Drug Related Problems and Glycaemic Control among Adult Type 2 Diabetic Patients at Wolaita Soddo University Teaching Hospital, Southern Ethiopia

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Abstract

Background: A drug-related problem is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes of patients. Type 2 diabetic patients generally use multiple medications for comorbidities increasing the risk of drug related problems and resultant poor glycemic control in this population.

Objective: To assess epidemiology and predictors of drug related problems and glycaemic control among adult type 2 diabetic patients at Wolaita Soddo University teaching hospital, Southern Ethiopia.

***Method*:** A facility based cross-sectional study design was employed and data was collected from medical record reviews and using structured questionnaire. Drug related problems were identified by using Cipolle's drug related problems identification method which was adapted to diabetes patients and was further evaluated by experts. To examine the influences of different variables on drug related problems and on glycaemic level, both binary and multiple logistic analyses were performed. The 95% CI was used to show the accuracy of data analysis and P value $\leq$0.05 was considered as statistically significant.

Results: A total of 243 adult type 2 diabetic patients were included, of these, two hundred twenty two patients with a total of 378 drug related problems were identified. Among these, 83.1% had at least one drug related problem, averaging 1.8 ± 0.751 problems per patient. Need additional drug, 137(56.37%) and non-compliance 126(51.9%) were the most common types while age≥ 65 [AOR=9.079, 95%CI= (2.213-37.241)], comorbidity [AOR=7.004, 95% CI= (1.285-18.194)], polypharmacy [AOR =3.311, 95% CI= (1.366-30.329)], and history of hospitalization [AOR=0.403, 95%CI= (0.176-0.925)] were independent predictors of the problems. Non–compliance [AOR=2.860, 95% CI= (2.947-5.715)], dose too low [AOR=2.277, 95%CI= (1.091-4.753)] and too high [AOR=0.105, 95%CI= (0.025-0.435)] independently predicted poor glycemic control among the patients.

Conclusion: The large number of drug related problems identified showed that optimal medication management in type 2 diabetes remains a major challenge in clinical practice. Hence, the hospital should optimize utilization of statins, antiplatelet, metformin and, also make efforts to increase medication adherence of the diabetic patients.

Key words: drug related problems, type 2 diabetes, Wolaita Soddo University teaching hospital, glycaemic control.

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Abbreviations and Acronyms

AHA :-American heart association

ADA: - American Diabetes Association

ACEIs: - Angiotensin Converting Enzyme Inhibitors

ADR: -Adverse Drug Reaction

AOR: Adjusted Odds Ratio

CHF: - Congestive Heart Failure

CrCl: - Creatinine clearance

COR: Crude Odds Ratio

DM: - Diabetes Mellitus

DRP: - Drug related problems

FBS: - Fasting blood sugar

IDF: - International Diabetes Federation

JUSH: - Jimma University Specialized Hospital

MMAS:- Morisky Medication Adherence Scale

NSAID: -Non-steroidal anti-inflammatory drug

PCNE: - Pharmaceutical Care Network Europe

PUD: - Peptic Ulcer Disease

SSA: - Sub-Saharan Africa

STG:- Standard treatment guideline

T2 DM: - Type 2 Diabetes Mellitus

WHO: - World health organization

WSU: - Wolaita Soddo University

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1. Introduction

1.1. Background Information

Diabetes is a group of metabolic diseases characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. The two broad categories of DM are designated as type 1 and type 2. Type 2 DM which accounts for 90 –95% of all diabetes cases, is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production. Risk factors for developing type 2 diabetes are associated with obesity, older age, family history of diabetes, and history of gestational diabetes, impaired glucose metabolism, physical inactivity, and race/ethnicity(1–3).

The worldwide prevalence of DM has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 285 million in 2010.Based on current trends, the International Diabetes Federation projects that 438 million individuals will have diabetes by the year 2030.Although the prevalence of both type 1 and type 2 DM is increasing worldwide, the prevalence of type 2 DM is rising much more rapidly, presumably because of increasing obesity, reduced activity levels as countries become more industrialized, and the aging of the population(2,4).

Type 2 diabetes is frequently not diagnosed until complications appear. It can affect many parts of the body and is associated with serious complications including macro vascular events in the heart and blood vessels as well as micro vascular complications including retinopathy, nephropathy, and neuropathy, which can finally lead to blindness, kidney failure, foot ulcers, gangrene, erectile dysfunction and complications of pregnancy (3,5,6).

Appropriate medication management targeting glycemic control, hypertension, and lipid management is important for reducing morbidity and mortality, and improving long-term quality of life for patients diagnosed with type 2 diabetes mellitus (T2DM). Particularly, in patients with type 2 diabetes, diet and physical activity are essential first line therapies, and many clinical practice guidelines now recommend initiating metformin at diagnosis (7,8).

A drug-related problem (DRPs) is defined as ‘an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes. An actual problem has resulted in clinical manifestations like adverse drug reaction or therapy failure due to incorrect dosage. A potential problem is not manifest, but if left unresolved, it may lead to drug-related harm to the patient. DRPs are associated with negative effects on patient outcomes and have the potential to increase the cost of care. Drug therapy problem has not achieved uniform meaning in most of the published articles. Hepler used the terms like drug-related problem, drug treatment failure and pharmacotherapeutic problem in one article to describe DRP. Other researchers used the term medication errors, which is the error in the hospital medication use process(9–11).

DRPs include all issues that can potentially affect the success of pharmacotherapy in a given patient, in particular medication errors, adverse drug events and adverse drug reactions. Many investigations show that DRP may stem from: non-compliance, lack of knowledge about the medication, adverse drug events, drug interactions, dosage problems, and practical problems. Events associated with such DRPs include changes in drug therapy following hospital discharge, patient’s cognition and poly-pharmacy(12).

Various classifications were published in the literatures regarding definitions and classifications of DRPs. According to Cipolle, Morley and Strand, all patient problems involving medications can be categorized into one of seven types of drug therapy problems which fall under four patient drug related needs; i.e. indication includes unnecessary drug therapy and needs additional drug therapy, effectiveness includes ineffective drug and dosage too low, safety which includes ADR and dosage too high and finally compliance when the patient is not able or willing to take the drug therapy as intended. When drug therapy problems are identified, they are resolved by changing products, doses, or by educating the patient on how to maximize the effectiveness of the medication and then a care plan is developed for each patient, including individualized goals of therapy for each medical condition (13).

1.2. Statements of the problem

Diabetes is a leading cause of illness and death in our society. Significant cost has been invested to positively impact this disease from its prevention to its treatment. Since patients with diabetes have a significant number of co-morbidities, a situation makes it difficult to focus only on the diabetes since many of the co-morbidities influence its management, either directly or indirectly that can result in DRPs which necessitates a comprehensive medication management services that identify and resolve drug therapy problems and improve patient outcomes(14).

Researches show that drug-related problems are a significant burden to the health care system of a country. Accordingly, the annual drug related morbidity and mortality in US was estimated to be approximately $177 billion. Other studies also support as preventable morbidity associated with drug usage in ambulatory care has considerable economic, clinical and humanistic impact. Therefore, effective interventions to reduce this significant problem will avoid unnecessary patient harm and waste of health care resources which has a great importance for low income countries like Ethiopia (15–17).

Drug therapy problems are also considered as the dominant reasons for hospital admission of patients. A study conducted in Canada showed that approximately 25% of patients were hospitalized for drug-related causes; over 70% of these causes were deemed preventable. It was also evidenced by another research on DRP conducted in Norway, as the majority of hospitalised patients (81%) had DRPs, and an average of 2.1 clinically relevant DRPs was recorded per patient (18–20). Therefore procedures for identification of, and intervention on, actual and potential DRPs, are important elements of drug therapy and may contribute to diminishing drug-related morbidity and mortality.

Since patients with type 2 diabetes generally use multiple medications for comorbidities, the prevalence of DRPs in this population is unquestionable. A study conducted in Malaysia on patients with T2DM and dyslipidaemia showed that 91.8% of patients had at least one DRP, averaging 1.94 ±1.10 problems per patient and of this, drug-drug interaction (18.0%) was the most common DRP type identified. It was also revealed as the drug classes that most likely to be associated with DRPs were anti-hypertensive, lipid-modifying and anti-diabetic agents. Similar findings were also obtained among patients with T2DM and hypertension in the same country suggesting that patients with type 2 DM have comorbidities that substantially increase prevalence of DRPs (21–23).

Furthermore, evidences show that DRPs have impact on health outcomes like poor clinical outcomes, cost and quality of life. A study conducted in Switzerland showed that 91% of the included patients had at least one DRP and the odds ratios indicated that not being exposed to DRPs was associated with a higher chance of reaching the clinical target, of having a better physical quality of life than the median and having lower total health care costs. Similarly, studies conducted to identify DRPs among T2DM patients showed that patients with DRPs are more likely to have poor glycemic control than those without DRPs (5, 21, 24, 49).

Even though there is lack of study findings concerning DRPs in Ethiopia particularly in type 2 DM, a study conducted on DRPs among Patients with Cardiovascular Diseases showed that 96.1% of patients had one or more DRPs and the mean number of DRPs was 1.38 $\pm$ 0.8 per patient. Similarly, other study also showed that 73.5% of patients had DRPs and of these 32.6% cases were related to untreated condition (25,26).

Hence, this study will try to assess types, prevalence and predictors of DRPs and their impact on glycemic control among patients with type 2 DM as this plays an important role in the quality assurance of the pharmaceutical care process and the quality development of pharmacy practice. Furthermore, identification and documentation of DRPs is un-doubtfully important in achieving treatment goals of patients' clinical, economic and humanistic outcomes.

2.1. Literature review

2.1.1. Diabetes general information

Globally, diabetes prevalence is increasing and is responsible for 5% of all deaths annually. The majority of the 382 million people with diabetes are aged between 40 and 59, and 80% of them live in low- and middle-income countries. All types of diabetes are on the increase, type 2 diabetes in particular: the number of people with diabetes will increase by 55% by 2035. Myriad of literatures showed that diabetes rose from the eighth to the fifth leading cause of death globally for the year 2000 with an excess mortality of 2.9 million deaths which accounted for 5.2% of all deaths(1,27–29).

It was estimated that 10.8 million people have diabetes in sub-Saharan Africa in 2006 of which type 2 diabetes accounts for well over 90% and that this would rise to 18.7 million by 2025, an increase of 80%, as such exceeding the predicted worldwide increase of 55%. The rising prevalence of diabetes in the region has largely been ascribed to changes in lifestyle and urbanisation, resulting in greater levels of obesity and physical inactivity. According to IDF Atlas 6th edition, 2012 report, and number of cases of diabetes in Ethiopia to be estimated about 1.4 million in 2011. Studies on diabetes since 1990 reported that 20-year survival rates were found in 60% USA, Addis Ababa Ethiopia 63% as well as in African-American and these mortality figures remain unacceptably high, although an even higher mortality (60% at 5 years) was found in a large group of insulin-requiring patients (1,30).

Patients with type 2 diabetes have long asymptomatic pre-clinical phase of about 12 years in which complications are commonly present at the time of diagnosis and the disease frequently goes undetected. A study conducted in Netherlands showed that retinopathy was found in 7.6% of people with screen-detected diabetes, impaired foot sensitivity in 48.1% and micro albuminuria in 17.2%, myocardial infarction in 13.3%, ischaemic heart disease in 39.5% and peripheral arterial disease in 10.6%(4).

2.1.3. Epidemiology and Categories of DRPs

Even though there is limited number of researches done on DRPs in type 2 diabetic patients, there are well established findings that show prevalence and types of DRPs among patients with chronic diseases associated with multiple comorbidities. According to a study conducted in ambulatory patient populations in Minnesota and South Australia, of 1,598 individual patients in Minnesota, 70% experienced one or more DRPS and the need for additional drug therapy, dosage too low and non-compliance were frequently occurring DRPs types. In South Australia, from a total of 982 patients, 90% experienced one or more DRPs but the common types of DRPs were non-compliance, additional drug therapy and ineffective drug therapy. Similarly, a prospective study in two general hospitals in Jordan reported that 88% of the patients had one or more DRPs, with an average of 1.9 DRPs per patient and the most prevalent DRP was incorrect dosing regimen which was represented by (22.2%), followed by drug-drug interaction (19.4%) (12,31).

A retrospective, cross-sectional study in patients on polypharmacy in Singapore revealed that out of 347 patients (aged 16–97) 10.8% of the study population had DRPs on admission and 71.9% of which were dominant reasons for admission, and DRPs contributed partly in the remaining cases. These DRPs were mostly avoidable, and can be broadly classified into non-compliance, adverse drug reactions, require synergistic therapy, inappropriate dose and untreated condition. Another study on DRPs done in southern India showed that most of the DRP observed in the study resulted from the inappropriate drug dosing problems (25.35%) followed by drug selection (23.94%) (32,33).

In Thailand a retrospective cross-sectional study conducted on type 2 diabetic patients' showed that of 1,630 type 2 diabetic outpatients,19.3% had at least one contraindication to metformin use, with chronic renal impairment being the most frequent risk (78%) and among those with a contraindication, 84.4% were metformin users. Similarly, a cross sectional study that involved type 2 diabetic patients who were on chronic treatment with metformin in Australia revealed that metformin was prescribed for 28% of patients with impaired renal function (CrCl < 60ml/min.) and 5% with CrCl < 30ml/min who are listed in the guidelines as having standard contraindications to its use(34,35) .

According to a cross-sectional, descriptive study done in Qatar, a total of 173 DRPs were identified with an average of 3.3 DRPs per patient and the most commonly encountered DRPs were non-adherence (31 %),need for education (23 %), and adverse drug reactions (21 %). Still relatively high number of DRPs compared to other studies was identified by a study conducted on DRPs among patients with type 2 diabetes in Denmark which showed an average of 2.8 DRPs were identified per angina pectoris patient; 4.1 DRPs per type 2 diabetes patient and 4.0 DRPs per asthma patient and inappropriate use of medicines by the patient was the most common DRP sub-category identified(36,37) .

Furthermore, a study on co-morbidities and drug therapy problems in patients with diabetes in Minnesota showed that 84% of patients had at least one DRPs of which the most frequent category is need of additional drug therapy (33%) for which underutilization of lipid lowering drugs and antiplatelet for cardiovascular prevention was found to be the most common causes of its occurrence. The second frequent type was ineffective drug or dosage too low (27%) which was identified as a very costly drug therapy problem since the patient continues to suffer and many medical problems are precipitated. The study also identified that DRPs in patients with diabetes resulting from dosages that are assessed to be too low to produce the desired outcomes involve not only the patient's anti-diabetic medications, but also commonly involved insufficient dosages of their statin medication, ACE inhibitors, or their medications to control chronic pain. In addition, a study in Australia found need additional drug therapy and non-compliance as frequent types of DRPs identified among T2DM patients (14,49).

Similarly, a study on drug related problems among T2DM patients in Nigeria identified 94% of patients had at least one DRPs of which unnecessary drug therapy, non-compliance and need additional drug therapy as the most frequent categories of DRPs. It showed that prescribing drugs without clear indication, lack of understanding for diseases and medication and underutilization of antiplatelet and lipid powering drugs for cardiovascular prevention as the most reasons for these types of DRPs in study patients (59).

2.1.4. Predictors for occurrence of DRPs

A study conducted in India showed that drug related problems identified were more commonly seen in patients aged above 60 years, (53.10 %) and in males. In Malaysia also a study on diabetic dyslipidaemia patients showed that male gender, renal impairment, polypharmacy and poor lipid control were factors that were significantly associated with DRP. Similarly, a cross-sectional, study on DRPs conducted in Qatar showed that elderly patients tended to have more DRPs compared to younger patients and there was a linear relationship between age and DRPs(21,32,36) .

As shown by a study conducted in Minnesota and South Australia, frequent DRPs were associated to addition of new therapies for comorbidities such as arthritis, hypertension, hyperlipidaemia and allergic rhinitis, while in the South Australian it was a compliance issues with conditions such as asthma, diabetes mellitus, angina and digestive disorders. Still another study revealed as 78% of patients with diabetes had at least one additional co-morbidity with the median number of four requiring drug therapy management(31).

A study in Norway revealed that class of drugs had association with frequency of DRPs occurred. The most common DRPs were ADR (22%) and wrong drug or dose used by patients (14%) which were associated with anti-diabetic and lipid modifying drugs. Identification of potential drug-related problems in the elderly conducted in Netherlands showed that use of NSAIDs and digoxin was associated with the highest risk for potential DRPs (38,39) .

Furthermore, a significant association between poly pharmacy and occurrence of DRPs was shown by a study done in Qatar as patients receiving six or more medications had significantly higher number of DRPs compared to those receiving three medications(36). In addition, a hospital based general cohort study done in Ethiopia showed that; most of the patients (23.7%) with multi co-morbidity had DRPs (26).

2.2. The conceptual frame work

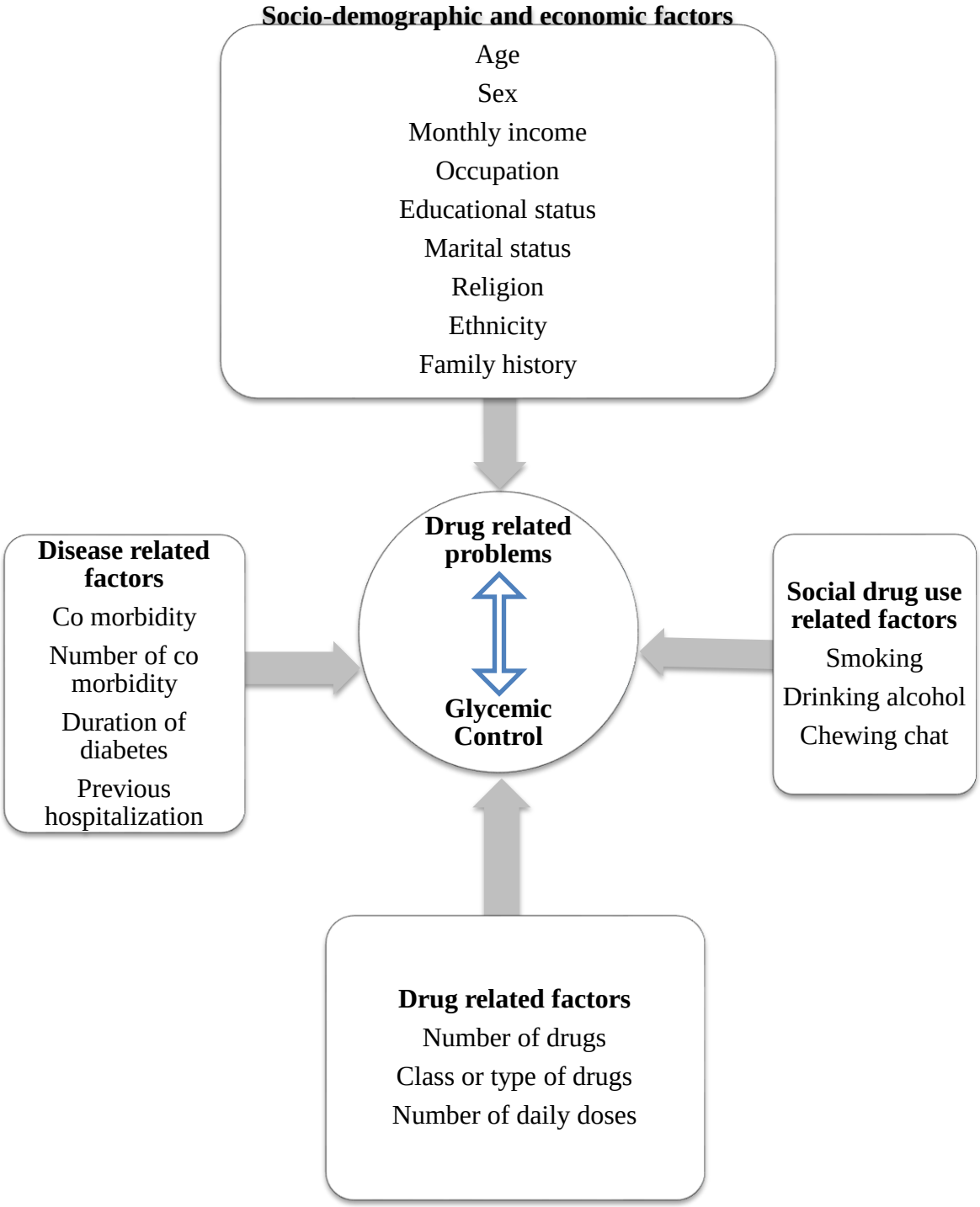


Figure 1 : Conceptual frame work adapted from literatures

2.3. Significance of the study

Type 2 diabetes substantially contributes to many complications increasing risk of DRPs which can result in poor clinical outcomes, increased healthcare costs and impaired quality of life in T2DM patients. Hence, the optimization of its management by early identification of types of DRPs and factors associated to them is essential. Categorizing and identifying drug related problems will also enable the practitioner in collaboration with the patient to construct a better care plan.

Therefore, the findings of this study:-

- Can be used as an input for policy makers to prepare treatment guidelines and to provide trainings for healthcare professionals so as to prevent and minimize frequency of DRPs.
- Will help to know the magnitude, type and predictors of DRPs experienced by type 2 diabetic patients.
- Will help the hospital by pointing out areas need to be focused in its health care plans
- Can be used as an input in movement to organize and empower pharmaceutical care service in the hospital.
- Will serve as base line for further studies or serve as secondary data for other studies as there is lack of studies on DRPs in T2DM patients especially in Ethiopia.

3. Research questions and Objectives

3.1. Research questions

- What is the prevalence of DRPs among adult type 2 DM patients at Wolaita Soddo University Teaching Hospital?
- What are common causes for the occurrence of DRPs among adult type 2 diabetic patients?
- Which drug classes are commonly involved in DRPs among adult type 2 diabetic patients?
- What are common independent predictors of DRPs among adult type 2 diabetic patients?
- Which type of DRPs is an independent predictor for poor glycemic control among adult type 2 diabetic patients?

3.2. General objective:-

To assess epidemiology and predictors of drug related problems and glycaemic control among adult T2DM patients at Wolaita Soddo University Teaching Hospital, Southern Ethiopia.

3.3. Specific objectives:-

1. To determine prevalence of drug related problems among adult type 2 diabetic patients.
2. To identify common causes of drug related problems among adult type 2 diabetic patients.
3. To identify common drug classes involved in drug related problems among adult type 2 diabetic patients.
4. To determine independent predictors of drug related problems among adult type 2 diabetic patients.
5. To determine independent predictors of poor glycemic control among adult type 2 diabetic patients.

4. Methods and Participants

4.1.Study area and period

The study was carried out among patients with type 2 diabetic patients at Wolaita Soddo University Teaching hospital. The Hospital (WSUTH) is found in South Nations Nationalities and People Region States (SNNPRS), Ethiopia. It is located in Soddo town of Wolaita Zone, SNNPRS which is 380 km away from the national capital Addis Ababa and 170 km far from the regional capital Hawassa. The teaching hospital was established in 1923 and serving people in catchment area of above 2 million people including neighboring Dawro zone, Gamo Gofa zone and Kambata Tambaro zone. It has the total capacity of about 195 inpatient beds.

According to the data obtained from the hospital approximately 48,036 people visits outpatient department per year and 5998 people admits inpatient department per year. The hospital has different wards. Among these wards medical wards, surgical wards, and ICU wards have total patient service per year was 1836, 1452 and 348 respectively (42).

The study was conducted from mid-February to March 30, 2015.

4.2.Study design

A facility based cross-sectional study design was used.

4.3.Population

4.3.1. ***Source population;*** *all* type 2 diabetes patients who visit Wolaita Soddo University Teaching Hospital for diabetes follow up care.

4.3.2. ***Study Population:*** All type 2 diabetes patients who came to the clinic during data collection and who fulfilled the inclusion criteria.

Inclusion criteria: -

- Patients who were diagnosed with type 2 DM
- patients who had received at least one ant diabetic medication
- Those on follow up for at least 3 months with their FBS measurements available before data collection.

Exclusion criteria;

- Patients not willing to take part in the study
- Age < 18 years
- Critically ill patients
- Patients with documented psychiatric problems
- Pregnant patients(Gestational DM)

4.4.Sample size and sampling technique

4.4.1. Sample size Determination

The sample size for the study was determined based on the following formula:-

$$n = \frac{(Z\alpha/2)^2 P(1-p)}{d^2}$$

Where:

n= sample size required

Z= 95% confidence interval (1.96)

D= margin of error (5%)

P= prevalence rate taken as 0.5 since no study was done on the same patient population in the country.

Then $$n = \frac{(1.96)^2 (0.5*0.5)}{(0.05)^2} = 384$$

By using population correction formula:-

$$n = \frac{n * N}{n + N}$$

Where, N= 520 total numbers of T2DM patients in the hospital,

$$n = \frac{384*520}{384+520} = 221$$

Adding 10% of non-response rate = 22. So, the total sample size = 221+22=**243** patients.

4.4.3. Sampling technique

All patients coming to the clinic during data collection period according to their appointment date and who fulfil the inclusion criteria were consecutively included in the study.

4.5. Variables

4.4.4. Independent variables

Socio-demographic and economic Variables

- ✓ Age
- ✓ Sex
- ✓ Educational status
- ✓ Religion
- ✓ Ethnicity
- ✓ Family history
- ✓ Income
- ✓ Marital status
- ✓ Occupation

Drug related variables

- ✓ Class or type of drugs
- ✓ Number of daily doses
- ✓ Number of drugs

Social drug use

- ✓ Smoking
- ✓ Drinking alcohol
- ✓ Chewing chat

Disease related variables

- ✓ Co morbidities
- ✓ Previous hospitalization
- ✓ Duration of diabetes

4.4.5. Dependent variables

Primary outcome variable:

- ➲ Drug Related Problem

Secondary outcome variable:

- ➲ Glycemic control

4.6.Data collection procedures

Data was collected through medical record reviews of patients using a prepared data extraction format and structured questionnaire which was translated to the local language for patient interview to collect information on adherence, socio-demographic, socio-economic and medication and disease related issues. The content of the data extraction format included patient details, investigations, current and past medications, daily doses, comorbidities and their management, duration of DM, and treatment targets. The data collection involved six pharmacists and one General practitioner for supervision.

4.7.DRPs Identification and classification

The Cipolle's method of identification and classification(43) was used to identify and assess DRPs in this study. The method was refined based on literature review and standard treatment guidelines(1,44) with further revision, and endorsement by panel of experts including Internists and Clinical Pharmacy Specialists. Information on drugs, such as recommended dosages, frequency, drug interactions and side-effects, was based on the Handbook of Clinical Drug data, British National Formulary, Medscape Drug interaction checker, and Stockley's drug interactions (45–47). DRPs due to patient non-compliance was identified by using validated Morisky Medication Adherence Scale (MMAS). It consists of 8 items with a dichotomous response (yes/no) with questions asking the patient to respond "yes" or "no" to items 1–7 and a 5 point Likert response for the last item. A positive response indicates a problem with adherence. The total score for each patient is the summation of the scores in each item. Therefore, a score greater than or equal to 3 indicates that the patient's medication adherence is poor.

Finally, the identified DRPs were classified as unnecessary drug therapy, needs additional drug therapy, ineffective drug, dosage too low, adverse drug reaction, dosage too high and noncompliance.

Table 1: DRPs identification criteria adapted from Cipolle, Morley and Strand method

S. NO	*DRP category*	*Criteria to identify as DRP*	*Expert's opinion*		*Comments*
			Agree	*Disagree*	
1	***Needs additional drug therapy***	**Statin therapy is needed :-** *(according to ADA 2014/2015, Eth STG 2014)* ✓ Irrespective of lipid profile if , Overt CVD , age >40 years and or ≥ 1 other CVD risk factors* ✓ Without CVD and <40 years:- if LDLc >100mg/dl or have multiple CVD risks			
		Antiplatelet therapy is needed ;- *(according to ADA 2014/2015, Eth STG 2014)* a. 10-year risk >10% (by calculating Framingham risk) **b.** Men >50 years of age or women >60 years of age who have at least one additional major risk factor *			
		➢ For a patient who has been taking metformin in its max daily dose (2-2.5g) and not achieved target glycemic level…needs addition of Glibenclamide and or insulin			
		➢ For a patient started on Glibenclamide, initiation of metformin (if available and no C/I) with slow titration is needed for its additional beneficial effects while adjusting the dose of Glibenclamide ¥			
		➢ For a hypertensive patient taking a drug in its max daily dose for >3months and not achieved target BP (<140/90mmHg), addition from other classes of drugs (ACEIs/diuretics/CCB/BB) in low dose is needed (based on the compelling indications)			
2	***Unnecessary drug therapy***	➲ Use of statins and antiplatelet in a patient without the criteria mentioned in No-1			
		➲ Patients on metformin with good glycemic control(av. FBS <130mg/dl), addition of Glibenclamide and or insulin			
		➲ For HTN patient without other compelling indications who has been taking ACEIs(Enalapril) and good BP control, addition of other antihypertensive is considered as unnecessary drug therapy			

¥ C/I=contraindication to metformin (CHF, CKD, lactic acidosis)

Table 1: DRPs identification criteria adapted from Cipolle, Morley and Strand method continued…

S. NO	*DRP category*	*Criteria to identify as DRP*	*Expert's opinion*		*Comments*
			Agree	*Disagree*	
3	***Dose too low***	If a patient with poor glycemic or BP control has been taking his/her medications below max recommended daily dose,			
		If a medication is being taken concurrently with known enzyme inducing or absorption affecting medication based on Medscape DI checker and Stockley's drug interactions 2009.			
4	***Ineffective drug therapy***	If a medical condition is refractory: ✍ When a patient's glycemic or BP is poorly controlled despite the combination therapy is used in its max daily dose, then the drug is said to be ineffective.			
		Use of drugs reducing effectiveness of the medications (by worsening the disease condition)			
5	***Dosage too high***	If the dose of medication is above max recommended daily dose,			
		If the dosing frequency is too short,			
		If dose adjustment for renal impairment is not done.			
		If a medication is being taken concurrently with known enzyme inhibiting medication (according to Medscape DI checker and Stockley's drug interactions 2009).			
6	***ADR***	If the drug product is contraindicated due to risk factors or If a safer drug product is required due to risk factors.			
		If a drug interaction causes an undesirable reaction that is not dose-related			
7	***Non compliance***	If the patient scores $\geq$ 3 according to validated Morisky Medication Adherence Scale (MMAS), then it is said to be poor adherence/non adherence.			

* *CVD risk factors: - Hypertension, Smoking, Dyslipidaemia, and family history of CVD*

4.8. Operational definitions and Terms

A 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 goals of therapy(13) .

Comorbidity:-any chronic disease which coexists with diabetes (45).

Polypharmacy: if greater or equal to five chronic medications for at least one month (21).

Glycemic control: good when the average FBS is 70-130mg/dl whereas ≥130mg/dl is poor(44).

CVD risks*:* HTN, smoking, dyslipidaemia, albuminuria and family history of CVD(1)

Unnecessary drug therapy: when there is no valid medical indication for the drug therapy at this time, multiple drug products are being used for a condition that requires single drug therapy, the medical condition is more appropriately treated with nondrug therapy, Drug therapy is being taken to treat an avoidable adverse reaction associated with another medication, (13) .

Need for additional drug therapy: if a medical condition requires the initiation of drug therapy, Preventive drug therapy is required to reduce the risk of developing a new condition, a medical condition requires additional pharmacotherapy to attain synergistic effects(13) .

Ineffective drug: Use of drugs reducing effectiveness of the medications (by worsening the disease condition), the medical condition is refractory to the drug product (13) .

Dosage too low: when drug interaction reduces the amount of active drug available, and a drug interaction reduces the amount of active drug available, the duration of drug therapy is too short to produce the desired response, the dosage interval is too infrequent to produce the desired response (13) .

Renal impairment: - CKD, chronic interstitial nephritis, chronic glomerulonephritis, and CrCl < 35 mL/min, and or as stated in the medical records (45).

Liver impairment refers to liver cirrhosis, chronic hepatitis, hepatocellular carcinoma, elevations of liver enzymes (more than 3 times the upper normal limits) or as stated in the medical records (45).

Adverse drug reaction: if drug product causes an undesirable reaction that is not dose-related, a safer drug product is required due to risk factors, a drug interaction causes an undesirable reaction that is not dose-related, and the drug product causes an allergic reaction, the drug product is contraindicated due to risk factors(13) .

Dosage too high: if dose is too high, the dosing frequency is too short, the duration of drug therapy is too long, a drug interaction occurs resulting in a toxic reaction to the drug product, the dose of the drug was administered too rapidly(13) .

Noncompliance: if the patient scores $\geq$3 in Morisky scale due to the reasons like; the patient does not understand the instructions, the patient prefers not to take the medication, , the drug product is too expensive for the patient, the patient cannot swallow or self-administer the drug product appropriately, and the drug product is not available for the patient(13) .

4.9. Data quality assurance

4.9.1. Pre-test

Questionnaires were prepared in English and translated into Amharic and back translated into English to check its consistency. The Amharic versions was used for data collection after pretesting on 5% (12) of the actual sample size in Soddo Christian General hospital and based on the finding appropriate correction was taken (including estimation of the time needed for data collection, respondents reaction to questions, respondents ability to understand etc.).

4.9.2. Data collectors training and supervision

The data collectors were trained on how to collect the data in an orientation session on study requirements including objectives of the study, definitions, and ways to approach patients, and the documentation processes, prior to data collection. The data collection process involved rigorous patient chart review and contacting patients who were eligible for inclusion in the study, explaining the purpose of the study, and obtaining their consent to participate. The patient card number was used, to check validity and completeness of the response. The data collectors were also strictly supervised daily and the principal investigator reviewed all filled format so that any suggestion and corrections was given soon.

4.10. Data analysis

Completeness of the data was checked every day and entered and cleaned using Epi-data version 3.1 and exported to SPSS version 21.0 for analysis by the principal investigators. Descriptive analysis was computed as frequency, mean and standard deviation (SD) for continuous variables and for categorical data. To examine the influences of different variables on DRPs as well as DRP categories on glycemic level and controlling for potential confounders, both binary and multiple logistic analyses were performed using at least three months average glycemic level(FBS) as the dependent variables. The 95% CI was used for data accuracy and P-value $\leq$0.05 was considered as statistically significant. The out puts of processed data was presented using tables, graphs, & figures accordingly.

4.11. Ethical consideration

Formal letter was obtained from Research Ethics Committee of Jimma University Ethical Board Review and given to the hospital .There was a written consent taken so that the patient will agree to give his/her medical information. Patients were assured that lack of willingness to involve in the study will not affect the service they get from the hospital. Pertinent drug information inquiry from patients regarding the concerns about his/her medications was provided to the patient during the data collection. To ensure patient confidentiality, name and address of the patient was not recorded in the data collection format. The patients were informed that that his/her medical information would not be disclosed to any external subjects/media.

4.12. Dissemination plan of the study finding

The result of this study will be presented to Jimma University as part of Masters of Clinical Pharmacy thesis and it is disseminated to JU College of Health Science, department of Pharmacy, summarized report to WSU teaching hospital, and to the targeted health facilities and Non - governmental organizations working on health sector in the study area. Effort will be made to publish it on national and international scientific journals.

5. Results

Socio-demographic characteristics of the study population

A total of 243 adult type 2 diabetic patients were included, of these 129(53.1%) were males. Of the total, 105(43.2%) fell within the age range of 45-54 years followed by age range of 55-64 year old 82(33.7%). The mean age of patients was 53(SD=±8.36 years) ranging from 26 to 88 years old. The highest percent of patients were married (70.8%), having primary education (45.3%) and merchants (29.6%). Most of patients (96.7%) did not use tobacco, did not chew chat (90.9%), while 18.5% drink alcohol and 22.6% had family history of DM **[Table 2**].

Table 2: Socio-demographic characteristics of T2DM patients in WSU teaching hospital, Southern Ethiopia, 2015(N=243)

Socio-demographic variable	***Frequency (%)***
Sex	
Male	129 (53.1)
Female	114 (46.9)
Age(years)	
Mean ± SD	53 ±8.362
Range	26-88
≤ 44	26(10.8)
45-54	105(43.2)
55-64	82(33.7)
≥ 65	30(12.3)
Marital status	
Married	172 (70.8)
Single	26 (10.7)
Divorced	15(6.2)
Widowed/er	30(12.3)
Education	
Illiterate	72 (29.6)
Primary education	110(45.3)
Secondary education	43(17.7)
College/University	18(7.4)
Occupation	
Employed	62 (25.5)
Merchant	72(29.6)
Farmer	33(13.6)
House wife	48(19.8)
Other*	28(11.5)

Table 2: Socio-demographic characteristics of T2DM patients continued…

Religion	
Protestant	135 (55.6)
Orthodox	73 (30.0)
Muslim	24(9.9)
Catholic	11(4.5)
Ethnicity	
Wolaita	161(66.3)
Amhara	29(11.9)
Gurage	20(8.2)
Gamo	19(7.8)
Others**	14(5.8)
Monthly income	
<750 birr	155(55.6)
≥750 birr	108(44.4)
Tobacco use	
Yes	8(3.3)
No	235(96.7)
Drinking alcohol	
Yes	45(18.5)
No	198 (81.5)
Chewing chat	
Yes	22(9.1)
No	221(90.9)
Family history of DM	
Yes	55 (22.6)
No	188(77.4)

**daily labourer, carpenter **Silte, Hadiya, Kambata*

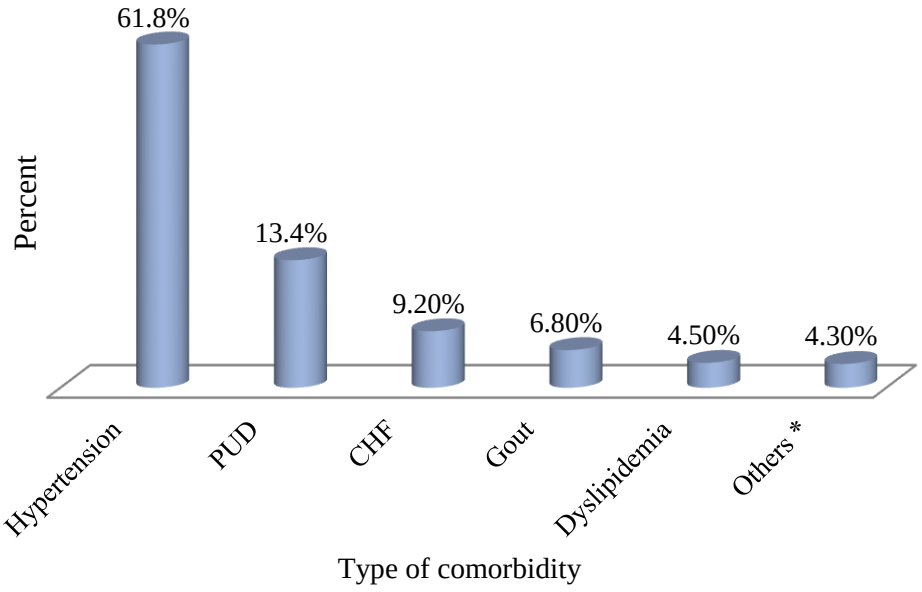
Disease related variables of study patients

The majority, 79% (192) of the patients had duration of T2DM of ≤ 10 years with the mean duration of 6.74± 5.02 years ranging from 7months to 25 years **[Table 3]**. More than half of patients, 56.0% (137) were with comorbidity of which hypertension contributed to the highest percentage (61.8%) followed by peptic ulcer disease (13.4%) **[Fig.2].** Majority 71% (97) of patients had one comorbidity with the mean number of comorbidities per patient was 2.54 ± 1.385 **[Fig.3]**. The average fasting plasma glycemic level of patients calculated from at least three consecutive values showed that 59.2% (144) of patients had poor glycemic control with the mean value of 130.06 ± 10.895 mg/dl ranging from 82 to 147mg/dl.

Table 3: Diseases related variables among T2DM patients in WSU teaching hospital, Southern Ethiopia, 2015(N=243).

Diseases related variables	***Frequency (%)***
Duration of diabetes (mean ± SD; years)	
Below (<=10 years)	6.74± 5.020
11-20 years	192 (79)
Above 20 years	43 (17.7)
	8(3.3)
History of hospitalization	
Yes	80(32.9)
No	163(67.1)
Presence of comorbidity	
Yes	137(56.0)
No	107(44.0)
Number of comorbidities (mean ± SD)	2.54 ± 1.385
Average Glycemic level*	
70-130 (good)	99(40.8)
Above 130 (poor)	144(59.2)
Average BP measure**	(N=85)
Above 140/90 mmHg	27(31.7)
90/60-140/90 mmHg	56(68.3)
Lipid profile	
Normal	15(6.2)
Dyslipidaemia	11(4.5)
Not available	217(89.3)
Renal function test	
Normal	73(30)
Impaired	6(2.5)
Not available	164(67.5)
Liver function test	
Normal	21(9)
Not available	222(91)

** calculated from at least three consecutive measures of FBS **those with HTN*



*=*CKD, asthma, HIV, epilepsy*

Figure 2 : Type of comorbidities among type 2 diabetes patients at WSU teaching hospital, Southern Ethiopia, 2015(N=137).

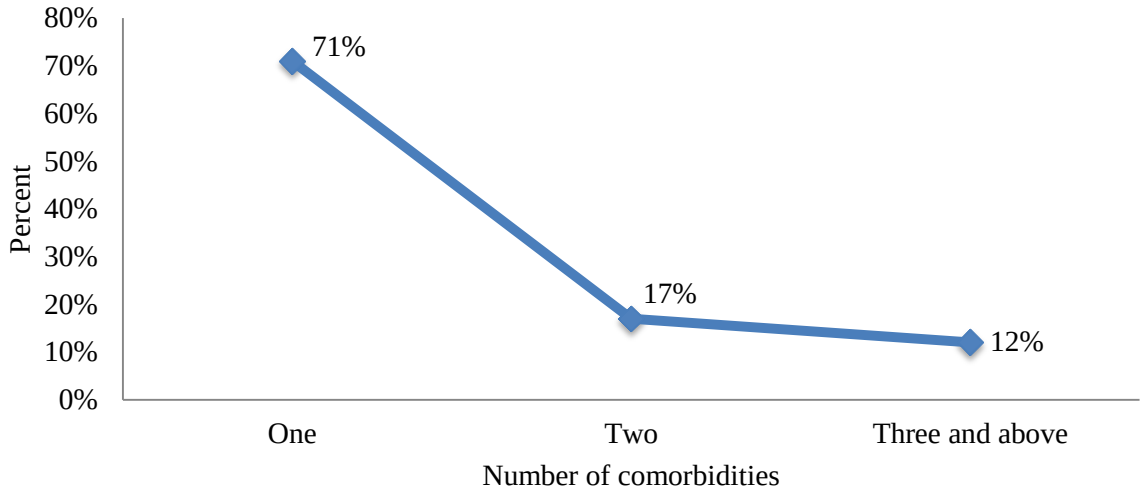


Figure 3: Number of Comorbidities among type 2 diabetes patients at WSU teaching Hospital, Southern Ethiopia,2015 (N=137).

Medication related variables of study patients

The highest percent, 76 (31.3%) of patients were taking three medications daily and 48 (19.8%) were taking more than or equal to five (polypharmacy) medications per day. The mean number of medications was 3.34 ± 1.383 ranging from one to seven medications. Majority (65.8%) of the medications were taken twice per day. The most commonly prescribed anti-diabetic medication type was a combination of Glibenclamide with metformin 116(47.7%) followed by monotherapy with Glibenclamide (25.9%) while monotherapy with ACEIs 39(46%) and a combination of ACEIs with calcium channel blockers 27(32%) were the most frequently prescribed antihypertensive medications. About quarter (26.7%) of patients were prescribed with lipid lowering medication of which almost all (91.67%) received simvastatin while 18.1% were prescribed with antiplatelet agent, aspirin. Among concurrently used medications other than anti-diabetics, antihypertensive, statins and antiplatelet, acid lowering drugs 32 (48.5%) and antibiotics 14 (21.2) were the most frequently prescribed medications [**Table 4].**

Table 4: Medication related variables among T2DM patients in WSU teaching hospital February 2015, (N=243)

Medication related variables	***Frequency (%)***
No of medications taken per day (mean ± SD)	3.33 ± 1.38
Below (<5)	195 (80.25)
Above (≥5) (polypharmacy)	48 (19.75)
Frequency/number of doses per day (mean ± SD)	2.34 ± 0.47
≤Twice	160 (65.8)
Three times and above	83 (34.2)
Type of anti-diabetic medications	
Metformin	13 (5.3)
Glibenclamide	62 (25.5)
Insulin	13 (5.3)
Metformin and Glibenclamide	**116 (47.7)**
Metformin and insulin	26 (10.7)
Insulin and Glibenclamide	12 (4.9)
Metformin + Glibenclamide + insulin	1 (0.4)

Type of antihypertensive medications	(N=97)
ACEIs	39 (40)
ACEIs + Calcium channel blockers	27(27.8)
Calcium channel blockers	6(6)
Diuretics +ACEIs	19(19)
Others ¥	8(8.2)
Statins	(N=60)
Simvastatin	55 (91.7)
Atorvastatin	5(8.3)
Antiplatelet	
Aspirin	44(18.1)
No Aspirin	199(81.9)
Other Concurrently used medications	(N=66)
Antiulcer drugs	32 (48.5)
Antibiotics	14 (21.2)
NSAIDs	11 (16.7)
Others*	9 (13.6)
MMAS**	
< 3	116(47.7)
≥ 3	127(52.3)

** ARV drugs, anti-asthmatics, anti-epileptics, steroids ** Morisky medication adherence score, ¥ beta blocker, other combinations*

Epidemiology of Drug related problems

A total of 202(83.1%) patients had at least one drug related problem. The mean number of DRPs was 1.8 ± 0.751 with a total of 378 DRPs identified .The maximum number of DRPs was four but most of the patients 85 (42%) had two DRPs **[Figure 4].** Based on patient drug related needs, indication 153 (63%), and compliance 127 (52.3%) related problems were found to be the most frequently occurring DRPs among T2DM patients [**Figure 5].**

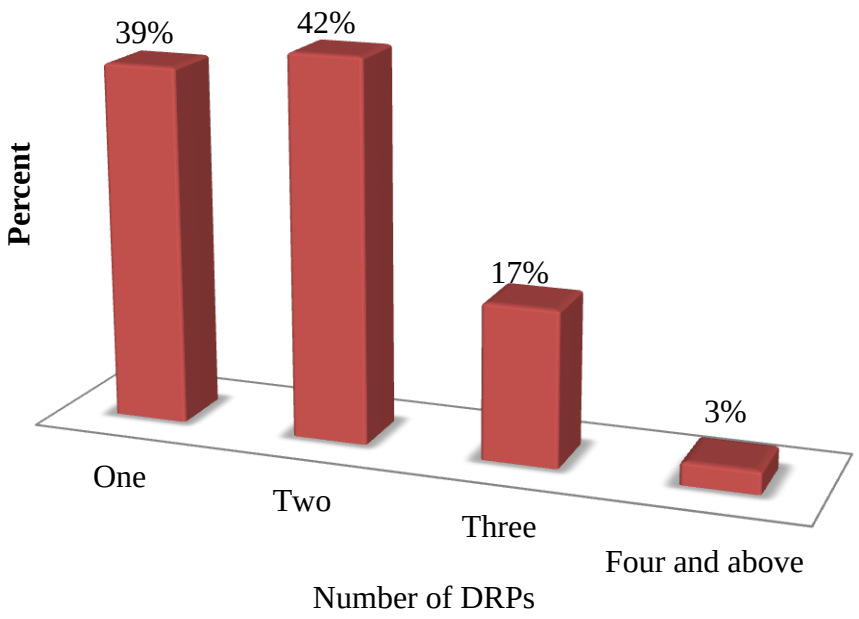


Figure 4: Number of DRPs among type 2 diabetes patients in WSU teaching hospital, Southern Ethiopia, 2015(N=243).

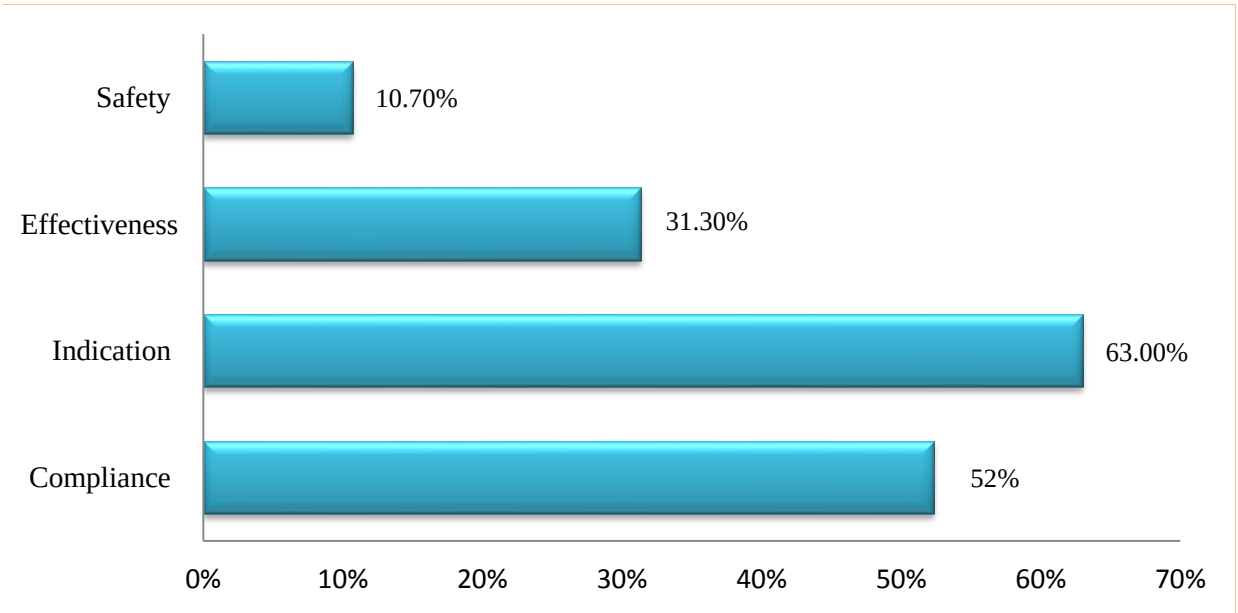


Figure 5: Patient drug related needs of the identified DRPs among T2DM patients in WSU teaching hospital, Southern Ethiopia, 2015 (N=243)

Of the seven categories of DRPs identified, need additional drug therapy was found to be the most frequent 137(67.8%) type **[Table 5].** It was found that requirement of preventive drug therapy 126(92%) was the most common reason for occurrence of this type of DRPs. A total 67(49%) and 26(18.9%) patients were not receiving statins and antiplatelet therapy respectively although they were at increased CV risk **[Table 7].** According to Validated Morisky Medication Adherence Scale (MMAS), 127 (52.3%) number of patients were not adhering to their medication giving non-compliance as the second most frequent type of DRPs. Majority 64(50.4%) of non- adherent patients reported that forgetting to take their medication followed by fear of side effects 36(28.3%) were the common reasons for their non-adherence **[Table 6].** Dosage too low 65(26.75 %) was found to be the third frequent DRP category for which Enalapril 42(64.6%) and metformin 21(32.4%) were common drugs involved.

Table 5: Types of the identified DRPs among T2DM patients in WSU teaching hospital, Southern Ethiopia, 2015

Categories of DRPs	***No of patients***	***% of total patients * (N=243)***
Need additional drug therapy	137	56.37
Non compliance	127**	52.30
Dose too low	65	26.75
Unnecessary drug therapy	16	6.58
Dose too high	14	5.76
Ineffective drug therapy	8	3.29
Adverse drug reaction	11	4.90

Total sum is greater than 100% as some patients had >1 reported DRPs. patients with MMAS ≥3*

Among drug classes commonly used by type two diabetes patients in the hospital, ant diabetic medications 78(38.6%) followed by statins 74(36.6%) were found to be the most frequently involved drugs in overall occurrence of DRPs. It was found that of patients requiring drug therapy for cardiovascular prevention, the most common cause was underutilization of lipid lowering drugs (statins) 67(49%) followed by antiplatelet 26(18.9%) **[Table7].**

Table 6: Common causes of each DRP identified among T2DM patients in WSU teaching hospital, Southern Ethiopia, 2015(N=202)

S.NO	*DRPs Category and causes*	*Frequency(N=243) (%)*
1	**Needs additional drug therapy**	**137(67.8)**
	Preventive drug therapy required	126(92)
	To attain synergistic effect	10(7.3)
	There is a medical condition that requires treatment	1(0.7)
2	**Non compliance**	**127(52.3)**
	Forgets to take medications	64(50.4)
	Fear of side of effects	36(28.3)
	Drug unavailability	15(11.8)
	Others*****	12(9.5)
3	**Dose too low**	**65 (26.7)**
	The dose is too low to produce the desired effect	56(86)
	The dosing is too infrequent to produce the desired effect	7 (4.6)
	There is drug interaction which reduces its effect	2(9.4)
4	**Unnecessary drug therapy**	**16 (6.5)**
	Duplicative drug therapy	14(87.5)
	There is no valid medical condition	2(12.5)
5	**Dose too high**	**14(5.7)**
	The dose given is too high	12(85.7)
	Drug interaction	2(14.3)
6	**Adverse drug reaction**	**11(4.5)**
	The drug is C/I due to risk or safer drug is available	4(41.7)
	The drug produces an undesirable effect(hypoglycaemia) **	7(33.3)
7	**Ineffective drug therapy**	**8(3.30)**
	The medical condition is refractory	1(12.5)
	Use of drugs reducing effectiveness of the medications	7(87.5)

** Unclear drug instruction, cost, and patient preference.*

*** At least one episode of hypoglycaemia prior to enrolment in the study*

Table7: Common drugs involved in each category of DRPs among type 2 DM patients at WSU teaching hospital, Southern Ethiopia 2015.

S. No	Category of DRPs	Commonly involved drugs	Frequency (%)
1	Needs additional drug therapy (N=137)	Statin	67(49)
		Aspirin	26(18.9)
		Metformin	14(10.2)
		Enalapril	11(8.0)
		Glibenclamide	7(5.1)
		Antiulcer drugs	1(0.8)
2	Unnecessary drug therapy (N=16)	Glibenclamide	9(56.25)
		Nifedipine	5(31.25)
		Aspirin	2(1.25)
3	Dose too low(N=65)	Enalapril	42(64.6)
		Metformin	21(32.4)
		Phenytoin	2(3)
4	Ineffective drug therapy (N=8)	NSAIDs	5(62.5)
		Prednisolone	2(25)
		Insulin + metformin + Glibenclamide	1(12.5)
5	Dose too high(N=14)	Glibenclamide	7(50)
		Cimetidine	2(14.3)
		Nifedipine	5(35.7)
6	Adverse drug reaction (N=11)	Metformin	3(27.3)
		Glibenclamide	6(54.5)
		Beta blockers	1(9)
		Cotrimoxazole	1(9)
7	Non-compliance (N=127)*	Metformin	14(11)
		Aspirin	10(7.8)
		Simvastatin	6(4.7)
		Atorvastatin	1(0.7)

**total sum is less than 127 as there are other non-drug related causes (forgetting, preferences, and instruction problem)*

Results of bivariate logistic regressions on factors associated with DRPs occurrence

Bivariate analysis was carried out to see the association between the independent variables with occurrence of DRPs in study patients. Accordingly , age range of 55-64 years [COR=2.993, 95% CI= (0.909-9.858)], diabetes duration 11-20 years [COR=2.3, 95% CI= (0.783-6.920)], frequency of daily dose (≥3 times per day) [COR=8.306, 95% CI= (2.48-27.389)], polypharmacy [COR=12, 95% CI=(1.007-22.814)], monthly income [COR=2, 95% CI= (1.000-3.964)], presence of comorbidity [COR=7.289, 95% CI = (3.198-16.617)], history of hospitalization [COR=0.23, 95% CI = (0.119-0.482)], use of ant-hypertensive drug [COR=4, 95% CI= (1.819-8.819)] and use of statins [COR= 0.862, 95% CI= (0.103-0.802) had association with occurrence of DRPs**[Table 8].**

Predictors of DRPs occurrence in study patients

Multivariable logistic regression analysis was carried out to identify independent predictors of occurrence of DRPs among the study participants. Accordingly, age of respondents, presence of comorbidity, polypharmacy, and history of hospitalization were found to be independent predictors of drug related problems among study patients. It was found that the likely hood of having DRPs increases as age of respondents increases. Patients with in the age range of 45-54 years were 4.8 times more likely to have DRPs [AOR=4.851,95%CI=(1.129-20.853)] whereas those above 65 years old were nine times more likely to have DRPs compared to those less than 45 years old[AOR=9.079,95%CI=(2.213-37.241)](p-value <0.001). It was also found that patients who were taking more than or equal to five medications per day were about three times more likely to have DRPs [AOR=3.311, 95%CI= (1.366-30.329)] compared to those who were taking less than five medications per day (p-value <0.025). Similarly, patients with comorbidity were seven times more likely to experience DRPs than patients without comorbidity [AOR=7.004, 95% CI= (1.285-18.194)]. However, it was also found that, patients with history of hospitalization were less likely to have DRPs [AOR=0.403, 95%CI= (0.176-0.925)] compared to those who did not **[Table 9].**

Table 8: Bivariate analysis of independent variables associated with DRPs among T2DM patients at WSU teaching hospital, Southern Ethiopia, 2015(N=243)

Variables	DRPs		COR	95% C.I.for COR		p-value
	Yes (%)	No (%)		Lower	Upper	
Polypharmacy						
Yes	47(19.3)	1(0.4)	12.129	1.007	22.814	0.015*
No	155(63.8)	40(16.5)	1			
Use of statins						
Yes	55(22.6)	5(2)	0.862	0.103	0.802	0.102*
No	147(60.4)	36(15)	1			
Use of antihypertensive						
Yes	49(20)	36(15)	4.005	1.819	8.819	0.001*
No	153(63)	6(3)	1			
History of hospitalization						
Yes	55(22.6)	25(10)	0.239	0.119	0.482	0.000**
No	147(60.5)	16(6.5)	1			
Presence of comorbidity						
Yes	129(53)	8(3.3)	7.289	3.198	16.617	0.000**
No	73(30)	33(13.7)	1			
Monthly income						
<750 birr	145(59.6)	23(9.5)	1.991	1.000	3.964	0. 050*
≥750 birr	57(23.4)	18(7.5)	1			
Educational status						
Illiterate	58(24)	14(5.8)	2.071	0.662	6.481	0.211*
Primary	95(39)	15(6.2)	3.167	1.032	9.716	0.044*
Secondary	37(15)	6(2.5)	3.083	0.836	11.376	0.091*
College/University	12(5)	6(2.5)	1			
Frequency of doses						
Twice or less	122(50)	38(15.6)	1			
Three times and above	80(33)	3(1.2)	8.306	2.480	27.389	0.001**
Age						
≤ 44 years	16(6.5)	10(4.1)	1			
45-54 years	93(38.3)	12(5)	1.359	0.493	3.749	0.553
55-64 years	67(27.5)	15(6)	2.993	0.909	9.858	0.072*
≥65 years	26(10.7)	4(1.6)	1.241	0.438	3.514	0.685
Duration of diabetes						
≤ 10 years	155(64)	37(15)	1			
11-20 years	39(16)	4(1.6)	2.327	0.783	6.920	0.129*
≥21 years	8(3.3)	0(0)	0	0	0	
Sex						
Male			1	0.415	15.91	0.545
Female			0.813			

*Note: *-significant results, 1-reference category **p-value<0.001, *p-value<0.25, CI=confidence interval, COR=crude odds ratio*

Table 9: Results of multiple logistic regressions for predictors of DRPs among T2DM patients at WSU teaching hospital, Southern Ethiopia, 2015(N=243)

Predictors	DRPs		COR	AOR	95% C.I.for AOR		p-value
	Yes (%)	No (%)			Lower	Upper	
Polypharmacy							
Yes	47(19.3)	1(0.4)	12.129	3.311	1.366	30.329	**0.025***
No	155(63.8)	40(16.5)	1	1			
Use of statins							
Yes	55(22.6)	5(2)	0.862	0.274	0.086	1.870	0.128
No	147(60.4)	36(15)	1	1			
Use of antihypertensive							
Yes	49(20)	36(15)	4.005	3.939	0.609	25.459	0.150
No	153(63)	6(3)	1				
History of hospitalization							
Yes	55(22.6)	25(10)	0.239	0.403	0.176	0.925	**0.032***
No	147(60.5)	16(6.5)	1	1			
Presence of comorbidity							
Yes	129(53)	8(3.3)	7.289	7.004	1.285	18.194	**0.024***
No	73(30)	33(13.7)	1	1			
Monthly income							
<750 birr	145(59.6)	23(9.5)	1.991	1.498	0.657	3.416	0.337
≥750 birr	57(23.4)	18(7.5)	1	1			
Frequency of doses							
≤ twice	122(50)	38(15.6)	1	2.930	0.664	12.920	0.156
≥Three times	80(33)	3(1.2)	8.306				
Age							
≤ 44 years	16(6.5)	10(4.1)	1	1			
45-54 years	93(38.3)	12(5)	1.359	4.851	1.129	20.853	**0.034***
55-64 years	67(27.5)	15(6)	2.993	6.878	1.930	24.511	**0.003***
≥65 years	26(10.7)	4(1.6)	1.241	9.079	2.213	37.241	**0.000***

*Note: *-significant results, 1-reference category, *p-value≤0.05, CI=confidence interval, COR=crude odds ratio, AOR=adjusted odds ratio*

Results of bivariate logistic regressions on factors associated with poor glycemic control in study patients

Bivariate analysis was carried out to see the association between the independent variables with poor glycemic control among study patients. Among all independent variables , age of respondents (above 55 years), dosing frequency, polypharmacy, presence of comorbidity, monthly income , use of statins ,use of anti-hypertensive, presence of DRPs, dose too low, adverse drug reaction and poor adherence were found to be significantly associated showing more likely hood of having poor glycemic control. But history of hospitalization and dose too high type of DRPs showed less likely hood of having poor glycemic control among study patients **[Table 10].**

Table 10: Bivariate analysis of independent variables associated with poor glycemic control among T2DM patients in WSU teaching hospital, Southern Ethiopia, 2015(N=243)

Variables	Ave. Glycemic level		COR	95% C.I.for COR		
	Poor (%)	Good (%)		Lower	Upper	p-value
Polypharmacy						
Yes	36(15)	12(8.4)	2.758	1.299	5.852	0.008*
No	108(44.5)	87(36)	1			
Use of Statins						
Yes	41(17)	19(8)	2.282	1.206	4.318	0.011*
No	103(42)	80(33)	1			
Use of antihypertensive						
Yes	58(24)	27(11)	4.005	1.819	8.819	0.148*
No	86(35.4)	72(29.6)	1			
Presence of DRPs						
Yes	137(56.4)	65(26.7)	4.065	1.999	8.266	0.000**
No	7(3)	33(13.5)	1			
Dose too low						
Yes	51(21)	14(5.7)	2.250	1.204	4.205	0.011*
No	93(38)	85(35)	1			
Dose too high						
Yes	5(2)	9(4)	0.316	0.102	0.974	0.045*
No	139(57)	90(37)	1			
ADR						
Yes	10(4)	1(0.4)	7.150	0.908	56.327	0.062*
No	134(55)	98(40.3)	1			
Poor-adherence						
Yes	98(40.3)	29(12)	3.821	2.206	6.619	0.000**
No	46(19)	70(29)	1			
History of hospitalization						
Yes	43(17.6)	37(15.2)	0.592	0.343	1.022	0.060*
No	101(41.5)	62(25.5)	1			

Table 10: Bivariate analysis of variables associated with poor glycemic control continued...

Presence of comorbidity						
Yes	93(38.3)	44(18)	1.749	1.035	2.955	0.037*
No	51(21)	55(22.6)	1			
Monthly income						
<750 birr	103(42)	52(21.7)	1.991	1.000	3.964	0.049*
≥750 birr	41(17)	47(19.3)	1			
Frequency of doses						
Twice or less	93(38.5)	67(27.5)	1			0.074*
Three times and above	51(21)	32(13)	1.671	0.951	2.939	
Age						
≤ 44 years	16(6.5)	10(4)	1			
45-54 years	64(26)	41(17)	2.545	1.062	6.102	0.969
55-64 years	47(19)	35(14.5)	2.132	0.872	5.214	0.036*
≥65 years	17(7)	13(5)	1.021	0.438	3.514	0.097*

*Note: *-significant results, 1-reference category **p-value<0.001, *p-value < 0.25, CI=confidence interval, COR=crude odds ratio*

Predictors of poor Glycemic control in study patients

Multivariable logistic regression analysis was carried out to identify independent predictors of glycaemic control among the study participants. It was found that patients having DRPs were about three times more likely to have poor glycemic control compared to those who did not have DRPs[AOR=2.804, 95% CI= (1.004-5.230)]. Among all categories of drug related problems identified; poor adherence, dose too low and dose too high independently predicted presence of poor glycemic control in this study. Accordingly, patients who had poor adherence to their medication were found to be 2.8 times more likely to have poor glycemic control [AOR=2.860, 95% CI= (2.947-5.715)] than those who had medication adherence (p-value <0.001). Similarly, patients having dose too low type of DRPs were about twice more likely to have poor glycemic control than others [AOR=2.277, 95% CI= (1.091-4.753)]. Nevertheless, it was found that patients who experienced dose too high type of DRPs were less likely to have poor glycemic control [AOR=0.105, 95% CI= (0.025-0.435)] [**Table 11 bellow].**

Table 11: Predictors of poor Glycemic control among T2DM patients in WSU teaching hospital, Southern Ethiopia, 2015 (N=243)

Predictors	Ave. Glycemic level		COR	AOR	95% C.I.for AOR		p-value
	Poor (%)	Good (%)			Lower	Upper	
Polypharmacy							
Yes	36(15)	12(8.4)	2.758	1.751	0.571	5.370	0.325
No	108(44.5)	87(36)	1	1			
Use of Statins							
Yes	41(17)	19(8)	2.282	1.601	0.652	3.933	0.304
No	103(42)	80(33)	1	1			
Use of antihypertensive							
Yes	58(24)	27(11)	4.005	0.421	0.138	1.281	0.128
No	86(35.4)	72(29.6)	1	1			
Presence of DRPs							
Yes	137(56.4)	65(26.7)	4.065	2.804	1.004	5.230	**0.011***
No	7(3)	33(13.5)	**1**	1			
Dose too low							
Yes	51(21)	14(5.7)	2.250	2.277	1.091	4.753	**0.016***
No	93(38)	85(35)	1	1			
Dose too high							
Yes	5(2)	9(4)	0.316	0.105	0.025	0.435	**0.009***
No	139(57)	90(37)	1	1			
ADR							
Yes	10(4)	1(0.4)	7.150	1.083	0.009	3.762	0.132
No	134(55)	98(40.3)	1	1			
Poor-adherence							
Yes	98(40.3)	29(12)	3.821	2.860	2.947	5.715	**0.000***
No	46(19)	70(29)	1	1			
Presence of comorbidity	93(38.3)	44(18)	1.749	1.109	0.338	3.635	0.865
Yes	51(21)	55(22.6)	1	1			
No							
History of hospitalization	43(17.6)	37(15.2)	0.592	0.901	0.458	1.772	0.762
Yes	101(41.5)	62(25.5)	1	1			
No							
Frequency of doses							
≤ twice	93(38.5)	67(27.5)	1	0.937	0.428	2.051	0.870
≥Three times	51(21)	32(13)	1.671	1			
Age							
≤ 44 years	16(6.5)	10(4)	1				0.231
45-54 years	64(26)	41(17)	2.545	3.264	1.174	9.072	0.717
55-64 years	47(19)	35(14.5)	2.132	2.517	0.905	7.004	0.910
≥65 years	17(7)	13(5)	1.021	1.075	.310	3.726	

COR=Crude Odds Ratio, AOR=Adjusted Odds Ratio, CI=Confidence Interval, *p-value ≤ 0.05, *1-refrence category*

6. Discussion

This facility based cross-sectional study was conducted with the aim of investigating epidemiology and predictors of drug related problems and glycaemic control among type 2 diabetes patients at Wolaita Soddo University teaching hospital, Southern Ethiopia.

The current study showed that 83.1 % of type 2 diabetic patients had at least one DRPs with the mean number of 1.8 ± 0.751DRPs which is relatively similar with a study by Cipolle et al conducted to identify DRPs among T2DM patients in Minnesota (84%)(14) and Sorensen et al in Denmark (81%)(48). But it is lower than a study on T2DM patients by Van Roosendaal et al in Australia that showed an average number of 4.6 $\pm$ 1.7 DRPs (49), by Eichenberger et al in Switzerland which found that all study patients(100%) had at least one DRP with the mean of 7.5 $\pm$ 2.5DRPs(50) and by Ogbonna et al in Nigeria (94%)(59). The discrepancy with the previous studies could be due to use of different references and methods to identify DRPs. Previous studies used PCNE classification of DRPs, and concurrent use of ACEIs and sulfonylureas was considered as potential DRPs in the study by Van Roosendaal et al. However, this combination of drugs was not considered potential DRPs in our study because there is lack of strong evidence of showing clinically significant interaction. Furthermore, Eichenberger et al used inclusion of patients of age above 60 years and intake of at least four prescribed drugs which could possibly contribute to the higher prevalence of DRPs in the study and use of Beer's criteria, older age of study population and inclusion of admitted T2DM patients could be reasons for the difference from the study in Nigeria.

The prevalence of DRPs in this study is also lower than studies conducted among T2DM patients with dyslipidaemia and with hypertension showing 91.8% and 90.5% respectively in Malaysia(21)(22). Its difference could be explained by the difference in DRPs classification tool used, inclusion of patients with comorbidity which could increase the possibility of number of medications and hence DRPs. Apart from that, the discrepancy with other study may be attributed to the differences in the study method and setting, and clinical knowledge of investigator(s) may also affect DRPs assessment.

The most common type of DRPs identified was needs additional drug therapy 137(56.37%). This is in line with a study by Van Roosendaal et al in Australia (49) and Cipolle et al in Minnesota(14). The cause for its high prevalence is absence of statins and antiplatelet for cardiovascular prevention which accounted 49% and 18.9% respectively. This is still in concordance with the finding from Australia which showed that 60.8% and 48.0% of patients were not receiving anti-platelet and statin therapy respectively although they were at increased cardio-vascular risk (49). In contrary to our study, unnecessary drug therapy accounted higher percentage than need additional drug therapy in Nigeria (59). This difference could be due to use of Beer's criteria which identifies potential DRPs in geriatric patients, use of different DRPs classification, and including admitted T2DM patients in the previous study.

The second most prevalent category of DRPs in our study was non-compliance accounting 127(52.3 %). This is in agreement with most previously done studies such as a comparative study in Minnesota and Australia (31), Huri et al study in Malaysia (21) and Ogbonna et al study in Nigeria (59). In contrary to this, a DRPs study by Cipolle on T2DM showed dose too low type of DRPs as the second frequently occurring DRPs rather than non-compliance. The discrepancy could be explained as the previous study used electronic therapeutic record system which is designed to document all types of drug therapies and difference in adherence assessment and in socio-demographics of study patients. The prevalence of non-compliance in this study is also higher than a study among T2DM patients in Bishoftu Hospital which showed that 28 % were non-compliant to their anti-diabetic medication(51). This could be due to difference in health care service of the hospitals and majority of study patients in Bishoftu were having educational level of secondary school and above which is the least in our study and age difference might also affect adherence of patients to their medications. The frequently reported reasons for non-compliance in this study were forgetting (45%) and fear of side effects of drugs (29%) which has agreement with a DRPs study in Australia (49) and Ethiopia(22).

In current study, ineffective drug therapy which accounted 2.20 % and ADR (3.31%) were the least frequent DRPs of all categories. In low prevalence of ineffective drug therapy, it is in line with a study in Minnesota (14) and Australia (49). The reason may be that in our study, there was rigorous evaluation and optimization of some of DRPs identification criteria by panel of experts. In contrary to our finding, ADR was found to be among the frequent types of DRPs in Australia(49). This could be due to considering concurrent use of ACEIs and sulfonylureas a ADR in previous study which is not in our study because of lack of strong evidence showing clinically significant interaction, lack of causality assessment and difference in documentation practice of adverse events and drug allergies in the two countries.

Multiple regression analysis indicated that age, polypharmacy, comorbidity and history of hospitalization independently predicted the occurrence of DRPs in this study. It was found that the likely hood of occurrence of DRPs was increasing as age of the respondents increases. Patients found within age range of 45-54years were about five times more likely to develop DRPs than those below 44years old [AOR=4.851, 95%CI= (1.129-20.853)] whereas the factor increased to nine times for elderly patients (age above 65 years) [AOR=9.079, 95%CI= (2.213-37.241)]. Association of advanced age with DRPs has prone scientific ground as it results in multiple disease conditions requiring multiple medications but from the literatures reviewed, some findings are conflicting. This finding is consistent with a study in Florida (41), in Jordan(20), in Nigeria (59) and a DRPs study in JUSH(25). But a study done among T2DM patients with dyslipidaemia in Malaysia (21) showed no significant association of age with DRPs. The discordance could be due to difference in study patients, and presence of standard geriatric drug guidelines like Beers criteria in the hospital might possibly reduce DRPs in geriatric population in previous study.

It was also found that there was significant association between polypharmacy and occurrence of DRPs. i.e. almost all patients(97.8%) taking $\geq$ five medications per day had DRPs and they were about 3 times more likely to have DRPs than who took less than five drugs per day [AOR=3.311, 95%CI=1.366-30.329)]. This finding is in agreement with myriad of studies on DRPs which showed that patients with multiple drug classes have a complex drug schedule which may contribute to the poor medication adherence problem, potential drug-drug interactions and side-effects of drugs and finally increased risk of DRPs(14,20,21,53,59).

Similarly, presence of comorbidity was also an independent predictor of DRPs in present study (P<0.001) which can be corroborated by previous studies on DRPs that identified comorbid conditions as major predictors of DRPs (14,31,40,59). This might be due to increase in number of medications(polypharmacy), complex drug taking schedule which contributes to high rate of non-compliance, increase in drug-drug interaction ,adverse effects and cardiovascular risk that necessitates need of additional therapy which collectively result in increased likely hood of experiencing DRPs in the study patients.

Another factor that had strong association with occurrence of DRPs in present study was history of hospitalization. We found that patients having history of hospitalization while on treatment were less likely to have DRPs compared to those who had not. We could not get such finding in previously conducted DRPs studies among ambulatory patients with chronic illness but the reason might be partly explained as further investigation and assessment of patient's condition by physicians, increased awareness about medication adherence and change in attitude they got from health professionals at the time of hospitalization could result in lower prevalence of DRPs in this patients.

Among common drug classes identified as causes for overall DRPs ant diabetic medications 82(40.5%) followed by statins 74(36.6%) and antihypertensive (31.6%). This finding agrees with a study in Malaysia (21) and in Australia (49). This could be due to a higher possibility to develop DRPs secondary to the wide range of use of these drugs by the study patients.

Predictors of poor Glycemic control of study patients

In present study,144(59.2%) patients were found to have poor glycemic control which goes in in line with a DRPs study on T2DM by Van Roosendaal et al (49), Khattab et al in Jordan(65.1%) (58) and study of medication adherence among T2DM patients in Ethiopia in JUSH (58%) and in Bishoftu Hospital(56%)(51)(52). But it is lower than a study in Malaysia (76.4%)(21) which could be due to difference in glucose monitoring methods.

More over, it was also found that presence of DRPs was significantly associated with patient's poor glycemic control ($P<0.05$). This is consistent with study in Malaysia(21) which showed that pateints with DRPs had higher HbA1c level than those who did not. Of all categories of DRPs identified, non-compliance, dose too low and dose too high independently predicted poor glycemic control of the study patients. Patients with poor adherence to their medication were found to be 2.8 times more likely to have poor glycemic control [AOR=2.8, 95%CI= (2.947-5.715) (at p-value <0.001). This finding is in agreement with a DRPs study by Van Roosendaal et al in Netherlands (49), Al-Qazaz et al ,Huri et al in Malysia(5)(21) and Kalayou et al study in Ethiopia(28) which showed that potentially non-adherent patients had a significantly higher HbA1c level than patients who adhered to therapy. Additionally, the current study found that patients with dose too low type of DRPs were twice more likely to have poor glycemic control than those who did not have this type of DRPs. But patients with dose too high type of DRPs were less likely to have poor glycemic control than others. It scientifically seems true that patients taking sub-therapeutic dose of a drug may have uncontrolled glycemic level because the dosage is not sufficient to produce the desired goal of therapy. Likewise, high dose may decrease their glycemic level. To date,locally or globally there is lack of study for comparison.

7. Limitations of the study

Even though the study has strengths such as use of DRPs identification criteria which is evaluated and accepted by experts, determining association between different categories of DRPs and glycaemic control and selecting a hospital providing clinical pharmacy service, it is limited by; chance of recall bias in adherence assessment as it was based on respondents self-report, absence of causality assessment and herbal drug use, missing of some data by chart review, absence of HbA1C monitoring for glycaemic level, lack of adequate organ function tests like RFT, LFT and lipid profiles.

8. Conclusion

In conclusion, the current study showed that majority of type 2 diabetic patients included in the study had at least one drug related problem showing optimal medication management in type 2 diabetes remains a major challenge in clinical practice. Need additional drug therapy due to underutilization of statins and antiplatelet for cardiovascular prevention, non-compliance and dose too low were the most common categories of drug related problems identified. Age of respondents, presence of comorbidity, polypharmacy, and history of hospitalization were found to be independent predictors of occurrence of drug related problems in this study. It was also found that of all categories of drug related problems in type 2 diabetes patients, non-compliance, dose too low and dose too high independently predicted poor glycemic control among T2DM patients.

9. Recommendations

Based on the above findings in order to minimize the prevalence and predictors of DRPs as well to improve glycemic control in T2DM patients, we forwarded the following recommendations:-

- MOH and FMHACA should establish a DRPs identification guideline at the national level to provide quality pharmaceutical care service.
- The hospital should provide comprehensive care for T2DM including periodic measurement of BMI, BP, RFT, LFT, and lipid profiles.
- The hospital should also make efforts to increase the medication adherence of the diabetes patients.
- Health care professionals should receive focused training for proper utilization of statins, antiplatelet, metformin and ACEIs in this population.
- Further study should be conducted to investigate other factors affecting management of T2DM patients.

10. References

1. American Diabetes Association. Standards of Medical Care in Diabetes. 2015. p. 14–80.
2. American Diabetes Association. Definition and classification of Diabetes Mellitus. 2010.
3. Centres for Disease Control and Prevention. National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States. 2014.
4. International Diabetes Federation (IDF). Global Guideline for Type 2 Diabetes. 2012.
5. Harith Kh, Sulaiman S, Hassali A. Diabetes knowledge, medication adherence and glycemic control among patients with type 2 diabetes. 2011; 33:1028–35.
6. George L. Bakris M; James R. Treatment of Hypertension in Patients with Diabetes. American Society of Hypertension Position Paper. J Clin Hypertens. 2008; 10(9):119–24.
7. Richardson CR, Wyckoff JA, Funnel MM, Herman WH, Release I, Recent M, et al. Management of Type 2 Diabetes Mellitus. 2014.
8. Redmond B, Caccamo D, Flavin P, Michels R, Myers C, Connor OP, et al. Diagnosis and Management of Type 2 Diabetes Mellitus in Adults. 2014.
9. American Society of Hospital Pharmacists. ASHP Statement on Pharmaceutical Care. Am J Hosp Pharm. 1993;50: 1720–3.
10. Al-arifi M, Abu-hashem H, Al-meziny M, Said R. Emergency department visits and admissions due to drug related problems at Riyadh military hospital (RMH), Saudi Arabia. Saudi Pharm J. King Saud University; 2014;22(1):17–25.
11. Adepu A and. Drug Related Problems : An Over View of Various Classification Systems. Asian J Pharm Clin Res. 2014;7(4):7–10.
12. Khdour MR, Jarab AS, Adas HO, Samaro EZ, Mukattash TL, Hallak HO. Identification of Drug-Related Problems : A Prospective Study in Two General Hospitals. 2012; 2–7.
13. Marley S, Charles D, Hepler L. Opportunities and Responsibilities in Pharmaceutical Care. 1990.
14. Cipolle R, Marley S, Linda M. Co-morbidities and Drug Therapy Problems in Patients with Diabetes. Medicat Manag Syst. 2013.
15. Pereira M, Ana G, Martins P, Cantrill JA. Preventable drug-related morbidity in community pharmacy : development and piloting of a complex intervention. 2012; 699–709.
16. Lester P, Corey A, Helmke M, Jennifer L. Integrating Components of Medication Therapy Management Services into Community Pharmacy Workflow. 2014; 5(2):1–9.

17. Andreazza, Roberta S MS. Causes of drug-related problems in the emergency room of a hospital in southern Brazil. Gac Sanit. 2011 Jan; 25(6):501–6.
18. Salvesen B. Drug-related Problems in Hospitalised Patients: A Prospective Study in General Hospitals. 2004;651–8.
19. Samoy L, Peter J WK. Drug-Related Hospitalizations in a Tertiary Care Internal Medicine Service of a Canadian Hospital : A Prospective Study. 2006.
20. Aburuz SM, Bulatova NR. Comprehensive assessment of treatment related problems in hospitalized medicine patients in Jordan. 2011; 33: 501–11.
21. Huri HZ, Ling LC.Drug-related problems in type 2 diabetes mellitus patients with dyslipidaemias. *BMC Public Health 2013*; 13:1192.
22. Huri HZ, Wee HF. Drug related problems in type 2 diabetes patients with hypertension : a cross-sectional retrospective study. BMC Endocrine Disorders; 2013; 13(1):1.
23. Emslie-smith A, Dowall JON, Morris A. The problem of polypharmacy in type 2 diabetes. 44(0):54–6.
24. Niquille A, Bugnon O. Relationship between drug-related problems and health outcomes : a cross-sectional study among cardiovascular patients. 2010;512–9.
25. Tigabu BM, Daba D, Habte B. Drug-related problems among medical ward patients in Jimma University specialized hospital, Southwest Ethiopia. J Res Pharm Pract. 2014 Jan;3(1):1–5.
26. Tegegne GT, Yimam B, Yesuf EA, Gelaw K. Drug Therapy Problem among Patients with Cardiovascular Diseases in Felege. Int J Pharm Teach Pract. 2014;5(3):989–96.
27. Kanavos P, Aardweg S Van Den. Diabetes expenditure, burden of disease and management in 5 EU countries. 2012 ;(January).
28. Kalayou K, Asrat D AB et al; Diabetes Self Care Practices and Associated factors among Type 2 Diabetic Patients in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia- A Cross Sectional Study. Int J Pharm Sci Res. 2012;3(11):4461–71.
29. International Diabetes Federation ; Diabetes Atlas Sixth edition, 2013.
30. Levitt NS. Diabetes in Africa : epidemiology, management and healthcare challenges. 2008; 1376–83.
31. Deepa G, Andrew S, Linda M et al. Drug therapy problems found in ambulatory patient populations in Minnesota and South Australia. 2007; 647–54.

32. Satish B, Kumar D. Assessment of Clinical Pharmacist Intervention in Tertiary Care Teaching Hospital. Asian J Pharm Clin Res. 2013;6:2–5.
33. Koh Y, Li SC. Therapy related hospital admission in patients on polypharmacy in Singapore : a pilot study. 2003; 25(4):135–7.
34. Awadhi SS Al, Clifford RM, Sunderland VB, Hackett LRP, Farah H, Do contraindications to metformin therapy deprives type 2 diabetic patients of its benefits ? 2008; 81–4.
35. Pongwecharak J, Tengmeesri N. Prescribing metformin in type 2 diabetes with a contraindication : prevalence and outcome. 2009; 481–6.
36. Kheir N, Awaisu A, Sharfi A. Drug-related problems identified by pharmacists conducting medication use reviews at a primary health centre in Qatar. 2014; 702–6.
37. Stig L, Ellen H, Sorensen W. Drug-related problems in patients with angina pectoris, type 2 diabetes and asthma – interviewing patients at home. 2006; 239–47.
38. Lange D, Egberts T. Identification of potential drug-related problems in the elderly : the role of the community pharmacist. 2006;33–8.
39. Gerd A, Christian G, Vidar B, Cecilie H, Horn AM. Evaluating categorisation and clinical relevance of drug-related problems in medication reviews. Pharm world Sci PWS Sci PWS. 2010; 32:394–403.
40. Ahmad A, Mast MR, Hugtenburg JG. Identification of drug-related problems of elderly patients discharged from hospital. 2014; 155–65.
41. Kevin T. Bain, Douglas J. Weschules, and Patti Tillotson. Prevalence and Predictors of Medication-related Problems. Medicare Patient Management. 2006.
42. WSU. Wolaita Soddo University Teaching Hospital Annual report; 2014.
43. Cipolle J, Strand M. Pharmaceutical care practices: The clinician's Guide, 2nd ed. 2004.
44. FMHACA. Food, Medicine and Healthcare Administration and Control Authority of Ethiopia, Standard Treatment Guidelines for General Hospital Diseases. 2014.
45. British National Formulary (BNF). *BMJ Group and RPS Publishing;* 2009.
46. Anderson PO. Handbook of Clinical Drug Data. 10th ed. McGraw-Hill Medical; 2002.
47. Baxter K. Stockley's Drug Interactions.2009.

48. Haugbolle LS, Sorensen EW. Drug-related problems in patients with angina pectoris, type 2 diabetes and asthma--interviewing patients at home. Pharm World Sci. 2006; 28(4):239–47.
49. Van Roozendaal BW, Krass I; Development of an evidence-based checklist for the detection of drug related problems in type 2 diabetes. Pharm World Sci. 2009 Oct;31(5):580–95.
50. Eichenberger PM, Haschke M, Lampert ML, Hershberger KE. Drug-related problems in diabetes and transplant patients : an observational study. Int J Clin Pharm. 2011.
51. Asres T, Gobezie T, Belayneh K, Amsalu D MA. Non Adherence and Its Contributing Factors Among Ambulatory Type two Diabetic Patients in Bishoftu General Hospital, South East, Ethiopia. 2014;3(August):13–27.
52. Wabe NT, Angamo MT, Hussein S. Medication adherence in diabetes mellitus and self-management practices among type-2 diabetics in Ethiopia. 2011;3(9):5–10.
53. Hajjar ER, Cafiero AC, Hanlon JT. Polypharmacy in elderly patients. Am J Geriatr Pharmacother. 2007 Dec;5(4):345–51.
54. Hussein M, Lenjisa JL, Woldu MA, Tegegne GT, Umeta GT, Dins H. Clinical Pharmacology Assessment of Drug Related Problems Among Hypertensive Patients on Follow up in Adama Hospital Medical College , East Ethiopia. 2014; 3(2):2–7.
55. Vogt-Ferrier N. Older patients, multiple comorbidities, polymedication… should we treat everything? Eur Geriatr Med. Elsevier; 2011 Feb 2;2(1):48–51.
56. Nguyen JK, Fouts MM, Kotabe SE, Lo E. Polypharmacy as a risk factor for adverse drug reactions in geriatric nursing home residents. Am J Geriatr Pharmacother. 2006 Mar;4(1):36–41.
57. Ernst ME, Iyer SS, Doucette WR. Drug-Related Problems and Quality of Life in Arthritis and Low Back Pain Sufferers. Value Heal. International Society for Pharmacoeconomics and Outcomes Research (ISPOR); 2003;6(1):51–8.
58. Khattab M, Khader YS, Al-khawaldeh A, Ajlouni K. Factors associated with poor glycemic control among patients with Type 2 diabetes. J Diabetes Complications. Elsevier Inc.; 2010; 24(2):84–9.
59. Ogbonna B. Ezenduka C. Opara C. Ahara L. Drug Therapy Problems in Patients with Type-2 Diabetes in a Tertiary Hospital in Nigeria. *International journal of innovative research & development.* 2014; 3(1); 494-502.

Annex I: English Questionnaire

A questionnaire to assess Drug related problems and Glycemic control among type 2 diabetic patients in WSU Teaching Hospital, Southern Ethiopia, 2015

Informed Consent

Greeting: Good morning/Good afternoon .Thank you for taking the time to provide answers to this questionnaire. My name is _____. I am here today as a data collector of a study conducted by college of Public health and medical Sciences, Jimma University. We are asking some questions on your health conditions and medication related issues. Whatever we ask you and get as a response will be confidential. Please remember there is no right and wrong answers to the questions only correct information is needed .Your name will not be written on this paper. Information about your family and your compound will be told to nobody. It will be used only for the study purpose. So would you participate in our study?

I, the, undersigned, with full understanding of the study objective I agree to give the informed consent voluntarily to the researcher.

Study participant: Signature_____ Date_____

Data collector: Name _____Signature _____ Date _____

Supervisor: Name_____ signature _____Date_____

Notice:-

- Start the interview if the patient agrees to participate.
- It does not include age <18 years, pregnant, critically ill and those with psychiatric problems and if the last three FBS measure is absent.

Section one: General information

Serial no	***Question/variables***	***Response***	***When to skip***
Part 1: Socio demographic characteristics.			
1.	Card number of the patient	_____	
2.	Sex of respondent	1.Male____ 2.Female___	
3.	Age of the respondent	_____	
4.	Marital status	1. Married 3. single 2. Separated /divorced 4. widowed (er)	
5.	Religion	1. Protestant 2.Orthodox 3. Muslim 4. Catholic 5.Other specify_____	
6.	Ethnicity	1. Wolaita 2.Gurage 3.Gamo 4.Gofa 5.Amhara 6.others____	
7.	Educational status	_____	
8.	Occupation	_____	
9.	Monthly income	_____in Birr	
10.	Do you use tobacco?	A. Yes B. No	
11.	Do you drink alcohol?	A. Yes B. No	
12.	Do you chew chat?	A. Yes B. No	

Part 2: Disease conditions & medication related variables			
1.	Have you ever been admitted while on DM treatment?	A. Yes B. No	
2.	Do you have a family with diabetes?	A. Yes B. No	
3.	How many medications do you take per day?	_____	
4.	What is the maximum numbers of doses taken per day?	1. Once 3. Three times 2. Twice 4. > three times 5. If other, specify_____	
Please refer to the patient's chart for the following questions			
5.	Duration of the diabetes in year	_____year	
6.	Comorbidity	_____	
7.	Number of comorbidities	1. One 3. Two 2. Three 4. More than three 5. If other, specify_____	

Part 3;- Adherence(***Morisky 8-Item Medication Adherence Questionnaire)***

Please write ''1'' if the response is ''yes'' and write ''0'' if the response is ''No'' (Except for Q-5) Scores: 0- 2 = Good adherence 3-8 = poor adherence		*(Yes=1/ No=0)*
1.	Do you sometimes forget to take your medicine?	
2.	People sometimes miss taking their medicines for reasons other than forgetting. Thinking over the past 2 weeks, were there any days when you did not take your medicine?	
3.	Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it?	
4.	When you leave home, do you sometimes forget to bring along your medicine?	
5.	Did you take all your medicines yesterday? (Yes =0, No=1)	
6.	When you feel like your symptoms are under control, do you sometimes stop taking your medicine?	
7.	Do you ever feel hassled about sticking to your treatment plan?	
8.	How often do you have difficulty remembering to take all your medicine? ___A. Never ___ B. Once in a while ___C. Sometimes ___ D. Usually ___E. All the time	A = 0; B-E = 1
Total score		

9. If the patient scores**≥3** for the Morisky Scale above, what could be the possible causes for non-compliance?
    A. Does not understand the instruction.
    B. Prefer not to take the medication.
    C. The drug product is too expensive for the patient.
    D. Forgets to take medications
    E. Cannot swallow or self-administer the drug product appropriately.
    F. The drug product is not available for the patient.

10. If the patient is non-adherent, which drugs caused noncompliance and what are the causes?

Indication	Drug regimen with the problem	Cause (Write Letter)

Section 2: Data extraction formats

I. Glycaemic control

1. Patient's glycemic level in last three visits

Date				
FBS				

2. Antidiabetic medications types and daily dose given

Medication	dose and frequency
Glibenclamide	
Metformin	
Insulin	

II. BP control

1. BP of the patient's for the last three visits

Date				
BP				

2. *Antihypertensive medications* and daily dose given

Medications	dose and frequency

III. Lipid control

1. Patients lipid panel

Total cholesterol (mg/dl) _____ LDL cholesterol (mg/dl) _____

HDL cholesterol (mg/dl)_____ Triglycerides (mg/dl)_____

2. Is the patient using any lipid-lowering medications? Yes_____ No _____

3. If yes to above question, which lipid lowering medication?

Medications	dose and frequency
Lovastatin	
Simvastatin	
Atorvastatin	

IV. Platelet control

1. Is the patient using any antiplatelet medication? Yes _____No_____
2. If yes, what is the antiplatelet used and its daily dose?

Antiplatelet drug	dose and frequency
Aspirin	
Clopidogrel	

V. Other medication information

1. Concurrently used drugs other than antihypertensive, statins, and antiplatelet

Drug name	Dose	Frequency	Duration	Medical condition

2. *Current PRN Drug Therapy*

Drug Name/Dose/Strength/Route	Schedule	Medical condition

3. Organ function tests

4.1. Renal function tests: CrCl (ml/min) _____, BUN (mg/dl) _____

4.2. Liver function tests: ALT (mg/dl) _____ , AST (mg/dl) _____

4. History of drug allergies if available.

Date	Drug therapy	Past allergies

Annex II: Amharic Questionnaire

<u>ለስኳር ህመምተኞች ህክሚና ከሚሰጡ መዲኃኒቶቸ ጋር ተያይዞ የሚመጡ ችግሮቸን ለማጥናት የተዘጋጀ መጠይቅ፣</u>

<u>ቃለመጠይቁን ከማድረግ በፊት የተሳታፊዎች ፈቃደኝነት መጠየቂያ ቅጽ</u>

ጤና ይስጥልኝ ፣እኔ ---------- እባላለሁ፡፡ እዚህ የመጣሁት ከጅማ ዩንቨሪስቲ ነው፡፡የዚህ ጥናት ዋና ዓላማ በሶዶ ሆስፒታል ለስኳር ህመምተች ህክሚና ከሚሰጡ መዲኃኒቶቸ ጋር ተያይዞ የሚመቱ ችግሮቸን ለማጥናት የተዘጋጀ ነው፡፡በመሆኑም ይህንን መረጃ ለማግኘት ቃለመጠይቅ በማካሄድ ላይ እገኛለሁ፡፡

ይህ ጥናት ሲጠናቀቅ የስኳር ህመምተኞችን ጤና ለማሻሻል በሚደረገው ጥረት ከፍተኛ እገዛ ይኖረዋል፡፡ በጥናቱ የማሳትፍዎ የእርስዎን ሙሉ ፈቃዳኝነት ሳገኝ ብቻ ነው፡፡ ከእርስዎ የማገኘውን ማንኛውንም መልስ በሚስጥር እጠብቃለሁ፡፡ ስለ ሙሉ ፈቃደኝነትዎና ስለሚያደርጉት ድጋፍ ሁሉ ከፍተኛ ምስጋና እያቀረብኩኝ ፤ከሁሉም በላይ ይህ ጥናት በእርስዎ ላይ ምንም ዓይነት ጉዳት እንደማያስከትል ማረጋገጥ እወዳለሁ፡፡በውይይቱም ጊዜ የማይስማማዎ ነገር ካለ የማቋረጥ መብትዎ በማንኛውም ሰዓት የተጠበቀ ነው፡፡

የጥናቱ ዓላማናተ ግባር ከተብራራልኝ በኃላጥያቄውን ለማስተናገድ ተጠይቄ፡-

ሀ. ተስማምቻለሁ ለ. አልተስማማሁም

በጥናቱ ለመሳተፍ መስማማቴን በፊርማዬ አረጋግጣለሁ፡ ፊርማ----------

የጠያቂው ስም----------ፊርማ ----------

የአረጋገጠው ሱፐቫይዘር ስም ----------ፊርማ ------ቀን ----------

መጠይቅ አቅራቢዎች በተጨማሪ ሊከተሉት የሚገባ መመሪያ፣

1. ውይይት ሊካሄድ የሚገባው ተጠያቂዎች መጠይቁን ለማካሄድ ከተስማሙ ብቻ ይሆናል፡፡
2. መጠይቁ የሚሞላው በእስክርቢቶ ብቻ ይሆናል
3. በሚሰጠው መልስ መሰረት በተገቢው መልኩ የምርጫ መልሱን ማክበብ
4. መጠይቁከ18 ዓመት እድሜ በታች፣ እረጉዝ ሴቶችን ፤በጠና የታመሙትን ና የስነ ዓእምሮ ችግር ያለባቸውን አይበለከታቸውም፡፡

የሚከተሉት ጥያቄዎች የስነ–ህዝብ ገጽታና ማህበራዊ ሁኔታ፤ ከህመምተኛዉ ጋር የተያያዙ ሁኔታዎችን፤ከህመሙ እና ከመድሀኒቶቹ ጋር የተያያዙ ሁኔታዎችን ለማጥናት የተዘጋጁ ናቸዉ።። ተጠያቂዉን በመጠየቅ፤ አማራጭ መልሶችን በመክበብ ወይም ባዶ ቦታዉን በመሙላት መልሳቸዉ።።

ተ.ቁ	ጥያቄዎች	አማራጭ መልሶች
	ሀ. የማህበራዊ ና የሥነ -ሕዝብ ገፅታዎች	
1.	የካርድ ቁጥር	_____
2.	ፆታ	1. ወንድ 2. ሴት
3.	ዕድሜ	----------ዓመት
4.	የጋባቻ ሁኔታ	1. ያገባ 2. የፈታ/የፈታች 3. ያላገባ 4. ባል/ምስት የሞተበት/ባት
5.	ሀይማኖትዎ ምንድ ነው?	1.ፕሮተስታንት 2.ኦርቶዶክስ 3. ሙስሊም 4. ካቶልክ 5.ሌላ --
6.	ብሄረሰብዎ ምንድ ነው?	1.ወላይታ 2.ጉራጌ 3.ጋሞ 4. ጎፋ 5. አማራ 6. ሌላ-
7.	የትምህርት ደረጀደዎ?	_____
8.	የሥራ ሁኔታ	_____
9.	የወር ገቢዎ በብር ስንት ነው	---------- ብር
10.	ስጋራ ያጨሳሉ ?	1. አጨሳለሁ 2. አላጨስም
11.	አልኮል ይጠጣሉ?	1. እጠጣለሁ 2. አልጠጣም
12.	ጫት ይቅማሉ ?	1. እቅማለሁ 2. አልቅምም
	ለ. ከህመሙ ና ከመድኃንትጋር የተያያዙ መረጃዎች	
13.	የስኳር በሽታ ያለበት የቅርብ ዘመድ አለዎት ?	1. አለ 2. የለም
14.	በቀን የምወስዱት የመድኃንት ብዛት ስንት ነዉ ?	_____
15.	በቀን ምን ያህል ጊዜነዉ መድኃንት የሚወስዱት ?	ነአንድ 2. ሁለት 3. ሶስትና ከዚያ በላይ 4. ሌላ ይጻፉ---------
16.	የስኳር በሽታ ህክምና ከጀመሩ ሆስፒታል ተኝተዉ ያዉቃሉ?	1. አዎ 2. አላዉቅም
	እባኮን ቀጥለው የተዘረዘሩትን ጥያቄዎች የበሽተኛውን ካርድ በመመልከት ይሙሉ	
17.	ለስኳር በሽታ ህኪምና ከጀመሩ ስንት ዓመት ነዉ ?	----------ዓመት
18.	ከስኳር በሽታ ዉጭ ሌላ በሽታ አለብዎት ወይ ?	----------
19.	ከስኳር በሽታ ዉጭ ሌላ በሽታ ካለብዎት ብዛቱ ስንትነው ?	----------

ሐ. ከመዲኃኒት አወሳሰድ ጋር የተያያዙ ጉዳዮች (MMAS)		
ከዚህ ቀጥለው ለተዘረዘሩ ጥያቄዎች መልሱ "አዎን" ከሆኔ "1' አይደለም ከሆኔ "0' ይጻፉ (ከ5ኛ ጥያቄ ውጭ) ፡ ጠቅላላ ድምሩ ፤ ከ"0-2" ከሆኔ "ጥሩ ነው" ፤ "3-8" ከሆኔ "ዝቅተኛ" ነው።።		*አዎን(1) አይደለም(0)*
1.	አንዳንዴ መዲሓኒትን መውሰድ ረስተው ያውቃሉ?	
2.	ባለፉት ሁለት ሳሚንታት መዲሃኒት መውሰድ የረሱበትን ቀን ያስታወሳሉ ?	
3.	ህመሙን ያባብሳል ብለው ሀኪመዎን ሳያማክሩ መድሃኒትን መውሰድ አቁመው የውቃሉ ?	
4.	መንገድ ወይም ሥራ ሲወጡ መድሀኒት ሳይዙ ሄደው ያውቃሉ ?	
5.	በትናንትና ዕለት ሁሉንም መድሀኒት ወስደዋል ? *("አዎን" ፡ "0" "አይደለም" ፡"1")*	
6.	የህመም ስመት ሲቀንስ መድሀንት መውሰድ አቁመው ያውቃሉ ?	
7.	በርግጥ መዲሀኒትን በየቀኑ መውሰድ ለአንዳንድ ሰዎች አስቸጋር ሊሆን ይችላል።። እንዲያው ኤርሶ የመዲሀኒት መውሰጃ ሰዓትን ማስታወስ አቅቶት ተቸግረው ያውቃሉ ?	
8.	መቼ መቼ ነው የሁሉንም መዲሀኒቶች መወሰጃ ሰዓት ለማታወስ የሚቸገሩት? (ሀ (0)፤ለ-መ(1)) ሀ. በፍጹም ለ. አንዳንዴ ሐ. በአብዛኛው መ. ዘወትር	
ጠቅላላ ድምር		

9. የመዲሀኒት አወሳሰዱ ዝቅተኛ ከሆኔ ፤ ምክንያቱ ምንድ ነው ?

ሀ. የመድሀኒት መረጃ አሰጣጥ ግልጽ አይደለም

ለ. አለመውሰድን እመርጣለሁ

ሐ. የመድሃኒቱ ዋጋ በጣም ውድ ነው

መ. መድሀኒቱን መውሰድ እረሳለሁ

ሠ. መዋጥ አልችልም ወይም ብቻዬን መውሰድ አልችልም

ረ. መድሃኒቱ ሆስፒታል ውስጥ አይገኝም

ሸ. ሌላ ምክንያት ካለዎት ይጥቀሱ----------

የመድሃኒቱ ሥም	የተሰጠበት በሽታ	ለአወሳሰዱ ችግር የሆኑ ነገሮች (ከላይ የተመረጠውን ፊደል የጻፉ)

Section three: Assessment of DRPs of the patient

1. Is there a **need for additional** drug therapy? Yes___ No_____
2. If yes for no. 1, what is the reason for additional drug therapy need?
   a) A medical condition that requires initiation of drug therapy.
   b) Preventive drug therapy required to reduce the risk of developing a new condition.
   c) To attain synergistic effect or additive effect
   d) Others (Specify) _____
3. If 'Yes' for no. 1, please list those medical problems needing additional medication

Date	Indication	Drug regimen with the problem	Cause(Write letter)

4. Is there any **unnecessary drug** therapy for the patient? a) Yes b) No
5. If Yes for no. 4, what are the reasons for unnecessary drug therapy?
   a) No valid medical indication for the drug therapy at this time
   b) Multiple drug products are used for a condition that needs single drug therapy.
   c) The medical condition is more appropriately treated with non-drug therapy.
   d) Drug therapy is used to treat an avoidable ADR associated with a drug
   e) Drug abuse, alcohol use, or smoking is causing the problem
   f) Only Life style can be used to control the condition
6. If yes, for no.4 , list unnecessarily prescribed medication and the causes

Date	Indication	Drug regimen with the problem	Cause(Write letter)

7. Is there any **ineffective drug** therapy used? a) Yes b) No

8. If yes for no.7, what was the cause?

   a) The drug is not the most effective for the medical problem
   b) The medical condition is refractory to the drug product.
   c) The dosage form of the drug product is inappropriate
   d) Use of drugs reducing effectiveness of the medications
   e) Others (Specify) _____

9. If yes for no.7, List the ineffective medications used ,

Date	Indication	Drug regimen with the problem	Cause(Write letter)

10. Is there any medication with **too low dosage**? a) Yes b) No

11. If 'Yes' for no. 10, what is the cause for dosage to be too low?

   a) The dose is too low to produce the desired response
   b) The dosing is too infrequent to produce the desired response
   c) There is a drug interaction which decreases the concentration of drug
   d) The duration of drug therapy is short to produce the desired response
   e) Others (Specify) _____

12. If 'Yes' for 10, please list those with dose too low with their causes

Date	Indication	Drug regimen with the problem	Cause (Write letter)

13. Is there any medication with **too high dosage**? a) Yes b) No

14. If Yes for no. 13, what is the cause for dosage to be too high?

a) The dose given is too high
b) There is a drug interaction which results in a toxic reaction to the drug product
c) The dosing frequency is too short
d) The duration of drug therapy is long for a given condition
e) The dose of the drug was administered too rapidly
f) Adjustment for renal impairment was not done

15. If 'Yes' for 13, please list those with dose too high with their causes

Date	Indication	Drug regimen with the problem	Cause(Write letter)

16. Is there any adverse drug reaction? A. yes B. no

17. If yes, what was the cause for the ADR?

A. A safer drug product is required due to risk factors.
B. A drug interaction causes an undesirable reaction that is not dose-related
C. The drug product causes an undesirable reaction that is not dose-related.
D. Others _____

Annex III: Categories and common causes of drug related problems

DRPs	**Common causes of drug Related problem**
Unnecessary drug therapy	There is no valid medical indication for the drug therapy at this time. Multiple drug products are being used for a condition that requires single drug therapy. The medical condition is more appropriately treated with nondrug therapy. Drug therapy is being taken to treat an avoidable adverse reaction associated with another medication.
Need for additional drug therapy	A medical condition requires the initiation of drug therapy. Preventive drug therapy is required to reduce the risk of developing a new condition. A medical condition requires additional pharmacotherapy to attain synergism
Ineffective drug	The drug is not the most effective for the medical problem. The medical condition is refractory to the drug product. The dosage form of the drug product is inappropriate. Use of drugs reducing effectiveness of the medications
Dosage too low	The dose is too low to produce the desired response. The dosage interval is too infrequent to produce the desired response. A drug interaction reduces the amount of active drug available. The duration of drug therapy is too short to produce the desired response.
Adverse drug reaction	The drug product causes an undesirable reaction that is dose-related. A safer drug product is required due to risk factors. A drug interaction causes an undesirable reaction that is not dose-related. The dosage regimen was administered or changed too rapidly. The drug product causes an allergic reaction. The drug product is contraindicated due to risk factors.
Dosage too high	Dose is too high. The dosing frequency is too short. The duration of drug therapy is too long. A drug interaction occurs resulting in a toxic reaction to the drug product. The dose of the drug was administered too rapidly.
Noncompliance	The patient does not understand the instructions. The patient prefers not to take the medication. The patient forgets to take the medication. The drug product is too expensive for the patient. The patient cannot swallow or self-administer the drug product appropriately. The drug product is not available for the patient.

Annex IV: DRPs identification flow sheet

Part 1:Glycaemic control			
101	What is the patient's current glycaemic control?	1. FBS ≥130mg/dl → poor 2. FBS 70-130mg/dl → good	
102	Is the patient using any of the following drugs?	1. Antipsychotics 2. Beta -2 agonists 3. Phenytoin 4. Glucocorticoids 5. COC	(hyperglycaemic drugs)
103	Is the patient taking a sulphonylurea (**Glibenclamide**)?	1. Yes 2. No	**If NO, go to Q-109**
104	If yes to above Q, assess for adverse effects of the drug;	Hypoglycaemia	
105	Does the patient have any one of the following?	1. renal impairment 2. hepatic impairment 3. Age above 65 years	(risk of hypoglycaemia)
106	Is the daily dose within the recommended range?	1. Yes 2. No Glibenclamide: 2.5 – 20 mg in 1 – 2 dose	If No, needs dose adjustment
107	Is the patient also taking any of the following drugs?	1. Rifamycins → ↓SU metabolism 2. High dose aspirin → ↑hypoglycaemia 3. Cotrimoxazole	**Glucose monitoring and Dose adjustment**
108	Is the patient taking **metformin**?	1. Yes 2. No	**If no, go to Q-112**
109	Check whether the patient has any of the following	1. CHF (class III/IV) 2. moderate to severe renal impairment 3. hepatic impairment 4. over 85 years of age	(C/I=risk of lactic acidosis)
110	Is the daily dose within the recommended range? (500 – 2500 mg in 1 – 3 doses)	1. Yes 2. No	If no, consider dose adjustment
111	Is the patient using **insulin**?	1. Yes 2. No	**If no , go to part 2 -**
112	If yes assess for adverse effects;	1. hypoglycaemia	
113	Check if the patient	1. Has renal impairment 2. Has hepatic impairment	Risk of hypoglycaemia
114	Is the patient also using the following drugs with insulin?	High dose aspirin	Risk of hypoglycaemia

Part 2 : Blood pressure control			
201	Current BP is:	1. BP≤140/90mmHg → (good) 2. BP>140/90mmHg → (poor)	
202	Is the patient using one or more antihypertensive?	1. Yes 2. No	**If no; go to Part 3**
203	Is the patient using any one of the following drugs?	1. NSAIDs 2. Corticosteroids 3. COC 4. Oral decongestants 5. Cyclosporine	May increase BP
204	Is the patient using thiazides diuretics?	1. Yes 2. No	**If no, go to Q-207**
205	Is the patient suffering from Severe renal impairment?	1. yes 2. no	(CI/ineffective)
206	Is the daily dose within the recommended range?	1. Yes 2. No HCTZ: 12.5 – 25 mg in 1 dose	(adjust dose / frequency)
207	Is the patient using **BB**?	1. Yes 2. No	**If no, go to Q-213**
208	If yes assess for adverse effects;	Hypotension	
209	Is the patient suffering from;	1. Bradycardia(HR <55) 2. Severe asthmatic disease	C/I
210	Which β-blocker is the patient using?	1. Atenolol 2. Metoprolol 3. Carvedilol 4. Propranolol	Non-selective β-B (can mask the symptoms of hypoglycaemia to a greater extent than selective ones: recommend atenolol or metoprolol)
211	Is the daily dose within the recommended range?	1. Yes 2. No Atenolol: 25 – 100 mg in 1 dose Carvedilol: 12.5 – 50 mg in 1 dose Metoprolol: 50 – 200 mg in 1 – 2 doses Propranolol: 40 – 320 mg in 2 – 3 doses	If not, Contact prescriber to adjust dose / frequency
212	Is the patient also using;	1. Verapamil 2. Diltiazem } additive effect 3. Rifamycins…decreased effects of BB	
213	Is the patient using **ACEIs**?	1. Yes 2. No	**If no, go to Q-217**
214	Is the patient suffering from renal failure?	1. Yes 2. No	
215	Is the daily dose within the recommended range?	1. Yes 2. No Captopril: 25 – 100 mg in 2 doses Enalapril: 5 – 40 mg in 1 – 2 doses Lisinopril: 5 – 40 mg in 1 dose	

216	Is the patient also using:	1. Potassium sparing diuretics 2. Potassium supplements 3. ARBs 4. Lithium …..Li toxicity	Risk of hyperkalaemia
217	Is the patient using **CCB**?	1. Yes 2. No	**If no go to part 3**
218	Which calcium channel blocker is the patient using?	1. Amlodipine… 2. Nifedipine 3. Diltiazem 4. Verapamil (less Antihypertensive)	
219	Is the patient also using:-	1. Rifamycins 2. Phenytoin 3. Carbamazepine 4. Norfloxacin 5. Imidazoles (e.g. fluconazole)	(effects of CCB might be decreased) (effects of CCB might be increased)
220	Is the patient suffering from:	1. NYHA class I-IV HF 2. Brady cardia	(Diltiazem and verapamil are CI)
221	Is the daily dose of CCB is within the recommended range?	1. Amlodipine: 2.5 – 10 mg in 1 dose 2. Nifedipine: 20 – 80 mg in 2 doses (CR): 20 – 120 mg in 1 dose 3. Diltiazem: 180 – 360 mg in 1 dose 4. Verapamil: 120 – 480 mg in 1 dose	
222	Is the patient using alpha selective blockers?	1. Yes 2. No	(Not the preferred agent in the HTN management of type 2 diabetes)
Part 3: Lipid control			
301	What's the patient's lipid profile?	1. Total cholesterol > 200mg/dl 2. LDL cholesterol >160mg/dl 3. HDL cholesterol < 45mg/dl 4. Triglycerides > 160mg/dl	(A dose change or other lipid-lowering agent might be needed)
302	Does the patient have any one of the following diseases?	1. Hypothyroidism 2. Obstructive liver disease 3. Nephrotic syndrome	(might be secondary causes of dyslipidaemia and ***need to be treated***)
302	Is the patient using **statin**?	1. Yes 2. No **If no go to part 4**	(Nearly all patients with type 2 diabetes should be using lipid-lowering medication(s)
303	Is the patient suffering from hepatic impairment?	1. Yes 2. No	(Increased risk of hepatotoxicity)
304	Is the daily dose within the recommended Range?	1. Atorvastatin:10 – 80 mg in 1 dose 2. Simvastatin: 10 – 80 mg in 1 dose(in age > 75 years max 40mg) Lovastatin : 10 – 80 mg in 1 or 2 doses	
305	Which statin is the patient using?	1. Atorvastatin 2. Simvastatin	(Metabolized through CYP3A4)

306	Is the patient also using:	1. Imidazoled (fluconazole) 2. Macrolides (e.g. erythromycin) 3. Protease inhibitors 4. Rifamycins 5. Carbamazepine	(higher risk of adverse effects) (levels may be decreased)
307	Is the patient also using Warfarin?	1. Yes 2. No	(risk of bleeding)
Part 4 ; Platelet control			
401	Is the patient using any anti-platelet Medications?	1. Yes 2. No	
403	Is the patient using low- dose aspirin (< 150 mg)?	1. Yes 2. No	
404	Is the patient suffering from any of the following?	1. PUD 2. Allergy to aspirin or NSAID 3. Bleeding disorder 4. Sever renal impairment 5. Hepatic impairment	ASA is CI Increased risk of bleeding
406	Is the daily dose within the recommended range? (75 – 150 mg in 1 dose)	1. Yes 2. No	
407	Is the patient also using	1. Clopidogrel…….(↑bleeding) 2. Other NSAIDs 3. Corticosteroid	***(increased risk of GIT irritation)***
408	Is the patient using clopidogrel?	1. Yes 2. No	
409	Is the patient suffering from:	1. Active bleeding → Contraindicated 2. Hepatic impairment → Risk of bleeding	
410	Is the daily dose within the recommended range? (75 mg in 1 dose)	1. Yes 2. No	

Declaration

This is to certify that the thesis prepared by **Hailu Chare**, entitled: "***Drug Related Problems and Glycemic control among Adult Type2 Diabetes Patients at Wolaita Soddo University Teaching Hospital, Southern Ethiopia***." for the preparation of senior paper in partial fulfilment of the requirements for the degree of Master of Science in Clinical Pharmacy.

I declare that this research thesis is original work and all sources of material used for this thesis and peoples involved are fully acknowledged.

Name: _____

Signature_____ Date _____

Approved by:

1st Advisors' Name:_____

Signature_____ Date_____

2nd Advisor's Name:_____

Signature _____Date_____