drugs. The likelihood of DRP among patients with comorbidity was 4.15 times higher as compared to non-comorbid patients. Being divorced and widowed increase the probability of developing DRPs by 5.088 times and 2.59 as compared to housewives and merchants.

Table 6: Predictors of occurrence of drug related problems patients attending at Medical Referral Clinic of Menelik II Referral Hospital, 2019.

Variables	DRPs		COR (95% CI)	AOR (95% CI)	P. value	
	Yes	No				
Age in years	75 and above	20 30	0.938 (0.703, 1.250)	1.095 (0.511 2.347)	0.816	
	65-74	96 90	1.00	1.00		
Marital status	single	12 14	1.00	1.00	0.582	
	Married	72 37	0.514 (0.346, 0.764)	0.787 (0.335 1.848)		
	Divorced	12 31	2.583 (1.327, 5.030)	5.088 (1.813 14.281)		0.002*
Employment status	widowed	20 38	1.900 (1.106, 3.265)	2.590 (1.045 6.415)	0.040*	
	unemployed	33 64	1.939 (0.274, 2.952)	2.866 (0.361 6.037)		0.06
	employed	24 7	0.292 (0.126, 0.677)	0.355 (0.110 1.146)		
retire	43 35	0.814 (0.521, 1.272)	1.456 (0.646 3.280)	0.365		

	other	16	14	1.00	1.00	
Number of drugs	Five and above	36	13	1.337 (1.001, 1.787)	3.01 (0.130, 0.696)	0.005*
	0-4 drugs	80	107	1.00	1.00	
Comorbidity	Yes	96	71	3.40 (0.544, 1.005)	4.15(0.209, 0.823)	0.012*
	No	71	49	1.00	1.00	

Table 7: Examples of drug related problems identified in patients attending the Medical Referral Clinic of Menelik II Referral Hospital, 2019.

No	Description of cases	Types of DRP
1	A 66 years old male patient with DM and hypertension was on NPH 36/18, and enalapril 5mg PO BID. He had two consecutive BP records of 155/103 mmHg and 179/102 mmHg	Dosage too low of Enalapril ✓ BP not controlled
2	A 70 years old male patient with HF and hypertension with nifedipine 20 mg PO BID. His Bp was not controlled with nifedipine alone. Two consecutive Bp records, 155/80 and 160/80mmhg.	Need additional therapy of ACEI
3	A 70 years old female patient with HTN and T2DM was on enalapril 5mg PO/day, amlodipine 5 mg PO/day, NPH 20/10, ASA 81mg PO/day, atorvastatin 40mg/day, metformin 500 mg PO bid and omeprazole 20mgpo/day, since she complained epigastric pain. Her two consecutive FBS records were 326 and 255 mg/dl.	Dosage too low of metformin drug interaction (aspirin + metformin)
4	A 65 years old female patient with HTN and atrial fibrillation was on ASA 81mg PO/day, enalapril 2.5 mg PO bid and nifedipine 20mg PO bid. Enalapril was substituted by HCT 25mg PO/day because of cough. Bp= 120/70, 130/100, EF =60%	ADR of enalapril (unsafe drug) Ineffective drug ✓ Nifedipine

5	A 74 years old female patient with HTN and had previous ischemic stroke attack on ASA 81mg/d and enalapril 2.5mg PO/day. Bp 150/80 mmHg.	Need additional therapy of statin
6	A 66 years female patient with DM and on second visit HTN was on Enalapril 10 mg PO/bid and NPH 35/20. She had two consecutive BP records of 150/100 mmHg and 155/81 mmHg.	Dosage too high, starting dose of Enalapril
7	A 65 years old female patient with T2DM on glibenclamide 5mg PO/bid and MTF 850 mg PO bid, due to availability issue, she discontinued metformin 850 mg preparation and changed to MTF 500 mg PO bid. She had two consecutive FBS records of 172mg/dl and 252mg/dl LDL= 98 mg/dl HDL= 60 mg/dl TC = 220 mg/dl	Non-compliance Need additional therapy of statin Dose too low of MTF PIM- Glibenclamide
8	A 66 years old female patient with HTN and DM was on MTF 500 mg PO bid, glibenclamide 5 mg PO bid, and Enalapril 5mg PO/bid. She had two consecutive FBS and BP records of 357mg/dl, 213mg/dl, and 160/90 mmHg, 175/95 mmHg respectively.	Dosage too low of MTF Dosage too low of Enalapril PIM- Glibenclamide
9	A 65 years old male patient with CHF secondary to CRVHD was on furosemide 40mg PO/day, spironolactone 25mg PO/day, enalapril 2.5mg/d, atenolol 25mg/day, ASA 81mg/day and warfarin 2.5mg/d. He had MR, TR, ischemic cardiomegaly on and ECG	Drug interaction ✓ ASA and furosemide ✓ ASA and warfarin ✓ Enalapril and spironolactone Ineffective drug - Atenolol
10	A 75 years old female patient with HTN and DM was on NPH 10 IUam, glibenclamide 5 mg PO/day enalapril 10mg/day, methyldopa 250mg PO bid and omeprazole 20mgpo/day. She had two consecutive FBS and BP	Methyldopa - PIM: high risk of adverse CNS effects Omeprazole- PIM: Risk of Clostridium difficile

	records of 170mg/dl, 110mg/dl, and 110/80 mmHg, 144/84 mmHg respectively.	infection and bone loss and fractures. Glibenclamide - PIM: prolonged hypoglycemia in older adults
11	A 66 years old female patient with T2DM was on metformin 500mg PO/day, NPH 20/10 IU, atorvastatin 40 mg PO/day, and amitriptyline 25mg/day.	Amitriptyline - PIM

6 Discussion

Optimal drug therapy is necessary for caring for elder patients since; they are vulnerable population groups because of the increased prevalence of chronic diseases and drug consumption. DRPs are a major concern in drug therapy and have been identified as contributing to poor clinical outcomes and undesired drug response. DRPs in older people are increasing and becoming a major health problem because of physiologic changes, different comorbid disease and increased number of drugs. Therefore, this study was done to asses DRPs in elderly ambulatory patients in one of the referral hospital in Ethiopia.

More than two-thirds of patients have at least two comorbid diseases. Hypertension 170(48.4%) was the highest prevalent disease. About 187(79.2%) of the patients received less than five drugs per day and the most commonly prescribed drug classes were ACEIs (50.8%). From 236 participants, 118 (49. 2%) patients encountered at least one DRP with an average number of 0.5 DRPs per patient and 122(16.5%) drugs were from the Beers medication list. Employment status, number of drugs and having comorbid conditions were the only factors associated with the occurrence of DRP.

In this study, the majority of the patients had comorbid disease conditions (70.8%), comparative with a study done in India with most patients who had comorbidity (83%) (Tamilselvan et al., 2018). This and other previous reports might lead to conclude that elders are prone to more disease complications and comorbidities. Hypertension and DM were the commonest encountered disease, which is similar to the study done in Nigeria (Kv & Nedumballi, 1991), India (Tamilselvan et al., 2018) and in the Netherlands (Ahmad et al., 2014).

The average number of medications used per day was 3.14 ± 1.658 per patient which is higher than studies done in Bonga Ethiopia (1.5 ± 0.8) per patient (Gizaw & Dubale, 2017) and 2.57 ± 1.05 per patient in Dire- Dawa, Dil- Chora Referral Hospital (Hussen & Daba, 2017). The discrepancy might be due to only elders were included in the present study, usually; elders were prone to more number of medications. This finding is lower than study done in Toronto Canada 5.7 medications (Courtman & Stallings, 1995), in India tertiary care hospital 7 ± 2.8 (Inamdar & Kulkarni, 2016) and another Indian study, on admission (7.61 ± 3.37) and on discharge (5.48 ± 2.46) (Salwe, Kalyansundaram, & Bahurupi, 2016). The reason might be due to differences in the study area,

usually admitted patients are exposed to more medications and medication related problems. This study was conducted in ambulatory patients but the former studies were in different wards. Another possible reason might be due to the time gap between the studies specifically in Canada study.

Of 236 participants (49.2%), patients encountered at least one drug related problem. This is magnitude is lower compared with other Ethiopian hospital by Gelchu & Abdela's (Gelchu & Abdela, 2019). However, lower than studies done in the Netherland (95.9%) (Ahmad et al., 2014), in Indian elders (87%) (Subeesh et al., 2017) and in Sweden (66%) (Pfister et al., 2017). The difference in the prevalence of DRP might be due to only patients on five and above medications included in Netherlands and Indian study and follow up interventional study design in Sweden. This finding is also lower as compared to other Ethiopian studies, in Dire-Dawa (71%) (Hussen & Daba, 2017) and in Bahir Dar (96.1%) (Tegegne et al., 2014), level of the institution and cohort study design in Bahir Dar teaching hospital may increase the prevalence.

Two and above DRPs in (19.1%) of patients were identified which is lower than Netherlands findings (78%) of patients (Ahmad et al., 2014). The average number of DRPs per patient is 0.5 which is comparative with studies done in Hiwot Fana Hospital in Ethiopia 0.6 per patient (Gelchu & Abdela, 2019) but the prevalence is lower than systematic review reports of 3.2 DTPs per patient (Lau & Dolovich, 2005).

Patients do not take medications as directed because of forgetfulness; do not understand the directions on the prescription labels or due to cost and availability issues. Noncompliance (45.8%) was the second most prevalent DRPs. This finding is lower as compared with a study done in Nigeria (33.1%) (Kv & Nedumballi, 1991) and systematic review of reported (35.2%) (Lau & Dolovich, 2005) but higher than what had reported in Netherlands (4.7%) (Lange & Egberts, 2006) and Toronto Canada (14.5%) (Courtman & Stallings, 1995), in Scotland (10.4%) (Cunningham et al., 1997). This discrepancy in prevalence might be due to difference in socioeconomic status, availability of medication in the country and literacy level of the study participants. The subjective nature of noncompliance measurement may lead to bias, which might be a cause for the difference in the report. Forgetfulness, patient preference, and unavailability were common reasons for patients' noncompliance.

This study concluded that the prevalence of needs additional DRP was (24.6%). This finding is higher than in the Netherlands' (16.1%) (Ahmad et al., 2014), India (7.15%) (Inamdar & Kulkarni, 2016), in Portuguese (6.9%) (Costa et al., 2016) and Scotland (Cunningham et al., 1997). Due to a high level of health care facility may reduce under treatment.

Adverse effects of drugs from patients' cards and interview is commonly underestimated. The prevalence of ADR was (11.2%) consistent with Sweden studies (Pfister et al., 2017). Prevalence of ADR or unsafe drug in Portuguese (43.7%) (Costa et al., 2016), in Singapore (31.7%) (Ting, Yin, Si, & Chew, 2015) and in Scotland (41.8%) (Cunningham et al., 1997) which is higher than the present finding. Study design, study setting and samples included in the study might be reason for the discrepancy, commonly patients with polypharmacy increases prevalence of drug interaction and undesired effects. The finding were not consistent with other study done in India (2.75%) (Inamdar & Kulkarni, 2016). This discrepancy might be due to samples included and study design used, in Inamdar & Kulkarni study, only DM patients with or without comorbidities were enrolled and randomized controlled clinical trial study design in Pfister et al. A study done in Toronto Ontario, Canada adverse drug reactions (25.8%) (Courtman & Stallings, 1995). Being tertiary care institutions in Canada might be the reason for the difference in prevalence.

Inappropriate dosage, dose too low and dose too high had a prevalence of (14.3%) and (2.4%) respectively which is in line with what had reported in Singapore 8.5% were under-dosed (Ting et al., 2015). But lower prevalence as compared to the Netherlands, dose too low (4.8%), dose too high (11%) (Ahmad et al., 2014) and in Sweden, dosage too high (14.2%), dosage too low (4.5%), (Pfister et al., 2017), but higher than in Indian findings, suprathereapeutic dose (0.55%), duration of therapy too short (0.27%) (Inamdar & Kulkarni, 2016). The level of institution and level of the health care professional might decrease the prevalence of inappropriate dosage. However, this finding is lower than Belgium (34%) university hospital geriatric ward (Somers, Paepe, & Maele, 2013), which might be being observational and follow up study able to identify more DRPs.

Prescribing Ineffective drug where more effective drug available (1.7%) is the least frequently documented DRPs in this study. But prevalence is higher in Netherlands finding (1.9%) (Ahmad et al., 2014), in Scotland before (6.0%) and after an intervention (4.9%) (Cunningham et al., 1997) and in Sweden (17.4%) (Pfister et al., 2017). The discrepancy may be due to only patients having

five and above medications included in the Netherlands' study and in Sweden RCT; study design can identify more DRPs.

Drug interaction accounts magnitude of 21.6% which was in line with Indian study (40.93%) (Inamdar & Kulkarni, 2016), but in other Ethiopian studies need additional drugs was the highest prevalence DRP (Hussen & Daba, 2017; Tegegne et al., 2014). The prevalence was high as compared with other findings (Fog et al., 2017; Somers, Paepe, & Maele, 2013). A possible explanation could be applying different drug interaction analysis databases tool to identify drug interaction, being an intervention study in Fog et al and Somers et al studies and level institutions might lead to the difference. A prospective, observational study at Vivekanandha hospital in India, indicated that interaction between ondansetron and tramadol had the highest prevalence (Tamilselvan et al., 2018) but aspirin and metformin had the highest frequency in this study.

About half of the participants (44.1%) exposed at least one potentially inappropriate medication. This finding is comparative with the Chinese study (53.5%) and (44.7%) based on Beers 2015 and 2012 criteria respectively (Zhang et al., 2017) and in India (52%) (Subeesh et al., 2017). But prevalence is lower than in the USA (73%) at admission and during discharge (Osei, Berry-cabán, Haley, & Rhodes-pope, 2016). Possible justification might be due to the availability of beers list medications in the USA. This report was higher than Indian findings (35.71%) (Inamdar & Kulkarni, 2016), the increased prevalence might be due samples included in the study, only DM patients were enrolled in the former study. The prevalence is high as compared with other Ethiopian studies, in Ayder teaching hospital 28.6% (Dinkashe et al., 2016), in Gondar (27.72%) (Mekonnen & Bhagavathula, 2014) and in Dessie Referral Hospital 23% (Sada, 2017). This lower prevalence is may be due to the highest number of antibiotics is prescribed since the beers list contains more nonantibiotics drugs. Glibenclamide omeprazole, diclofenac, and Amytryphylin have frequently prescribed beers list medications.

Similarly with other finding (Gizaw & Dubale, 2017), expensive cost, Patient preference, forgetfulness were reasons for patient's non-adherence. Needs preventive drug therapy and drug-drug interaction were common reasons for needs additional drug therapy and drug interaction respectively. Marital status, number of drugs and having comorbid conditions were the only factors associated with the occurrence of DRP. Similar findings were reported in Dil-Chora Referral

Hospital, in Dire-Dawa (Hussen & Daba, 2017) but Gelchu & Abdela reported the number of drugs is the only factor associated with DRPs (Gelchu & Abdela, 2019). Multi centered study in Norway, the number of DRPs per patient increased linearly with the increase in the number of drugs (Viktil, Blix, Moger, & Reikvam, 2006). In Jimma University specialized hospital, polypharmacy was the only independent predictor for unnecessary drug therapy (Tigabu, Daba, & Habte, 2013).

6.1 Limitation of the study

- The cross-sectional nature of the study did not allow a follow-up.
- ADRs were considered based on patients' responses and/or from medical records without the establishment of a causal relationship.
- The result of the study may not be generalizable to all hospitals because of a single centered study conducted in a referral hospital.
- Unavailability of alternative medications for PIMs in beers lists may overestimate the prevalence.

7 Conclusion

In this study there is high prevalence of DRPs and PIMs. Marital status, number of comorbidity and number of drug prescribed have significant association with the occurrence of DRPs. Management of elderly patient's needs special concern since they are prone to different DRPs for several reasons, including the presence of comorbidity and a large number of concurrent medications

8 Recommendation

Based on the findings of this study, the following recommendations are suggested to

Federal Ministry of Health.

- The health sector policymakers should include clinical pharmacy services.
- The guideline should be developed and implemented on the treatment of elders based on parameters.

Menelik II Referral Hospital

- Clinical pharmacy service should also be started to identify, solve, and prevent DRPs in medical referral clinic of MIIRH.
- Further studies with a follow up of patients and with intervention should be considered.

Clinical Pharmacists and Physicians

- Clinicians should check for potential drug-drug interactions before starting a new drug.
- There should be a regular patient education program to increase patient compliance.
- Before prescribing drugs physicians should follow special guidelines developed for elderly patients

□

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Annexes

Annex I: Informed Consent Form

Dear Participant,

You have selected to be part of this survey and this is why we would like to interview you. This study is doing by an AAU pharmacy practice, postgraduate student. The aim of the study is only to asses drug-related problems in individuals aged 65 and above.

The information you provide is very confidential and will not be disclosed to anyone. It will only be used for research purposes. Your name, address, and other personal information will be removed from the instrument, and only code will be used to connect your name and your answers without identifying you.

Your participation is voluntary and you can withdraw from the study after having agreed to participate. You are free to refuse to answer any question that asked in the questionnaire. If you have any questions about this study, you may ask me or contact (name of institution and contact details) or (Principal Investigator at the site).

Consent to participate: Agreed in this consent indicates that you understand what will be expected of you and are willing to participate in this survey.

Read by Participant Interviewer

Agreed _____

Principal investigator address

Email: lingerendalifer@gmail.com

Phone: 0949903167

Annex II: Data Abstraction Format

I. Study Information

Study title: Assessment of drug-related problems in elder patients among chronic patients at Medical Referral Clinic at Menelik II Hospital.

Principal Investigator: **Bedilu Linger**

Date of screening..... CODE: -----

Part 1. Socio-demographic information (make √ a sign for your answer).

1. Age (year): _____
 2. Gender: Male Female
 3. Weight (kg) _____ Height (cm) _____ Body mass index (BMI)[kg/m²] _____
 4. Marital Status: Single Married Divorced widowed
 5. Educational status: No formal education primary secondary College and above
 6. Employment: Unemployed- employed retire other
 7. Religion: orthodox Muslim. Protestant
- Others _____
8. Social drug use: Yes No If yes, what? Cigarette Alcohol chat
other specify _____
 9. Source of medicine Free Payment

Part II: Medical and Medication information

10. Chief Complaint: -----

11. History of Present Illness:-----

12. Past Medical History: -----

13. past Medication History

No	Medication (Dose, route, Frequency)	Start date	Stop date (optional)
1			
2			
3			

3			
4			
5			

14. Main Diagnosis (ICD):

P1. _____ P2. _____ P3. _____

P4. _____ P5. _____ P6. _____

Current medication history:

No	medication (dose, Route, Frequency)	Start date	Stop date (optional)
1			
2			
3			
4			
5			

Part II: Vital sign and Investigation

15. Vital sign

Date	BP (mmHg)	PR (b/m)	RR (br/m)	T oC	Sa O2 %	

16. RFT

Date	Scr (mg/dl)	BUN (mg/dl)	Cr cl
Reference. Range			

17. Coagulation profile

Date	INR	PT	aPTT
Reference. Range			

18. LFT

Date	AST	ALT	ALP		

Reference. Range					

19. TFT

Date	TSH	T4	T3	
Reference. Range				

20. Electrolyte

Date	Na	K	Ca	mg	Cl
Reference Range					

21. Lipid profile

Date	T cholesterol (Mg/dl)	LDL (mg/dl)	HDL (mg/dl)	TG (mg/dl)
Reference Range				

22. Blood Glucose

Date	RBS (mg/dl)	FBS (mg/dl)	HgA1C %
Reference Range			

23. CBC

Date	WBC	RBC	PLT	HGB	HCT	MCV	MCHC	NEU	LYMPH
R. Range									

24. Imaging. X-ray_____

CT _____

MRI _____

Ultrasound _____

ECG _____

Other relevant investigations:

Date							
R. Range							

Part IV: MRP reported by the patients

A. Do you have trouble in swallow or administer your medicine? Yes No

B. Do you have trouble in understanding or remembering how to take your medicine?
Yes No

C. Do you sometimes stop taking your medicine by yourself? Yes No

If yes, what is your reason lead to stop taking medicine?

D. Does the cost of medicine make hard for you to take as prescribed?

Yes No

E. Does the availability of patient's medicine make it hard for you to take it as prescribed?

Yes No

F. Do you sometimes forget taking his/her medicine? Yes No

G. Do you experience any undesirable effect when you taking your medication? Yes

no If yes please select, Name of medicine _____

1. Headache 2. Forgetfulness 3. Weight gain 4. Blurred vision

5. Weakness 6. Hypersomnia 7. Confusion 8. Epigastric pain

11. Skin rash 12. Irritability, 13. Cough, 14. Falling,

15. Itching (skin rash) 16. Depression 17. Others. _____

H. DO you ever discontinue your medicine due to fear of the above side effects? Yes

No

	Incorrect administration		
	Allergic reaction		
	Dosage increase/decrease too fast		
Dose Too high:	Dose too high		
	Frequency too short		
	Duration too long		
Non-compliance	Does not understand instructions		
	Cannot afford drug product		
	Patient prefers not to take		
	Patient forgets to take		
	Drug product not available		
	Cannot swallow/administer drug		
Drug interaction:	Drug- drug interaction		

C. Did the patient have any PIM based on beers 2019 criteria? Yes No

If yes, drug involved in PIM

የታካሚው አጠቃላይ መጠይቅ

የታካሚ ማህበረሰባዊ ባህሪያቶች መረጃ በተመለከተ

1. እድሜ፤-----
2. ልጅ ወንድ ሴት
3. ክብደት ----- ቁጥር -----
4. ሀይማኖት; ክርስቲያን እስላም ፕሮቴስታንት ሌላ-----
5. የጋብቻ ሁኔታ፤ ያለገባ/ች ያገባ/ች አግብቶ/ታ የፈታ/ች ሚስቱ/በሊየሞተችበት/ባት
6. የትምህርት-ሁኔታ፤ ያልተማረ/ች; ከ1ኛ-8ኛ ክፍል ከ9ኛ-12ኛ ክፍል ኮሌጅ ዲፕሎማ እና ከዚያ በላይ
8. የስራ ሁኔታ: ስራ አጥ ተቀጣሪ ጡሮታ የወጣ/ች ሌላ-----
9. የማህበራዊ መድኃኒት አዎ የለም
10. አዎ ሲጋራ ጫት አልኮል ሌላ-----
11. መዲሃኒት የሚያገኙት በምን መሌኩ ነው; በግዢ በነጻ

መድሀኒት አወሳሰድ በተመለከተ

1. መድሀኒትዎን ለመዋጥ ወይም ለመጠቀም ተቸግረው ያውቃሉ? አዎ የለም
2. የመድሀኒትዎን አወሳሰድ ባለማስታወስዎ ምክንያት መድሀኒት ሳይወስዱ ቀርተው ያውቃሉ? አዎ የለም
3. የመድሀኒት ዋጋ ውድ በመሆኑ ምክንያት ሳይወስዱ ቀርተው ያውቃሉ? አዎ የለም
4. መድሀኒት ገበያ ላይ ባለመገኘቱ ምክንያት አቋርጠው ያውቃሉ? አዎ የለም
5. መድሀኒትዎን ረስተው ሳይወስዱ ቀርተው ያውቃሉ? አዎ የለም
6. መድሀኒትዎን በራስዎ ምክንያት ሳይወስዱ ቀርተው ያውቃሉ? አዎ የለም
7. ለተራ ቁጥር 6 መልስዎ አዎ ከሆነ በምን ምክንያት-----
8. መድሀኒትዎን በሚወስዱበት ጊዜ የጎንዮሽ ጉዳት አጋጥመዎት ያውቃሉ? አዎ የለም
9. ለተራ ቁጥር 8 መልስዎ አዎ ከሆነ በምን -----
 የራስ ምታት መርሳት ሳል
 የቆዳ ሸፍታ እንቅልፍ ማጣት የጨዋራ ማቃጠል
 ማሳከክ ድብርት መውደቅ ክብደት መጨመር
10. በጎንዮሽ ምክንያት መድሀኒት አቋርጠው ያውቃሉ? አዎ የለም

Annex IV: Ethical Clearance

በ ፋርማሲ ት/ቤት

የኢትዮጵያ ሪፊዌ. ቦርድ

አዲስ አበባ ዩኒቨርሲቲ
Addis Ababa University



School of Pharmacy

Ethical Review Board

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June 21, 2019

Date
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ERB/SOP/108/06/2019

Ref. No.

To: **Bedilu Linger**

School of Pharmacy

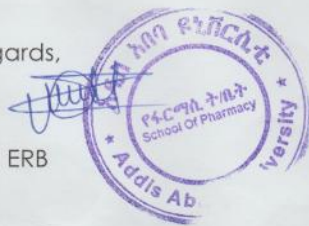
Re: **Ethical Clearance**

It is to be recalled that you submitted a study proposal entitled "**Assessment of drug related problems in elderly patients visiting Menelik II Referral Hospital Addis Ababa Ethiopia**" for ethical approval by the School's Ethical Review Board (ERB). The Board thoroughly reviewed the proposal based on its operational guidelines and found it to fulfill all ethical requirements stipulated in the guidelines. This is, therefore, to inform you that the proposal is ethically approved for implementation.

With best regards,

Arebu Issa

Chairperson, ERB



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