



A retrospective study of drug related problems and contributing factors among type 2 diabetes mellitus patients on follow up at public health institutions of kemisse town, north east Ethiopia

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ABSTRACT

Background: Drug related problems interfere with the desired treatment outcomes of type 2 Diabetes mellitus. This study was conducted to determine prevalence of drug related problems and associated factors among patients with type 2 Diabetes Mellitus in public health institutions of Kemisse town, northeast Ethiopia from May 01 to 30, 2019.

Methods: Institution based retrospective cross sectional study was conducted among type 2 Diabetes Mellitus patients on follow up at public health institutions of Kemisse town, northeast Ethiopia.

Result: From the total of 156 patients included in the study, 126 (80.8%) patients have at least one drug related problem with a total of 149 drug related problems. The most prevalent drug related problems were need for additional drug therapy 60 (40.3%) followed by non-compliance 51 (34.2%) and unnecessary drug therapy 12 (8%). Identified causes of need for additional drug therapy were the need for prophylactic drug therapy (statins and antiplatelet), 83.3%; presence of untreated medical condition (Hypertension, diabetic nephropathy and diabetic foot ulcer), 11.7%; and the need for combination therapy for better efficacy, 5%. This study revealed that age ≥ 45 years (AOR = 5.59, 95% CI = 1.38–20.64, P = 0.016), presence of comorbid condition (AOR = 3.22, 95% CI = 1.75–13.47, P = 0.014 and emergency visit in the last one year (AOR = 5.08, 95% CI = 1.14–18.71, P = 0.033) were significantly associated with the occurrence of drug related problems.

Conclusion: A total of 149 drug related problems were identified in 80.8% of type 2 diabetes mellitus patients. The three most prevalent drug related problems were need for additional drug therapy 60 (40.3%) followed by non-compliance 51 (34.2%) and unnecessary drug therapy 12 (8%). Additionally, age ≥ 45 years (AOR = 5.59, P = 0.016), presence of comorbidity (AOR = 3.22, P = 0.014) and emergency visit in the last one year (AOR = 5.08, P = 0.033) were significantly associated with the occurrence of drug related problem.

1. Background

Although medications play a vital role in the cure, palliation and inhibition of disease, they also expose patients to drug related problems (DRPs). Therefore, addressing DRPs has become a priority, due to the complexity of today's drug therapy, which consequently makes appropriate drug prescribing increasingly challenging [1–3]. A DRP is a clinical problem and it must be identified, resolved in a method similar to other clinical problems [4].

Drug related problems are among dominant reasons for patient

hospitalization. A review of the literature concerning DRPs has shown that 28% of all emergency department visits were drug-related, including adverse events of which 70%–90% were preventable [5,6]. Drug related problems are of a major concern in health care because of increased morbidity, mortality and health care cost. DRP is associated with prolonged length of hospital stay, increased economic burden, and an almost 2-fold increased risk of death [7,8]. More specifically, hospitalization resulting from DRPs is a major concern to both patients and healthcare providers due to its tremendous health and economic burdens [9].

Abbreviations: ACEI, Angiotensin converting enzyme inhibitor; ADR, Adverse Drug Reaction; DRP, Drug related problem; T2DM, Type 2 diabetes Mellitus.

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Table 1

Socio-demographic characteristics of adult patients with type 2 diabetes mellitus on follow up at public health institutions of Kemisse town, North East Ethiopia, May 1 to May 30, 2019.

Variable		Frequency	Percentage
Gender	Male	63	40.4
	Female	93	59.6
Age categories	25–44 years	40	26
	45–64 years	104	66.3
	>or = 65 years	12	7.7
Family history of DM	Yes	45	29
	No	111	71
Educational status	No formal education	63	40.4
	Primary	60	38.5
	Secondary	18	11.5
	College or University	15	9.6
Occupation	Farmer	87	55.8
	Merchant	32	20.2
	Government employee	15	9.6
	Sanitation worker	22	14.4
Marital status	Married	128	81.7
	Single/divorced/ widowed	28	18.3
Religion	Muslim	64	41
	Orthodox	62	39.8
	Protestant	24	15.4
	Catholic	6	3.8
Alcohol consumption	Yes	65	41.7
	No	91	58.3
Type of alcohol consumption	Beer	26	40
	Tej	6	9.2
	Tela	13	20
	Caticala	20	30.8
Chat chewing	Yes	26	16.7
	No	130	83.3

Table 2

Disease related factors among patients with type 2 diabetes mellitus on follow up at public health institutions of Kemisse town from May 1 to May 30, 2019.

Disease related factor		Frequency	Percentage
Duration since diagnosis of type two DM	<5 years	123	78.8
	≥5 years	33	21.2
Number of emergency visits in the last 1 year	Zero	44	27.9
	One	87	55.8
	≥two	25	16.3
Number of hospitalizations in the last 1 year	Zero	93	59.6
	One	56	35.9
	≥two	7	4.5
Duration on treatment	<5 years	123	78.8
	≥5 years	33	21.2
Presence of co-morbidity	Yes	81	51.9
	No	75	48.1

The diabetic patients are vulnerable in experiencing drug-related problems. Moreover, type 2 diabetes mellitus (T2DM) often accompanied by various co-morbidities resulting in increased risk of drug related problems [10]. According to an institutional based retrospective cross-sectional study conducted at Wolaitasodo university teaching hospital in Ethiopia, 83.1% of the type 2 diabetic patients had at least one drug related problem [4]. Studies show that blood glucose levels of diabetic patients remain poorly controlled despite the treatment they receive indicating the presence of a drug related problem [11]. Therefore; it is unequivocal that drug related problems (DRPs) may account the lion share of the problems in diabetes management. Thus, preventing and resolving drug related problems of T2DM patients has a positive impact on improving clinical, humanistic and economic outcomes of the patient. This study was conducted to assess the prevalence of drug related

problems and associated factors among type 2 diabetes mellitus patients in public health institutions of Kemisse town, northeast Ethiopia.

2. Methods

2.1. Study area and period

This study was conducted among patients with T2DM in two public health institutions (Kemisse General Hospital, Kemisse health center) which are located in Kemisse town. Kemisse town is located in special zone of Oromo, North east Ethiopia. It is 330 km far from the capital city of the country, Addis Ababa and 130 km far from the capital city of North shoa, Debre-Birhan. The hospital has a catchment population of 252,319 with 84 beds distributed in medical, pediatrics, surgical, and gynecology and obstetrics wards. The study was conducted from May 1 to May 30, 2019.

2.2. Study design

Institution based retrospective cross sectional study design was used.

2.2.1. Inclusion and exclusion criteria

Inclusion criteria: Patients with T2DM older than 18 years.

Exclusion criteria: Patients who have incomplete records.

2.2.2. Sample size determination and sampling technique

All T2DM patients at follow-up in Kemisse general hospital and Kemisse health center were included in the study as a result sampling was unnecessary. There were a total of 330 (220 from the hospital and 110 from the health center) type II DM patients at follow-up. Among these, 174 patients (116 from the hospital and 58 from the health center) were excluded due to incomplete record so that a total sample size of 156 patients was taken.

2.3. Study variables

Dependent variable: Drug related problem is the dependent variable.

Independent variables:

Patient related factors: Age, Sex, Educational level, marital status, and Social drug use.

Disease related factors: Presence of co-morbidity, duration of illness, emergency visit in the last one year, hospitalization in the last one year.

Drug related factors: type of drug utilized, no of medications utilized and duration of treatment.

2.3.1. Data collection instrument

Data collection questionnaire and checklist were developed in English which were then translated into Amharic and Afan Oromo.

2.3.2. Data collection process and management

The data were collected from patients with type 2 Diabetes Mellitus through interview using a pretested questionnaire and from patient card using a pretested checklist, and data were arranged and controlled for its completeness. It was checked whether all the collected data were arranged and kept well to avoid data loss.

2.3.3. Data processing and statistical analysis

The collected questionnaires and checklists were checked for completeness manually. Then it was entered in to Epi info version 4.0.2.101 and then it was exported to SPSS version 20 for analysis. The statistical significance and strength of the association between independent variables and the outcome variable was measured using bivariate regression model. A variable with p value less than 0.25 was transferred into multivariable regression model to adjust confounder effects and a p value less than 0.05 was considered as statistically

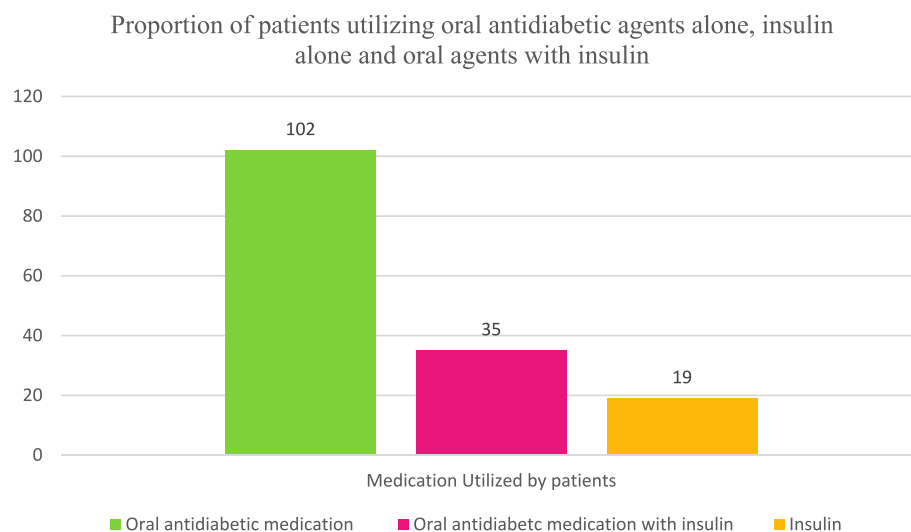


Fig. 1. Medications utilized by patient with type 2 diabetes mellitus attending public health institutions of Kemisse town from May 1 to May 30, 2019.

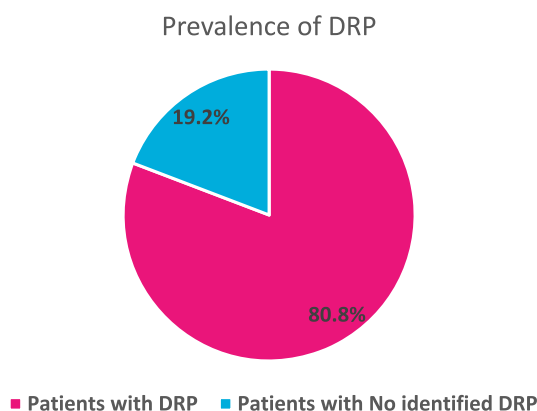


Fig. 2. Prevalence of drug related problems among patients with T2DM attending public health institutions of Kemisse town from May 1 to May 30, 2019.

Table 3
Type of DRPs among patients with T2DM attending public health institutions of Kemisse town from May 1 to May 30, 2019.

Type of drug related problem	Frequency	Percentage
Need for additional drug therapy	60	40.3
Noncompliance	51	34.2
Unnecessary drug therapy	12	8
Dosage too low	10	6.7
Ineffective drug	6	4
ADR	5	3.3
Dosage too high	5	3.3
Total	149	100

significant.

2.4. Ethical consideration

Before data collection, a formal letter was obtained from Department of pharmacy, College of medicine & Health Sciences and given to Kemisse General Hospital and Kemisse health center. After getting permission from the hospital, data collection was conducted. Verbal informed consent was obtained from each patient prior to the interview. Confidentiality of the information was assured and privacy of the

Table 4
Common causes of each DRP identified among patients with T2DM in public health institutions of Kemisse town from May 1 to May 30, 2019.

Type of DRP	Causes of DRP	Frequency	Percentage
Unnecessary drug therapy	No medical condition	7	58.3
	Drug with over lapping effect	5	41.7
Need for additional drug therapy	Untreated medical condition	12	20
	Need for Prophylactic drug therapy	45	75
	Need for combination therapy for better effect	3	5.0
Ineffective drug therapy	More effective drug available	6	75
	Inappropriate dosage form	2	25
Dosage too low	Wrong dose	6	60
	Long frequency	4	40
	Unsafe drug for the patient	3	60
ADR	Undesirable effect	2	40
	Wrong dose	2	40
Dosage too high	Short frequency	3	60
	Non-adherence	51	100

patients was maintained throughout the study. Additionally, the study was approved by the ethical review committee of college of medicine and health sciences.

Definition of terms:

Co-morbidity: Any documented chronic disease which coexists with diabetes [5].

Good Glycemic control: When the average fasting blood sugar is 70–130 mg/dl [5].

Poor glycemic control: When the average fasting blood sugar is greater than 130 mg/dl [5].

Drug related problem: Drug related problem is any undesirable event experienced by a patient which involves, or is suspected to involve, drug therapy, and that interferes with achieving the desired goal of therapy [12–14].

Adverse drug reaction (ADR): A DRP that occurs when the medication causes undesirable reaction which is not dose-related, or a safer drug is needed because of patient risk factors, or a drug interaction causes an undesirable reaction that is not dose-related [12–14].

Dosage too high: This DRP occurs when the dose is too high or the dosing interval is too short, or the duration of therapy is too long for the patient, or the dose was administered too rapidly, or a drug interaction

Table 5

Drugs involved in DRP among patients with type 2 diabetes mellitus in public health institutions of Kemisse town from May 1 to May 30, 2019.

No	Type of DRP	Causes of DRP	Drug involved in DRP	N (%)
1	Need for additional drug therapy	Untreated medical condition	ACEIs (9) and Antimicrobials (3)	12 (11.7)
		Need for Prophylactic drug therapy	Statins (33), Antiplatelet (12)	45 (83.3)
		Need for combination therapy for better effect	sulfonylureas (2) calcium channel blocker (1)	3 (5.0)
2	Unnecessary drug therapy	No medical condition	Insulin as initial therapy with oral agents	7 (58.3%)
		Drug with overlapping effect	Glibenclamide and glimepiride	5 (41.7%)
3	Ineffective drug therapy	More effective drug available	Glibenclamide as initial treatment	6 (75%)
		Inappropriate dosage form	Topical antimicrobial for diabetic foot ulcer	2 (25%)
4	Dosage too low	Two low dose to produce the desired effect	Glibenclamide 2.5 mg twice daily	6 (60%)
		Long frequency	Metformin 500 mg daily	4 (40%)
5	ADR	Unsafe drug for the patient	Metformin for CLD (2) & CHF (1) patients	3 (60%)
		Undesirable effect	Metformin caused lactic acidosis (1) and hypersensitivity reaction (1)	2 (40%)
6	Dosage too high	dose is too high	Metformin 2 g twice daily	2 (40%)
		Short frequency	Glibenclamide 10 mg three times a day	3 (60%)
7	Noncompliance	Non-adherence	Metformin	35 (68.6%)
			Glibenclamide	16 (31.4%)

Fasting blood glucose level of patients with DRP

■ FBS > 130mg/dl ■ FBS = 80 to 130mg/dl

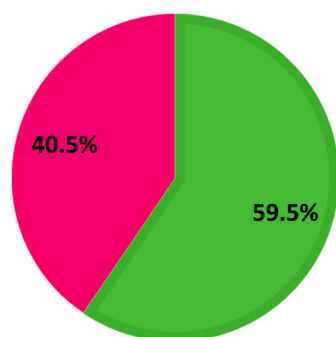


Fig. 3. Fasting blood glucose level of type 2 diabetes mellitus patients with DRP in public health institutions of Kemisse town from May 1 to May 30, 2019. FBS = Fasting Blood Sugar.

causes a toxic reaction to the drug product [12–14].

Dosage too low: It is a DRP that occurs when the dose is too low to produce the desired treatment outcome, or the duration of therapy is too short, or the dosage interval is too long, or a drug interaction reduces the amount of active drug available at the site of action [12–14].

Ineffective drug therapy: The drug is not effective or the most effective for the medical condition of the patient, or the dosage form of

the drug is inappropriate for effective therapy, or the condition is refractory to the drug product being used [12–14].

Noncompliance: A DRP that occurs when the patient fails to understand instructions of drug administration, or the patient can't self-administer the drug product appropriately, or the drug product is too expensive for the patient, or the patient prefers not to take the medication, or the drug product is not available for the patient [12–14].

Need for additional drug therapy: A DRP that occurs when there is a medical condition that requires the initiation of drug therapy, or preventive drug therapy is required to reduce the risk of developing a new condition, or a medical condition requires additional medication to attain synergistic effects [12–14].

Unnecessary drug therapy: A DRP that occurs when there is no valid medical indication for the drug therapy, or the medical condition is better treated with non-drug therapy, or drug therapy is being taken to treat an avoidable adverse reaction associated with another medication, or multiple drug products are being used for a condition that requires single drug therapy [12–14].

3. Result

3.1. Socio-demographic characteristics

A total of 156 patients were included in this study. Among the included patients, 93 (59.6%) were females, and about 104 (66.3%) of the study participants were in the age of 45–64 years with a mean age of 49.6 years. Regarding their marital status, 128 (81.7%) were married. Among the total study participants, 87 (55.8%) were farmers in occupation, 65 (41.3%) were alcohol users and 26 (16.3%) sometimes chew chat (Table 1).

3.2. Disease related factors

Among the total patients, 123 (78.8%) were diagnosed for T2DM in the past 5 years. About 87 (55.8%) of the patients visited emergency department once in the last one year, and 56 (35.5%) of the patients were hospitalized once in the last year. Additionally, 81 (51.9%) of the patients have co-morbidity (Table 2).

3.3. Medication utilized by patients

Among 156 patients included in the study, 102 (65.4%) were taking Oral antidiabetic drugs alone, 35 (22.4%) were taking oral antidiabetic drugs with insulin and the remaining 19 (12.2%) were taking insulin alone (Fig. 1).

3.4. Prevalence of drug related problems

From the total of 156 T2DM patients included in the study, 126 (80.8%) had at least one drug related problem (Fig. 2).

3.5. Types of drug related problems identified

A total of 149 DRPs were identified in 126 (80.8%) T2DM patients. From the seven drug related problems identified, the most prevalent DRPs were need for additional drug therapy, 60 (40.3%) followed by non-compliance, 51 (34.4%) and unnecessary drug therapy, 12 (8%) (Table 3).

3.6. Causes of drug related problems

Causes of each DRP were identified (Table 4). The three causes of the need for additional drug therapy were a need for prophylactic drug therapy, 45 (75%); a need for combined drug therapy, 3 (5%) and presence of untreated medical condition, 12 (20%).

Table 6

Bivariate and multivariate logistic regression of factors associated with the occurrence of Drug related problem in patients with T2DM at follow up in public health institutions of Kemisse town, North East Ethiopia from May 1 to May 30, 2019.

Variable	DRP present	DRP absent	COR	p-Value	AOR	p-value
Gender	Male	54	8	1.75 (0.61–4.99)	0.296	
	Female	72	21	1		
Age Category	25–44	19	21	1	1	
	≥45	107	9	13.79 (4.22–39.97)	0.001 ^a	5.59 (1.38–20.64) 0.016 ^b
Educational Status	Illiterate and primary	110	13	8.67 (1.54–43.69)	0.014 ^a	2.99 (0.31–23.75) 0.344
	Secondary	7	11	0.48 (0.086–2.63)	0.395	0.21 (0.02–2.69) 0.231
	Tertiary	9	6	1		1
Co morbidity	Yes	76	5	7.92 (1.81–27.34)	0.003 ^a	3.22 (1.75–13.47) 0.014 ^b
	No	50	25	1		1
Duration of diabetes	<5 years	101	22	1.31 (0.42–4.12)	0.64	
	>5years	25	8	1		
Marital status	Married	99	29	1		1
	Single/divorce d/widowed	27	1	5.18 (0.65–41.37)	0.121 ^a	5.64 (0.453–70.303) 0.179
Types of antidiabetic medication	Oral drugs	77	25	1		1
	Insulin with or without OA drugs	49	5	5.33 (0.92–42.57)	0.060 ^a	4.55 (0.29–35.91) 0.279
Duration on treatment	<5 years	101	22	1.31 (0.42–4.12)	0.64	
	≥5 years	25	8	1		
Hospitalization in the last one year	No	66	27	1		1
	Yes	60	3	14.73 (1.88–95.69)	0.011 ^a	4.66 (0.46–41.94) 0.191
Emergency Visit in the last one year	No	23	21	1		1
	Yes	103	9	11.60 (3.61–33.97)	0.001 ^a	5.08 (1.14–18.71) 0.033 ^b

AOR = Adjusted odd ratio, COR = Crude odd ration.

^a Variables that have p-value <0.25.

^b Factors significantly associated with the occurrence of drug related problem in patient with T2DM.

3.7. Drugs involved in drug related problem

Needs additional drug therapy: From the medications that should be used for prevention or treatment of DM complications or co-morbid conditions, there was underutilization of statins, 33 (55%); followed by Aspirin, 12 (20%); ACEIs for the treatment of hypertension and diabetic nephropathy, 9 (15%) and antimicrobials for the treatment of diabetic foot ulcer, 3 (5%) (Table 5).

3.8. Laboratory values

Among the total 126 patients with DRP, 75 (59.5%) had poor glycaemic control (Fasting blood sugar >130 mg/dl) (Fig. 3).

3.9. Factors associated with drug related problems

Bivariate and multivariate Analysis: Out of 10 variables entered into bivariate logistic regression, age, educational status, comorbidity, marital status, type of antidiabetic medication, number of emergency visit and number of hospitalization in the last one year have p-value less than 0.25 and selected for multivariate logistic regression. Age ≥45 years (AOR = 5.59, 95% CI = 1.38–20.64, P = 0.016), presence of comorbid condition (AOR = 3.22, 95% CI = 1.75–13.47, P = 0.014 and emergency visit in the last one year (AOR = 5.08, 95% CI = 1.14–18.71, P = 0.033) were significantly associated with the occurrence of drug related problem (Table 6).

4. Discussion

For most diseases, drug therapy enhances health-related quality of life [15]. However, inappropriate use of drugs may be harmful [16]. Drug-related problems have been identified as common causes of negative clinical and economic outcomes in health care systems worldwide [17–21]. Optimization of drug therapy and preventing drug-related problems are major factors to improve health care, reduce expenditure, and potentially save lives [22].

This study showed that 126 (80.8%) of patients with T2DM had at least one drug related problem. This is consistent with a study conducted

in Wolaitasodo hospital (83.1%) [4], but the prevalence of DRP in this study is lower than the study conducted in Malaysia, 91.8% [23] and Nigeria, 94% [11]. This discrepancy with the previous studies might be due to differences in sample size and methods of DRP identification. The most common type of drug related problem in the current study was need for additional drug therapy (40.3%), and similar studies conducted in Wolaitasodo hospital showed needs for additional drug therapy as the most prevalent DRP [4].

This study identified that age ≥45 years, presence of comorbidity and emergency department visits in the last one year were significantly associated with the occurrence of drug related problem. It was found that patients in ≥45 years of age were 5.59 times more likely to experience DRP than patients in the age group of 25–44 years. This is in line with a study conducted in wolaitasodo which identified that patients in the age group of 45–54 years were 5 times more likely to develop drug related problem than patients in the age of 25–44 years. This study also identified that those patients with co morbidities were 3.22 times more likely to develop DRP than those without comorbidity, and this is in line with the study conducted in wolaitasodo hospital [4] and Jimma University specialized Hospital [24].

Limitation of this study: It did not study economic status of the patients as it may affect the occurrence of Drug related problem. This study didn't identify the specific causes of noncompliance due to poor documentation. Identification of an ADR was only based on documented clinical assessment made by physicians; thus, the findings might be an underestimate of the number of ADRs.

5. Conclusion

A total of 149 DRPs were identified in 80.8% of T2DM patients included in the study. The three most prevalent drug related problems were need for additional drug therapy, 60 (40.3%) followed by non-compliance, 51 (34.2%) and unnecessary drug therapy, 12 (8%). Additionally, Age ≥45 years (AOR = 5.59, 95% CI = 1.38–20.64, P = 0.016), presence of comorbid condition (AOR = 3.22, 95% CI = 1.75–13.47, P = 0.014 and emergency visit in the last one year (AOR = 5.08, 95% CI = 1.14–18.71, P = 0.033) were significantly associated with the occurrence of drug related problem.

Ethics approval and consent to participate

The study has been approved by the ethical review committee of college of medicine and health sciences, Wollo University. Verbal informed consent was obtained from each patient prior to the interview.

Consent to publish

Not applicable.

Availability of data and materials

All the datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

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No funding was obtained for this study.

Authors' contributions

All authors were involved in the design, analysis and write up of the study. TM conducted the actual data collection at the hospital. All authors read and approved the final draft of the manuscript.

Declaration of competing interest

All the authors declare that there is no conflict of interest.

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References

- [1] Fernandez-Llimos F, Tuneu L, Baena MI, Garcia-Delgado A, Faus MJ. Morbidity and mortality associated with pharmacotherapy. Evolution and current concept of drug-related problems. *Curr Pharmaceut Des* 2004 Dec 1;10(31):3947.
- [2] Marathe PH, Gao HX, Close KL. American diabetes association standards of medical care in diabetes 2017. *J Diabetes* 2017 Apr;9(4):320–4.
- [3] Birarra MK, Heye TB, Shibeshi W. Assessment of drug-related problems in pediatric ward of zewditu memorial referral hospital, Addis Ababa, Ethiopia. *Int J Clin Pharm* 2017 Oct 1;39(5):1039–46.
- [4] Koyra HC, Tuka SB, Tufa EG. Epidemiology and predictors of drug related problems among type 2 diabetic patients at Wolaita Soddo University teaching hospital, southern Ethiopia. *Am J Pharmacol Sci* 2017;5(2):40–8.
- [5] Powers MA, Bardsley J, Cypress M, Duker P, Funnell MM, Fischl AH, Maryniuk MD, Siminerio L, Vivian E. Diabetes self-management education and support in type 2 diabetes: a joint position statement of the American diabetes association, the American association of diabetes educators, and the academy of nutrition and dietetics. *Diabetes Educat* 2017 Feb;43(1):40–53.
- [6] Redzuan AM, Ramli AR, Pheng MTH. Drug-related problems in hypertensive patients with multiple comorbidities. *J Pharm Res* 2017;1(3):000113.
- [7] Berenguer B, La Casa C, De La Matta MJ, Martin-Calero MJ. Pharmaceutical care: past, present and future. *Curr Pharmaceut Des* 2004 Dec 1;10(31):3931–46.
- [8] Nasution A, Khairunnisa HR. Drug related problems in management of hypertensive outpatients admitted to four Indonesian primary health centers. *Drug Ther* 2016;9(1).
- [9] Al Hamid A, Aslanpour Z, Aljadhey H, Ghaleb M. Hospitalization resulting from medicine-related problems in adult patients with Cardiovascular diseases and diabetes in the United Kingdom and Saudi Arabia. *Int J Environ Res Publ Health* 2016;13(5):479.
- [10] Zazuli Z, Rohaya A, Adnyana IK. Drug-related problems in type 2 diabetic patients with hypertension: a prospective study. *J Basic Clin Pharm* 2017 Aug 20;8(4).
- [11] Ogbonna BO, Ezenduka CC, Opara CA, Ahara L. Drug related problems in patients with Type-2 Diabetes in a tertiary hospital in Nigeria. *Int J Innov Res Dev* 2014;3(1):494–502.
- [12] Belayneh YM, Amberbir G, Agalu A. A prospective observational study of drug related problems in medical ward of a referral hospital in northeast Ethiopia. *BMC Health Serv Res* 2018 Dec;18(1):808.
- [13] Schwinghammer TL. Pharmacotherapy case book: a patient focused approach. eighth ed. 2011. p. 23–4.
- [14] Cipolle RJ, Strand LM, Morley PC. *Pharmaceutical Care practice: A Clinician's Guide*. second ed. New York: McGraw-Hill; 2004. p. 178–9.
- [15] Hohmann C, Radziwill R, Klotz JM, Jacobs AH. Health-related quality of life after ischemic stroke: the impact of pharmaceutical interventions on drug therapy (pharmaceutical care concept). *Health Qual Life Outcome* 2010;8:59.
- [16] Chiatti C, Bustacchini S, Furneri G, et al. The economic burden of inappropriate drug prescribing, lack of adherence and compliance, adverse drug events in older people: a systematic review. *Drug Saf* 2012;35(suppl 1):73–87.
- [17] Kempen TG, van de Steeg-van Gompel CH, Hoogland P, Liu Y, Bouvy ML. Large scale implementation of clinical medication reviews in Dutch community pharmacies: drug-related problems and interventions. *Int J Clin Pharm* 2014;36(3): 630–5.
- [18] Kheir N, Awaisu A, Sharfi A, Kida M, Adam A. Drug-related problems identified by pharmacists conducting medication use reviews at a primary health center in Qatar. *Int J Clin Pharm* 2014;36(4):702–6.
- [19] Kjeldsen LJ, Birkholm T, Fischer H, et al. Characterization of drug-related problems identified by clinical pharmacy staff at Danish hospitals. *Int J Clin Pharm* 2014;36(4):734–74.
- [20] Braund R, Coulter CV, Bodington AJ, et al. Drug related problems identified by community pharmacists on hospital discharge prescriptions in New Zealand. *Int J Clin Pharm* 2014;36(3):498–502.1.
- [21] Al-Arifi M, Abu-Hashem H, Al-Meziny M, Said R, Aljadhey H. Emergency department visits and admissions due to drug related problems at Riyadh military hospital (RMH), Saudi Arabia. *Saudi Pharmaceut J* 2014;22(1):17–25.
- [22] Al-Azzam SI, Alzoubi KH, AbuRuz S, Alefan Q. Drug-related problems in a sample of outpatients with chronic diseases: a cross-sectional study from Jordan. *Therapeut Clin Risk Manag* 2016;12:233.
- [23] Huri HZ, Ling LC. Drug-related problems in type 2 diabetes mellitus patients with dyslipidemia. *BMC Publ Health* 2013 Dec;13(1):1192.
- [24] Teklay G. Patients at Jimma university specialized hospital, southwest. *J Med Sci* 2013 Oct 1;13(7):578–84.