

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

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Abstract

Background: Drug therapy in the elderly needs an emphasis on the age related changes in pharmacokinetics and pharmacodynamics profiles of drugs. As age increase, people usually exposed to more health and medications related problems.

Objective: This study aimed to assess drug related problems among older patients in Addis Ababa, Ethiopia.

Method: A hospital based cross-sectional study was conducted among 236 chronic elderly patients who were on follow up-care from 25 June 2020 – 25 September 2020. Data collection was done through patient interview and medical chart review. Epi data version 4.2.0.0 and statistical package for social science version 23 were used for data entry and analysis respectively. Descriptive statistics was employed to describe percentage and frequencies. Univariable and multivariable binary logistic regressions were used to declare association between independent variables and dependent variables.

Results: More than two-thirds of patients exposed for comorbid conditions. In this study, 740 medications were prescribed; an average of 3.14 ± 1.658 per patient. Fifty-six percent of patients encountered at least one drug related problems. The average number of drug related problems per patient was 0.87. Drug interaction (42.4%) followed by non-compliance (26.3%) and needs additional drug therapy (14.2%) were major drug related problems. Being Employed (AOR: 0.214, 95%CI: 0.054, 0.857), number of drugs (AOR: 10.6, 95%CI: 3.363, 33.697), and having comorbid conditions (AOR: 3.682, 95%CI: 1.809, 7.494) were significantly associated with the occurrence of drug related problems.

Conclusion: There is a high prevalence of drug related problems encountered in older chronic patients. Number of disease and number of drugs contribute for the occurrence of drug related problems. Therefore, special attention should be given for this group to reduce drug related problems.

Keywords: Drug Related Problems; Drug Interaction; Older

Abbreviations

ADR: Adverse Drug Reaction; CVD: Cardio Vascular Disease; DRP: Drug-Related Problems; DM: Diabetes Mellitus

Background

Drug related problem (DRP) is an event involving drug treatment that actually or potentially affects the expected health outcomes [1] or any undesirable occasion experienced by the patient that includes, or suspected to include drug treatment, which interferes to achieve

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the specified goals of treatment. Pharmaceutical care professionals are responsible to prevent or resolve DRPs to optimize the outcomes of treatment, unless DRPs might lead to poor clinical outcomes [2]. DRP may happen during prescribing, transcribing, dispensing, and patient use of medication therapy [3]. Age related physiologic changes leads to a diminished capacity to respond to stresses and the ability to preserve homeostasis, making older adults vulnerable to decomposition in stressful circumstances. Old age is the major independent risk factors for chronic diseases such as cardiovascular disease, cancers, and neurodegenerative disorders. Consequently, older people have multiple comorbidities, usually in the range of 5 to 10 illnesses [4]. 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 older adults [5]. Older adults have at least five disease [6], they also utilize four to eight drugs per day [7]. The prevalence of DRPs in older adults ranges from 66% [8] to 87% [9] in developed countries whereas in African, it varies from 78.6% to (83.4%) [10-12]. More days of hospital stay, having more disease conditions and a large number of medications associated with the occurrence of inappropriate medication [13]. Identification and prevention of DRPs in older outpatients is a vital component for decreasing hospital admissions [14]. The purpose of identifying DRPs is to achieve the desired goals of therapy and realize the best possible outcomes; meanwhile, improving prescribing pattern in the elderly reduces the occurrence of ADRs, cost of treatment, and increase compliance in elderly patients [15]. All pharmacists should provide appropriate pharmaceutical care to the elder population [16]. Optimal drug therapy is necessary to care elders appropriately 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 them, in addition, no specialized physicians in gerontology. Studies regarding DRPs in elderly patients are limited, thus, this study was aimed to assess DRPs among chronic elderly patients.

Materials and Methods

Study setting and study period

The study was conducted from June 25 to September 25, 2020 at Menelik II Referral Hospital (MIIRH), which is located in the center of Addis Ababa, the capital city 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.

Study design and study population

A facility based cross-sectional study design was employed. All patients aged 65 years and above attending the medical referral clinic of Menelik II Referral Hospital were the study populations. Those patients with incomplete medical and medication information, first visitor patients, and patients having hearing and speaking problems were excluded from the study.

Sample recruitment strategies

Two hundred seventy three chronically ill patients were visited the hospital during the study period, however 17 and 15 patients were excluded due to unwilling to participate and first visit respectively while five were excluded due to incomplete medical record. By using convenient sampling 236 participants recruited. In Menelik II Referral Hospital, about 800 elder chronically ill patients refilled per year by approximate estimation of previous data. Due to small number of study population in the study period, researchers was used convenient sampling method. The study population accounts 29% of the general population, which can provide approximate generalizability.

Variables of the study

Dependent variable

The main outcome of interest in this study was the prevalence of DRPs in older adults.

Independent variables

Independent variables included were demographics variables (age, sex, educational status, marital status, occupation, source of medication, social drug use), Patient characteristics (class of prescribed drugs, number of prescribed drugs and number of comorbidities).

Data collection, procedure, and instrument

Information was collected through reviewing of medical records and interviewing of patients using a structured checklist and questionnaire, additionally the questionnaire was translated in to local language. The content of the checklist includes patient profiles, investigations, current and past medication and disease conditions. Others like biochemistry and hematology results were included in the checklist. 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, dosages, frequency of administration, duration of therapy, drug interactions, and ADRs were compared from the standard books and guidelines. Standard treatment guideline for Ethiopian hospitals, American geriatrics society updated Beers criteria 2019; American diabetes association: standards of medical care in diabetes - 2019; ACC/AHA/updated dyslipidemia guide line -2019, 2017 ACC/AHA HFSA/ focused update of the 2013 ACCF/AHA/ guideline for the management of heart failure and ACC/AHA 2017 guideline for the prevention, detection, evaluation, and management of high blood pressure in adults were used to identify DRPs. 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 and contraindicated 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.* with minor modification. Based on Cipolle., *et al.* DRPs were categorized into seven classes and 33 reasons for DRPs [1].

Data entry and analysis

The data was entered into EPI-data version 4.2.0.0 and analyzed using Statistical Package for IBM social sciences (SPSS) version 23. Descriptive statistics were used to present 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. Those variables with a p-value < 0.25 in univariable logistic analysis were further analyzed to multivariate logistic regression. Adjusted Odds Ratio (AOR) with a 95% confidence interval was applied to describe an association. Those variables with a p-value < 0.05 were considered as significant in multivariate analysis.

Data quality control technique

Content of the questionnaire was evaluated by senior experts who have published research work in DRPs. The tool was adopted from the previous published literatures to make the questionnaire more reliable. Translation was made to the local language for easy of understandability. Prior to actual data collection, sufficient training was given to data collectors on data collection methods, contents of the questionnaire and ethical issue. In addition, strict supervision was done during the entire data collection period and the filled questionnaires were checked at the end of the day. Pretest was done on 22 older chronic patients before actual data collection.

Ethical considerations

Study was approved by the ethical committee of the Addis Ababa University School of pharmacy ERB with an approval number of ERB/SOP/108/06/2020. Written informed consent from the study participants was taken before conducting this study. The confidentiality of information was assured by omitting personal identifier.

Operational definition and definitions of terms

- **DRPs:** Indicates an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes [2].
- **ADRs:** Refers to 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 [17]
- **Older adults:** Includes those patients aged 65 years and above according to Beers criteria [18].

- **Non-compliance:** Defined as the patients uses the drug differently as compared to the prescribed once because of either patient preference, cost, swallowing or administering problem, difficulty of understanding instructions, unavailability, or forgetfulness [2].
- **Co-morbidity:** Describes existence of more than one disorder or disease condition alongside primary diagnosed disease [19].
- **Drug interaction:** Is a change in the effect of the drug when the drugs taken together with a second drug. The effect may be decreased, increase or leads to toxic effects when it is given with another drug [20].

Result

Socio-demographic characteristics

A total of two hundred and seventy three patients visited medical referral clinic during the study period. From this, 236 patients were included with a mean age was 70.51 ± 5.892, ranging from 65 and 89 years 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 without payment (Table 1).

Variables	Category	Number	Percent		
Age (Mean ± SD)	70.51 ± 5.892				
	65-74	186	78.8		
	> 75	50	21.2		
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	34	14.4
		Alcohol	23		
		Chat	4		
	No	202	85.6		

Others*: Housewives, merchants; SD: Standard deviation

Table 1: Sociodemographic characteristics of study participants in Menelik II Referral Hospital, Addis Ababa, Ethiopia, 2020 (N = 236).

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 1). The most common disease encountered were hypertension 170 (72.0%), diabetes mellitus 135 (56.7%), heart failure 21 (8.8%), ischemic heart disease 16 (6.7%), primary open-angle glaucoma 15 (6.3%) and hyperthyroidism 14 (5.9%) (Table 2).

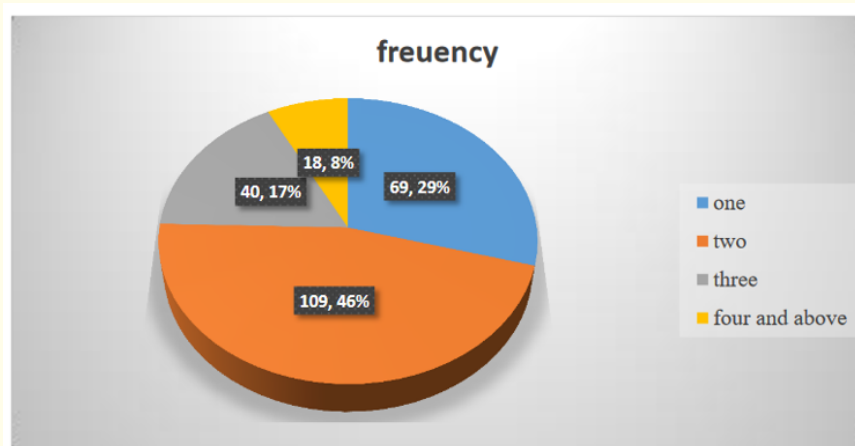


Figure 1: Number of comorbidities among patients in Menelik II Referral Hospital, Addis Ababa, Ethiopia, 2020.

Disease	Frequency	Percentage
Hypertension	170	72.0
Diabetes mellitus	135	56.7
Ischemic heart disease	23	9.6
Heart failure	21	8.8
Primary open-angle glaucoma	15	6.3
Hypertensive heart disease	12	5.0
Cardiomyopathy	12	5.0
Hyperthyroidism	14	5.9
Bronchial asthma	9	3.8
Dyslipidemia	9	3.8
Atrial fibrillation	6	2.5
Vulvar heart disease	5	2.1
Benign prostate hyperplasia	4	1.7
Other*	21	8.8

Table 2: Disease pattern among study participants in Menelik II Referral Hospital, Addis Ababa, Ethiopia, 2020.
 Others*: Glomerulonephritis, Arthritis, Chronic Otitis Media, Upper Respiratory Tract Infection, Pulmonary hypertension.

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 SD ± 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 angiotensin converting enzyme inhibitors (ACEIs) 121 (50.8%), oral hypoglycemic agents 94 (39.5%), calcium channel blockers (CCBs) 75 (31.5%), antiplatelet 69 (29.0%), diuretics 67 (28.2%) and insulin 63 (26.5%) (Figure 2).

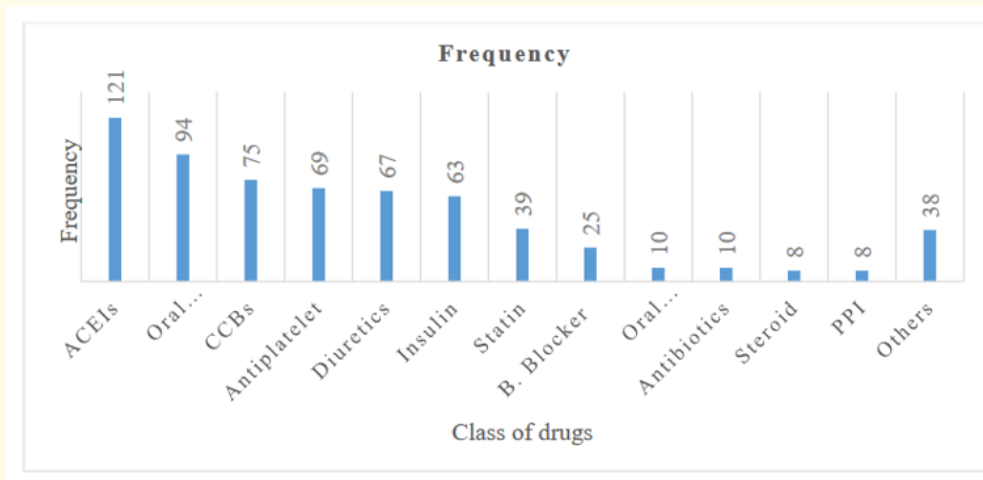


Figure 2: Pattern of medication use among patients in Menelik II Referral Hospital, Addis Ababa, Ethiopia, 2020.

Others: Propylthiouracil, Nonsteroidal Anti-Inflammatory Drugs, Xanthine Oxides Inhibitors, Digoxin. B. Agonists, Amitriptyline, Diphenhydramine, Methyl dopa, Dorzolamide/timolol, pilocarpine. ACEIs: Angiotensin-Converting Enzyme Inhibitors, CCBs: Calcium Channel Blockers, B. Blockers: Beta-Blockers.

Drug related problems

From 236 participants, 133 (56.4%) (95% CI: 50.4, 62.3) patients encountered at least one drug-related problem and a total of 205 DRPs were identified. The average number of DRPs per patient was 0.87. Regarding the number of DRPs the patient’s faced from totals, 80 (60.2%) patients suffered one, 37 (27.8%) patients faced to two, 13 (9.8%) exposed for three, and 3 (2.2%) suffered from four DRPs. Drug interaction 87 (42.4%) followed by non-compliance 54 (26.3%) and needs additional drug 29 (14.2%) were major DRPs identified in this study (Table 3).

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 3).

Factors associated with the occurrence of drug related problems

Age, marital status, employment status, number of drug and comorbidity have a P-value of less than 0.25 in univariable logistic regression and further analyzed in multivariable logistic regression analysis. Employment 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 10.6 (3.363,

DRP	Cause of DRPs	No. of DRPs	Total DRPs	Percent
Professional related factors				
Needs additional drug	Preventive drug therapy is required to reduce the risk of developing a new condition.	15	29	14.2
	A medical condition requires additional pharmacotherapy to attain synergistic effects.	10		
	Untreated disease condition	4		
Ineffective drug therapy	The drug is not the most effective for the medical problem.	2	2	0.9
Dose too low	The dose is too low to produce the desired response.	17	17	8.3
Dose too high	Dose is too high	3	3	1.5
Patient related factors				
Noncompliance	Patient forgets to take	31	54	26.3
	Patient 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		
Drug related factors				
Drug interaction	Drug-drug interaction	87	87	42.4
ADR	The drug product causes an undesirable reaction.	13	13	6.4
Total		205	205	100

No.= Number, DRP= Drug Related Problems, ADR= Adverse Drug Reaction

Table 3: Types of drug related problems identified from patients in Menelik II Referral Hospital, Addis Ababa, Ethiopia, 2020.

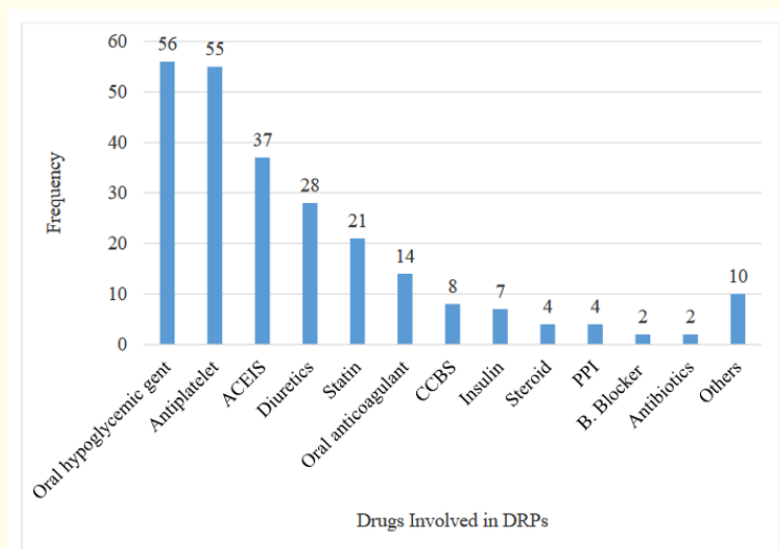


Figure 3: Drug classes involved in drug related problems in Menelik II Referral Hospital, Addis Ababa, Ethiopia, 2020. ACEIs: Angiotensin-Converting Enzyme Inhibitors, CCBs: Calcium Channel Blockers, PPI: Proton Pump Inhibitors. Others: Nonsteroidal Anti-Inflammatory Drugs, Digoxin, B. agonists.

33.697) 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 3.6 (1.809, 7.494) times higher as compared to non-comorbid patients. Being an employee decreases the probability of developing DRPs by 78.6% (8.7, 86.1) as compared to housewives and merchants (Table 4).

Variables		DRPs		COR (95% CI)	AOR (95% CI)	P. value
		Yes	No			
Age in years	75 and above	22	28	1.884 (1.003, 3.539)	0.927 (0.417, 2.060)	0.852
	65-74	111	75	1.00	1.00	
Marital status	Single	12	14	1.00	1.00	
	Married	78	31	0.341 (0.142, 0.818)	0.354 (0.112, 1.114)	0.076
	Divorced	19	24	1.083 (0.407, 2.879)	1.593 (0.450, 5.639)	0.470
	Widowed	24	34	1.214 (0.478, 3.082)	1.316 (0.405, 4.273)	0.648
Employment status	Unemployed	45	52	1.321 (0.581, 3.001)	1.135 (0.438, 2.940)	0.794
	Employed	25	6	0.274 (0.087, 0.861)	0.214 (0.054, 0.857)	0.02*
	Retire	47	31	0.754 (0.323, 1.761)	0.901 (0.324, 2.504)	0.842
	Other	16	14	1.00	1.00	
Number of drugs	Five and above	45	4	12.656 (4.375, 36.610)	10.645 (3.363, 33.697)	0.00*
	0-4 drugs	88	99	1.00	1.00	
Comorbidity	Yes	115	59	2.450 (1.456, 4.121)	3.682 (1.809, 7.494)	0.00*
	No	18	44	1.00	1.00	
COR: Crude Odds Ratio, AOR; Adjusted Odds Ratio, CI: Confidence Interval						

Table 4: Multivariable logistic regression analysis among elders in Menelik II Referral Hospital, Addis Ababa, Ethiopia, 2020 (N = 236).

Discussion

Special concern is needed to give care for older 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.

In the current study, DRPs were identified in 56.4% elderly patients. Professional (prescribers and pharmacists) related factors, patient related factors and drug related factors were origins for DRPs. Patient-related DRPs depends on knowledge, education, attitude and awareness of patients regarding to their treatment. Prescriber-related DRPs depends on level of education, level of expertise and experience of the prescriber. Drug-related DRPs are due to physical and chemical nature of the drugs and are usually difficult to avoid and prevent. Clinical pharmacist should put their role on the identification, evaluation and prevention of DRPs because these problems likely to be intervened by the clinical pharmacist. DRPs decrease the therapeutic outcome of drug therapy, there for health facility should establish clinical pharmacy service and assign geriatrician. Pharmacy professionals should give appropriate counseling and labeling of instruction with local language during dispensing to increase patient compliance. Clinical pharmacist should create good multidisciplinary team sprite to aware the effects of DRPs for care delivery. This figure is lower than studies done in Netherland [21], Indian [8], [22] and Sweden [23]. The difference in the prevalence of DRP might be due to those only patients on five and above medications included in Netherlands and Indian study and being follow up interventional study design in Sweden. Therefore, DRP studies in polypharmacy users increase the prevalence.

This finding is also lower as compared to other Ethiopian studies, in Jimma [11,12], level of the institution and study setting might contribute for the discrepancy, the former studies done in inpatients while the currents in ambulatory. Totally 22.5% of patients developed two and above DRPs and the mean DRP per patient was 0.87 which is lower than previous reports [11,12,21,24]. This is ascribed by due to the inclusion of all internal medicine admitted patient, difference in populations and study design used for the identification DRPs.

Drug interaction (42.4%) was the number one frequently encountered DRPs. This value is in line with Indian study (40.93%) [25]. The prevalence was high as compared with other findings [26,27]. A possible explanation could be applying different drug interaction analysis databases tool to identify drug interaction, and level of institutions might lead to the difference. A study done in India, indicated that interaction between ondansetron and tramadol had the highest prevalence [28] but aspirin and metformin had the highest frequency in this study. Pharmacy professional should identify the significance of interaction before prescribing drugs to minimize such problems.

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. In this study patients noncompliance accounts 26.3% of total the DRPs, consistent with Garedow, *et al.* finding [11]. Current report is lower as compared with a study done in Nigeria (33.1%) [10] and systematic review finding (35.2%) [24] but higher than what had reported in Netherlands (4.7%) [29], Canada (14.5%) [14], and Scotland (10.4%) [30]. The possible explanation for the difference might be variation in socioeconomic status, availability of medication in the country and literacy level of the study participants might have reason for variation of result. 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 drug was (14.2%). Can be due to no specific national treatment guideline for elders, workload and lack of expertise geriatrician. This finding is in line with the study done in the Netherlands' (16.1%) [21]. This figure is higher than previous studies [25,30,31] but lower than study done somewhere in Ethiopia [11]. Due to the presence of 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 6.4% was low as compared to other findings [12,31,32]. 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 was not consistent with other studies [23,25]. This discrepancy might be due to samples included and study design employed, in Inamdar and Kulkarni study, only DM patients with or without comorbidities were enrolled and being randomized controlled clinical trial study design in Pfister, *et al.* Inappropriate dosage, dose too low and dose too high had a prevalence of (8.3%) and (1.5%) respectively which is in line with what had reported in Singapore [32]. but higher than in Indian findings [25]. The level of institution and level of the health care professional might decrease the prevalence of inappropriate dosage. Prescribing Ineffective drug where more effective drug available (0.9%) is the least frequently documented DRPs in this study.

Similarly with other finding [33], drug 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-drug interaction respectively. Employment status, number of drugs and having comorbid conditions were the only factors associated with the occurrence of DRP. Other studies supported that number of disease condition and polypharmacy [11,12,34] but Gelchu and Abdela reported that number of drugs is the only factor associated with DRPs [35-37]. The prospective identification of DRPs might increase the acceptability of the finding.

Limitation of the Study

Being cross-sectional nature of the study did not allow knowing real causal relation and 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, small sample size and short study period.

Conclusion

This study showed that a high prevalence of DRPs encountered in older chronic patients. Being employed, comorbidity and number of drug have significant association with DRP. Management of elderly patients needs special concern since they are prone to different DRPs for various reasons, such as presence of comorbidity and a large number of concurrent medications. Health sector policymakers should include clinical pharmacy services to prevent DRPs in elderly patients. In general, this study provided hint to the prevalence of DRPs in ambulatory elderly chronic patients in developing country.

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Availability of Data and Materials

The datasets used for this manuscript are available from the corresponding author upon reasonable request.

Conflict of Interest

All authors have no conflicts of interest with the material presented in this article.

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