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RESEARCH PAPER

Epidemiology and Predictors of Drug Related Problems among Ambulatory Type 2 Diabetes Mellitus Patients at Jimma University Specialized Hospital, Southwest Ethiopia

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ABSTRACT

The optimal use of medications plays a key role in achieving treatment targets for glucose, blood pressure and lipids in diabetic patients. Efficacy of a medication regimen, however, may be limited by drug related problems and can negatively influence diabetes control. A prospective cross-sectional study was conducted among ambulatory type 2 diabetic patients at Jimma university specialized hospital. Data were entered into and analyzed using SPSS for windows version 20. Among 309 included in the study, 61.5% males. Nighty percent of study participants (n = 279) suffered at least one drug related problem. A total of 632 drug related problems were identified and the mean number of drug related problems per patient was 2.00 ± 1.32. Adverse drug reaction [AOR= 2.191, 95% CI= 1.176, 4.082], noncompliance [OR=2.788, 95% CI: 1.588, 4.896], type of antidiabetic medications [AOR=3.821, 95% CI: 1.236, 11.815], educational status [AOR= 3.994, 95% CI= 1.260, 12.659] and occupation [AOR= 2.644, 95% CI: 1.230, 5.685] were independent predictors of poor glycemic control. The prevalence of drug-related problems was high in this study. Factors associated with drug related problems were polypharmacy and comorbidities.

Key Words: Type 2 Diabetes mellitus, drug related problem, Epidemiology, Ethiopia.

INTRODUCTION

Pharmaceutical care is the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life. Evidence suggests that pharmaceutical care produces improvements in glycemic control, lipid profile, and economic outcomes as well as on humanistic outcomes such as health-related quality of life. Drug related problem (DRP) is a term describing an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes. There are several classifications for drug related problem. According to Cipolle and his colleagues, DRPs are classified into seven categories. These include unnecessary drug therapy, need for additional drug therapy,

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ineffective drug, dosage too low, dosage too high, adverse drug reaction and noncompliance [1,2].

Type 2 diabetes is a chronic metabolic disorder characterized by both defects in insulin secretion and/or tissue sensitivity to insulin. The latter is known as insulin resistance and forms part of a cluster of cardiovascular risk factors seen in a high proportion of patients with type 2 diabetes. It is known as the metabolic syndrome and also includes central obesity, hypertension and dyslipidemia[3]. Metabolic syndrome occurs in approximately 86% of patients with type 2 diabetes mellitus [T2DM], and the prevalence of cardiovascular disease increases substantially in patients with this syndrome.T2DM patient's high burden of multimorbidity has implications for health service utilization and polypharmacy[4].

Diabetes is a common and very prevalent disease affecting the citizens of both developed and developing countries and is the most common endocrine disorder globally. Comorbid illness such as hypertension in diabetics interfere with optimal treatment decisions in diabetes care and makes it more difficult to avoid multiple drug use; hence diabetics are more prone to have DRPs. Evidence suggests that a targeted, intensified, multifactorial intervention which includes lifestyle modifications and multiple pharmacotherapies is required to reduce or prevent macrovascular and microvascular complications[5, 6].

Metformin, if not contraindicated and if tolerated, is the preferred initial pharmacological agent for type 2 diabetes. In newly diagnosed T2DM patients with markedly symptomatic and/or elevated blood glucose levels or glycosylated haemoglobin [HbA1C], insulin therapy, with or without additional agents should be considered. If noninsulin monotherapy at maximal tolerated dose does not achieve or maintain the HbA1C target over 3-6 months, add a second oral agent, a glucagon-like peptide-1 receptor agonist, or insulin. A patient centered approach should be used to guide choice of pharmacological agents. Considerations include efficacy, cost, potential side effects, and effects on weight, comorbidities, hypoglycemia risk, and patient preferences. Due to the progressive nature of T2DM, insulin therapy is eventually indicated for many patients with T2DM [7].

The optimal use of medications plays a key role in achieving treatment targets for glucose, blood pressure and lipids. DRPs commonly occur among T2DM patients. Therefore, efficacy of a medication regimen may be limited by a range of DRPs including adverse

drug reactions [ADR], drug interactions [DI], contra-indications and non-adherence. Since patients with T2DM generally use multiple medications, DRPs are likely to occur in this population and these can negatively influence diabetes control. Few researches have shown that a substantial proportion of DRPs that exist within the health care system are related to patients with diabetes[8-10].

In diabetes, the key treatments to control blood glucose concentrations, the oral antidiabetic agents and insulin, have the potential to cause serious adverse effects. Profound and life-threatening hypoglycemia induced by treatment is a limiting factor in the management of diabetes. In addition, errors of omission can lead to hyperglycemia and potentially ketoacidosis or hyperosmolar coma. Awareness of errors that contribute to or worsen such effects allows safeguards to put in place[11]. The aim of this study was to assess epidemiology and predictors of drug related problems in diabetes patients at Jimma University specialized hospital, southwest Ethiopia.

METHODS AND PARTICIPANTS

Data collection and Analysis

A prospective cross-sectional study was used. The sample size was determined by using the formula for estimating a single population proportion. Sample size was calculated from study done in JUSH 2011, by taking the proportion of poor glycemic control which is 58.2 % on T2DM patients at diabetes Clinic of JUSH with 95% confidence level and 5% margin of error to get an optimum sample size that allowed the study to look into various aspect of poor glycemic control and drug related problems among T2DM patients[12].

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

$$= (1.96)^2 * 0.582(1-0.582)/\ (0.05)^2$$

$$= 374$$

Where: n= the required sample size

Z= the value of Z in the standard normal distribution that corresponds to level 0.05.

p= proportion of poor glycemic control taken from study was done in Diabetes Clinic at JUSH = 58.2%

d = the margin of error (precision) =5%

This yields a sample size of 374. Since the source population consisted of less than 10,000 respondents, the sample size was adjusted by using correction formula

$$n_f = n/\ 1+n/N$$

Where n_f = the final sample size, n= desired sample size 374 and N= number of total T2DM patients (1407). The calculated sample was 295. Considering a 10% non-response rate, which was 30, 325 T2DM patients were planned to be included in the study. Sixteen patients had no medication chart or medical

record and only 309 patients were included in the study.

All T2DM patients who had attended diabetic clinic during the study period and who were willing to give their informed consent to take part in the study were involved. All consecutively coming T2DM patients fulfilling the inclusion criteria were included in the study.

Data analysis

A descriptive analysis was conducted to indicate the frequency, consistencies and to identify missed values for independent variables. Binary logistic regression analysis was used to determine association of drug related problems and glycemic with independent variables. Multiple logistic regression analysis was used to determine the independent predictors of DRPs and glycemic control. 95% CI was calculated for data analysis. P values < 0.05 were considered as statistically significant. Independent variables having association with dependent variable on the bivariate analysis was entered into the multivariable logistic regression model to identify their independent effects.

Study variables

Independent variables included were patients Age, Sex, Educational status, Religion, Ethnicity, Social drug use, Marital status, BMI, Occupation, Comorbidities, Diabetic complication, Polypharmacy, Duration of DM Dependent variable were Drug related problems as Primary outcome and Glycemic control as Secondary outcome

RESULTS

Socio-demographic characteristics

A total of 309 T2DM patients fulfilled the inclusion criteria in this study. Males (61.5%) were present in greater proportion than female patients in this study. Majority (81.2%) of patients were married. The mean ± standard deviation of patients' age was 55.13 ± 10.83 years old with old with age ranges of 30 to 83 years old. The elderly population (>=65 years) constituted only 20.1% of the study population. In this study, one hundred seventy patients (55.0%) were Oromo by ethnicity and one hundred forty-four (46.6%) patients were Muslims by religion. One hundred eleven (35.9%) patients were with educational level of primary school and 85 (27.5%) patients were illiterate. Regarding to their occupation, 95 (30.7%) patients were farmer, 70(22.7%) patients were employed, and 68 (22.0%) patients were unemployed. Majority of the patients (94.2%) were non-smokers in this study. 260 (84.1%) patients were drinking coffee. This study results also showed that about 1 in 18 (5.5%) subjects consumed alcohol. Sixty (19.4%) patients were chat

chewers. Twenty-nine (9.4%) patients had BMI of >=30kg/m^2 and one hundred six (34.3%) patients had BMI of >=25kg/m^2 (Table 1).

Clinical characteristics

The mean ± standard deviation of patients' duration of diabetes was 7.16± 5.81 years old. The majority of the patient population had duration of T2DM of less 10 years (n = 249). Only 14(4.5%) patients had diabetic duration of more than 20 years. Seventy-seven (24.9%) patients had a family history of DM. One hundred sixty-six (53.7%) patients had one or more comorbidities from which hypertension contributed to the highest percentage (50.4%). Two hundred twelve (68.6%) patients had one or more diabetic complications. Among diabetic complications, neuropathy was present in 146 (47.2%) patients. 94 (30.4%) patients and 56 (18.1%) patients had retinopathy and nephropathy, respectively as a complication (Table 2).

Prescribed medications

The mean number of medications prescribed per patient was 3.77 ± 1.43 medications. The number of medications taken by patients ranged from 1 to 7. Polypharmacy was common as one hundred eleven (32.7%) of the patients were taking five or more medications.

The number patients prescribed with insulin only therapy was 81 (26.2%), combination insulin and oral antidiabetic therapy was 39 (12.6%), combination of oral antidiabetic therapy was 109 (35.3%) and monotherapy of oral antidiabetic agents 80 (25.9%). The most common anti-diabetic drug prescribed in the study was metformin either as a monotherapy or combination therapy (65.05%) followed by Glibenclamide (45.95%). Enalapril was the most prescribed antihypertensive agent taken by 143 (42.27 %) patients as a single or combination therapy with other antihypertensives. On the other hand, the most common lipid lowering agent prescribed in subjects was lovastatin (123 patients or 39.8%). The number of patients prescribed with antiplatelet medications was 198 (64.1%). Aspirin has accounted the major proportion being prescribed for 196 (64.3 %) patients and three (1.0 %) patients were taking clopidogrel (Table 3).

Glycemic control

Mean of FBS value was 162.12± 50.42 mg/dl. The minimum and maximum FBS values were 83.62 and 314.75 mg/dl, respectively in this study population. There were only 90 (29.1%) patients with FBS value within the targeted range (70-130mg/dl). 219 (70.9%) patients had glycemic level of >130mg/dl (Table 4).

Drug Related Problems

A total of 279 (90.3%) patients had at least one DRP. 632 DRPs were identified and the

mean number of DRPs per patient was 2.05 ± 1.32. Poor medication compliance was the most common DRP occurring at 143 (46.3%) patients and had accounted for 207 (32.75%) of DRPs. Dosage too low was present at 131(42.4) patients. Nighty six (31.1%) patients had an ADR to any one of the medications. The prevalence of need for additional drug was 30%. Ten (3.2%) patents had unnecessary drug therapy. The prevalence of both dosage too high and ineffective drug was 1 % (Table 5).

Drug related problems involved and their causes

Around half (49.47%) of poor medication compliance cases in this study were due to the patients forgetting to take medicines. 146 (89.02%) of the dosage too low were due to the dose is too low to produce the desired responses. Majorities (76.38%) of need for additional drug therapy were due to need for prevention or prophylactic treatments. 89 (80.9%) of adverse drug reactions were due to undesirable reaction that is not dose-related (Table 6).

Drugs involved in drug related problems

Metformin has contributed to the majority of drug related problems accounting for 207 (32.43%) of drug related problems. This was followed by glibenclamide (18.35%) and NPH (16.30%). Enalapril and other anti-hypertensives has also contributed to 73(11.66%) and 9(1.44%) respectively. Statins were involved in 70(11.18%) of the DRPs. Aspirin has contributed to 48(7.67%) of DRPs (Table 7).

Predictors for the occurrence of drug related problems

Presence of comorbidities, number of drugs used, and marital status were the factors that had showed association with DRPs on bivariate logistic regression analyses. Association between sex, age, ethnicity, religion, occupation, social drug use, diabetic complications, previous hospitalization and BMI with DRPS was tested in the bivariate analysis and found to have no association (Table 8).

Number of drugs and comorbidities was the factors which were significantly associated with DRPS on multivariate logistic analyses (Table 9).

There was a statistically significant association between total number of drugs used and DRPS. Patients who use five or more drugs were 4.6 times more likely to have DRPs than those who took less than five drugs (AOR= 4.608, 95% CI= 1.040, 20.412).

The presence of one or more Comorbidities was also significantly associated with DRPs. Patients with one or more comorbid conditions in addition to T2DM were 5.9 more

likely to have DRPs than those without any comorbidities (AOR=5.926, 95% CI: 2.111, 16.632).

Drug related problems, sociodemographic and medication related factors as predictors for the occurrence of poor glycemic control

Adverse drug reactions, noncompliance, use of combination of oral antidiabetic agents and insulin, illiteracy and being farmer were the variables that showed association with poor glycemic control on multivariate logistic regression analysis.

There was a statistically significant association between adverse drug reaction and poor glycemic control. Patients who develop ADR to one more of the medications were 2 times more likely to have poor glycemic control than those with no ADR (AOR= 2.191, 95% CI= 1.176, 4.082).

Patients who were noncompliant to medications were more likely to have poor glycemic controls than those who were compliant (AOR=2.788, 95% CI: 1.588, 4.896).

The type of antidiabetic medications used was also significantly associated with poor glycemic control. Patients who were on insulin and oral antidiabetic agents were 3.8 times more likely to have poor glycemic control than those on oral antidiabetic agents only (AOR=3.821, 95% CI: 1.236, 11.815).

Educational status of the study subjects was among the factors that showed association with glycemic control. Illiterate patients were about four times more likely to have poor glycemic control when compared with patients with educational status of college or university (AOR= 3.994, 95% CI= 1.260, 12.659).

Occupation of the study subjects was among the socio-demographic factors which were significantly associated with poor glycemic control. Farmer patients were 2.6 times more likely to develop poor glycemic outcome when compared to unemployed patients (AOR= 2.644, 95% (1.230, 5.685).

DISCUSSION

This study assessed drug related problems and glycemic control among ambulatory type 2 diabetic patients at Jimma University Specialized Hospital using information obtained from chart reviews and patient interviews.

The results of the current study showed that overall prevalence of drug related problems in the study population was 90.3%. This is somewhat similar with other studies done in Malaysia (90.5%, 91.8% [10,13]. This can partly be explained by the fact that patients with type 2 diabetes generally use many medications and emphasize the need for

adequate medication management in these patients.

In this study, the mean of 2 DRPs per patient was less than the levels found in other studies done in Denmark and Netherlands, which were about 4.1 and 4.6 DRPs per T2DM patient [3,14]. This could be explained by different DRP classification used.

Multivariate analysis result of this study showed that polypharmacy and comorbidities were among the factors which were significantly associated with DRPS.

Regarding polypharmacy, patients who used five or more drugs were 4.6 times more likely to have DRPs than those who took less than five drugs (AOR=4.608, 95% CI: 1.040, 20.412). It is a well-known fact that polypharmacy is strongly associated with DRPs and this has been shown by numerous studies [15-17].

Polypharmacy has been associated with problems such as poor medication adherence, potential drug-drug interactions, duplication of therapy, increased costs, emergency department visits, hospitalizations, additional medical or surgical interventions, decreased quality of life and side-effects of drugs. The frequent daily drug administration and different pill numbers for each medication may contribute to the poor medication compliance problem in these patients.

The presence of one or more co morbid medical condition was also significantly associated with drug related problems. Patients with one or more co morbid medical condition in addition to T2DM were 5.9 times more likely to have DRPs than those without any comorbidity (AOR=5.926, 95% CI: 2.111, 16.632). This is in line with other studies [18,19].

This may be due to the use of many drugs to manage individual co-morbidity accordingly. In addition, co-morbidities can create a challenging and uncertain environment to make isolated drug therapy decisions.

The four most common DRP categories identified in the current study noncompliance, dosage too low, need additional drug and adverse drug reaction. This is not in line with other studies which reported adverse drug reaction and noncompliance as the most common DRPs, respectively [14,20]. This variation frequency of DRPs may be due to drug regimen differences and types of DRPs classification used.

Poor medication compliance was the most common DRP occurring at in 141 patients (45.6%) and has accounted for 207 (32.75%) of DPRs. This disagrees with a study from the Netherlands, whereby 17.6% of T2DM patients were compliant to their medications [3]. This may be the use of different tool used

for the assessment of compliance and difference reports by the patients. More than 40% of poor medication compliance cases in this study were due to the patients forgetting to take medicines. Other reasons detected in this study were that patients had concerns over drugs due to their side-effects, were unable to purchase medications and drug unavailability.

This was not in line with a study done in Malaysia by which more than 90% of poor medication compliance cases were due to the patients forgetting to take medicines[10]. This difference may be due to the patient's inability to purchase medications has also contributed more to drug noncompliance in our study.

Dosage too low was the second most DRP. Metformin and enalapril were the two most drugs involved in the dosage too low category. This reduction in the doses of the drugs especially metformin and enalapril may be due to fear of the adverse reactions of the drugs since organ function tests are not done regularly.

The 'needs additional therapy' category was the third most frequent drug related problem in the study accounting for 124 (19.62%) of the total drug related problems. Aspirin and statins were the commonest drugs involved in the need for additional drugs category. This is in line with a study done in Netherlands[3].

This indicates that this category of DRP, either for treatment, prevention or synergistic effect, or therapy to achieve the desired goals of therapy, is substantial among diabetic patients. The results of the current study showed that cardiovascular risk was not adequately addressed in this population.

Adverse reactions were present in 96 (31.1%) patients. Hypoglycemic symptoms were the commonest occurring in 45 (14.56%) patients. This is in line with a study done in Netherlands by which 29.1% patients reported having experienced at least one episode of hypoglycemia[3]. Abdominal discomfort was the second most common adverse drug reaction occurring at 35(11.33%) patients.

In the present study, poor glycemic control (FBS >130 mg/dL) was found in most of participants (70.9%). This is similar with previous study done at JUSH, 2011 in which 73.1% of patients had FBS above the target level of 130 mg/dl [21]. The results of this study indicate that the pharmacotherapy given to patients need to optimized to improve glycemic control. The results obtained from multivariate logistic regression analysis showed that adverse drug reaction, noncompliance, use of combination of insulin and oral antidiabetic agents, educational status and occupation were the variables that showed association with poor glycemic control.

There was a statistically significant association between adverse drug reaction and poor glycemic control. Patients who had ADR to one more of the medications were 2.2 times more likely to have poor glycemic control than those with no ADR (AOR= 2.191, 95% CI= 1.176, 4.082). This finding is consistent with that reported by other studies (22, 23). This may be due to patients preferred not to take medications due to fear of side effects of medications.

There was a statistically significant association between noncompliance to medications and poor glycemic control. Patients who were noncompliant to medications were 2.8 times more likely to have poor glycemic controls than those who were compliant to their medications (AOR=2.788, 95% CI: 1.588, 4.896). This is consistent with a study done in Netherlands [3].

The type of antidiabetic medications used was also significantly associated with poor glycemic control. Patients who were on combination of insulin and oral antidiabetic agents were 3.8 times more likely to have poor glycemic control than those on oral antidiabetic agents only (AOR=3.821, 95% CI: 1.236, 11.815).

The association between treatment with combination of oral antidiabetic agents and insulin and poor glycemic control is consistent with a study done in Jordan[23]. This may be due to the complexity of the regimen.

Educational status of the study subjects was among the factors that show association with poor glycemic control. Illiterate patients were about four times more likely to have poor glycemic control when compared with patients with educational status of college or university (AOR= 3.994, 95% CI= 1.260, 12.659). This association between illiteracy and poor glycemic control is consistent with other studies [24,25]. This may be due to their poor ability to take medications appropriately and poor knowledge about diabetes and the medications.

Occupation of the study subjects was among the socio-demographic factors which were significantly associated with poor glycemic control. Farmer patients were 2.6 times more likely to develop poor glycemic outcome when compared to unemployed patients (AOR= 2.644, 95% (1.230, 5.685). This may be due to the farmers less knowledge about diabetes self-management, have inflexible work schedules, and be more likely to have unhealthy eating behaviors.

Conclusions

The prevalence of drug related problems was high among type 2 diabetes mellitus patients in this study. Polypharmacy and the presence

of comorbidities were independent predictors of drug related problems among ambulatory type 2 diabetes mellitus patients. The proportion of patients with poor glycemic control was high. Among different characteristics of drug related problems, adverse drug reactions and noncompliance were found to be independent predictors of poor glycemic control among ambulatory type 2 diabetes mellitus patients.

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Table 1: Distribution of socio-demographic variables among ambulatory type 2 diabetes mellitus patients, JUSH, southwest Ethiopia

Variables	Categories	N (%)
Sex	Male	190 (61.5)
	Female	119(38.5)
Marital status	Married	251 (81.2)
	Single	11(3.6)
	Divorce	11(3.6)
	Widowed	36(11.7)
Age in years	18-40	33(10.7)
	40-64	214(69.3)
	>=65	62(20.1)
Educational level	Illiterate	85(27.5)
	Informal education(can read and write)	23 (7.4)
	Primary school (1-8)	111(35.9)
	Secondary school (9-12)	46(14.9)
	College/university	44(14.2)
Occupation	Employed	70(22.7)
	Unemployment	68(22.0)
	Merchant	29(9.4)
	Farmer	95(30.7)
	Other[1]	47(15.2)
Ethnicity	Oromo	170 (55.0)
	Amhara	78(25.2)
	Dawro	8(2.6)
	Kefa	21(6.8)
	Gurage	10(3.2)
	Yem	8(2.6)
	Others[2]	14(4.5)
Religion	Muslim	144(46.6)
	Orthodox	138(44.7)
	Protestant	23(7.4)
	Others[3]	4(1.3)
Social drug use	Drinking coffee	260(84.1)
	Chewing chat	60(19.4)
	Smoking cigarettes	18 (5.8)
	Drinking alcohol	17(5.5)
BMI	<=18.5 kg/m2	23(7.4)
	18.5-24.9 kg/m2	151(48.9)
	25-29.9 kg/m2	106(34.3)
	>=30 kg/m2	29(9.4)

“1” =Daily laborers, pensioner
“2” =Tigire, wolayita, “3” =Catholics, Jehovah witness, apostolic church

Table 2: Clinical characteristics of ambulatory type 2 diabetes mellitus patients, JUSH, southwest Ethiopia.

Clinical characteristics	Categories	N (%)
Duration of diabetes	<10 years	249(80.6)
	10-20 years	46(14.9)
	>20 years	14(4.5)
Diagnosis	Type 2 DM	143(46.3)
	T2DM+others[1]	166(53.7)
Diabetic complications*	Neuropathy	146(47.2)
	Retinopathy	94 (30.4)
	Nephropathy	56 (18.1)
	Others [2]	56 (18.1)
Total number of drugs	<3 drugs	136(44.0)
	3-4 drugs	72(23.3)
	>=5 drugs	101(32.7)

"1"Renal impairment, bronchial asthma, ischemic heart disease, Dyslipidemia, gout, Parkinson's disease, congestive heart failure.

"2" Impotency, hypertension, myocardial infarction, infection

*One patient may have more than one diabetic complication or comorbidity

Table 3: List of medications used by ambulatory type 2 diabetes mellitus patients, JUSH, southwest Ethiopia

Class of medications	Frequency (%)
Antidiabetic medications	
Metformin	53 (17.2)
Glibenclamide	27(8.7)
NPH	81 (26.2)
Metformin + Glibenclamide	109 (35.3)
Metformin + Insulin	33(10.7)
Metformin + insulin + Glibenclamide	6(1.9)
Total	309(100)
Antihypertensives	
Enalapril	93(30.1)
Amlodipine	7 (2.26)
Enalapril +Amlodipine	17(5.5)
Enalapril + Atenolol	30(9.71)
Enalapril + Hydrochlorothiazide	2(0.63)
Atenolol	1 (0.3)
Total	309(100.0)
Lipid lowering medications	
Lovastatin	123(39.8)
Simvastatin	11(3.6)
Atorvastatin	5(1.6)
Total	309(100.0)
Antiplatelet medications	
ASA	195(63.1)
Clopidogrel	3(1)
Total	309(100.0)

NPH= Neutral Protamine Hagedorn, ASA= Aspirin

Table 4: Glycaemic level of ambulatory type 2 diabetes mellitus patients at JUSH, southwest Ethiopia

FBS Level	N (%)
70-130 mg/dl	90(29.1)
>130 mg/dl	219(70.9)
Total	309(100.0)

Table 5: Distribution of drug related problems among ambulatory type 2 diabetes mellitus patients at JUSH, southwest Ethiopia, from February 14 - April 9, 2014.

Category of DRP	Frequency(n=632)	Percentage (%)
Unnecessary drug therapy	16	2.53
Needs additional drug therapy	124	19.62
Ineffective drug	6	0.95
Dosage too low	167	26.68
Dosage too high	3	0.47
Adverse drug reactions	109	17.25
Noncompliance to medications	207	32.75
Total	632	100

Table 6: Drug related problems involved and their causes among type 2 diabetic patients, JUSH, southwest Ethiopia

Category of DRPs	Causes	N (%)
Unnecessary drug therapy	Duplicated therapy	11(73.33)
	No medical condition	4 (26.67)
Needs additional drug	Untreated indication	24(18.90)
	Preventive or prophylactic	97(76.38)
	Synergistic or potentiating effect	6(4.72)
Ineffective drug	Condition refractory to drugs	3(50)
	Not more effective for the condition	3(50)
Dosage too low	Dose is too low	146(89.02)
	Dose interval too infrequent	3(1.83)
	Drug interactions	15(9.14)
Dosage too high	Dose too high	2(66.67)
	Dosing interval too frequent	1(33.33)
Adverse drug reaction	Allergic reaction	9(0.82)
	Contraindications present	10(9.1)
	Drug interactions	5(4.54)
	Undesirable reaction that is not dose-related	89(80.9)
	Dosage regimen was administered or changed too rapidly	7(6.36)
Noncompliance	Forget to take medications	95 (49.47)
	The drug product is too expensive	37(19.27)
	Side-effects	23(11.98)
	Unavailability of drugs	19(9.90)
	Patient prefers not to take medications	18(9.38)

Table 7: Drugs involved in DRPs among ambulatory type 2 diabetes mellitus patients, JUSH, southwest Ethiopia

Drug	Drug related problem category							Total, n (%)
	Unnecessary drug, n (%)	Need additional drug, n (%)	Ineffective drug, n (%)	Dosage too low, n (%)	Dosage too high, n (%)	ADR, n (%)	Noncompliance, n (%)	
Metformin	0(.0)	0(.0)	3(.47)	82(12.97)	0(.0)	40(6.33)	82(12.97)	207(32.43)
Glibenclamide	5(.79)	5(.79)	3(.47)	30(47.47)	0(.0)	15(2.4)	58(9.18)	116(18.35)
Insulin	0(.0)	0(.0)	0(.0)	16(3.53)	2(.32)	36(5.69)	49(7.75)	103(16.30)
Enalapril	0(.0)	20(3.16)	0(.0)	37(5.85)	0(.0)	6(.95)	10(1.58)	73(11.55)
Other anti-hypertensives*	3(.47)	1(.16)	0(.0)	2(.32)	0(.0)	0(.0)	3(.47)	9(1.42)
Statins	1(.16)	67(10.60)	0(.0)	0(.0)	0(.0)	1(.16)	1(.16)	70(11.10)
Aspirin	3(.47)	31(4.91)	0(.0)	0(.0)	1(.16)	9(1.4)	4(.63)	48(7.59)
Other concomitant drugs	4(.63)	0(.0)	0(.0)	0(.0)	0(.0)	2(.32)	0(.0)	6(.95)
Total								632(100)

*Atenolol, Hydrochlorothiazide, Amlodipine

Table 8: Bivariate logistic regression analysis for factors associated with drug related problems among ambulatory type 2 diabetes mellitus patients, JUSH, southwest Ethiopia

Variables	Category	Drug related problems		COR	P-value	B	95% C.I
		Yes	No				
Sex	Male	174(56.3%)	16(5.2%)	1.450	0.336	0.372	(.680, 3.091)
	Female	14(4.5%)	105(34%)			1	
Age in years	>=65	57(18.4%)	5(1.6%)	1.284	.626	.250	(.471, 3.501)
	<65	222(78.1%)	25(8.1%)			1	
Marital status	Married	231(74.8%)	20(6.5%)	2.406	.036	.878	(1.059, 5.465)
	Not married	48(15.5%)	10(3.2%)			1	
Educational level	Illiterate	77(24.9%)	8(2.6%)	1.048	.914	.047	(.448, 2.454)
	Literate	202(65.4%)	22(7.1%)			1	
Occupation	Employed	64(20.7%)	6(1.9%)			1	
	Unemployed	59(19.1%)	9(2.9%)	1.561	.466	.445	(.471, 5.170
	Merchant	27(8.74%)	2(0.6%)	.959	.941	.411	(.317, 2.903)
	Farmer	86(27.8%)	9(2.9%)	2.36	.998	19.28	(.009, 2.872)
	Other[1]	41(13.3%)	6(1.9%)	1.398	.549	.335	(.466, 4.192)
Ethnicity	Oromo	152(49.2%)	18(5.8%)			1	
	Others[2]	127(41.1%)	12 (3.9%)	1.253	.564	.226	(.582, 2.700)
Religion	Muslim	125(40.5%)	19(6.1%)			1	
	Others[3]	154(49.8%)	11(3.6%)	2.128	.057	.755	(.976, 4.638)
BMI(kg/m^2)	<18.5	21(6.8%)	2(.6%)		.781	1	
	18.6-24.9	135(43.7%)	16(5.2%)	.804	.852	.219	(.172, 3.749)
	25-29.9	98(31.7%)	8(2.6%)	1.167	.571	.154	(.231, 5.893)
	>=30	25(8.1%)	4(1.3%)	.595		.519	(.099, 3.579)
Previous hospitalization	Yes	85(27.5%)	10(3.2%)	.876	.747	.132	(.393, 1.952)
	No	194(62.8%)	20(6.5%)			1	
Diabetic duration(years)	<=7	165(53.4%)	19(6.1%)			1	
	>7	114(36.9%)	11(3.6%)	1.193	.657	.177	(.547, 2.603)

Diabetic complications	Yes	193(62.5%)	19(6.1%)	1.299	0.513	0.262	(0.593, 2.848)
	No	86(27.8%)	11(3.6%)			1	
Number of medications	>=5	99(32.0%)	2(.6%)	7.700	.006	2.041	(1.797, 33.00)
	< 5	180(58.3%)	28(9.1%)			1	
Comorbidities	Yes	158(51.1%)	5(1.6%)	6.529	0.000	1.876	(2.429, 17.55)
	No	121(39.2%)	25(8.1%)			1	

"1"= reference group, COR-crude odds ratio, AOR-adjusted odds ratio, CI- confidence interval

Table 9: Multivariate logistic regression analyses of predictors of drug related problems among ambulatory type 2 diabetes mellitus patients at JUSH, southwest Ethiopia

Variables	Category	Drug related problems		AOR	P-value	B	95% C.I
		Yes	No				
Total number of drugs used	< 5	180(58.3%)	28(9.1%)			1	
	>=5	99(32.0%)	2(.6%)	4.608	.044	1.528	(1.040, 20.412)
Comorbidities	Yes	158(51.1%)	5(1.6%)	5.926	.001	1.779	(2.111, 16.632)
	No	121(39.2%)	25(8.1%)			1	

"1"= reference group, AOR-adjusted odds ratio, CI- confidence interval

Table 10: Predictors of poor glycemic control among ambulatory type 2 diabetes mellitus patients, JUSH, southwest Ethiopia

Variables	Categories	Glycemic level		COR	P-value	B	AOR	95% C.I
		>130mg/dl	70-130mg/dl					
ADRs	Yes	76(24.6%)	20(6.5%)	1.86	.013	.78	2.191	(1.176 , 4.08)
	No	143(46.3%)	70(22.7%)			1		
Noncompliance	Yes	116(37.5%)	27(8.7%)	2.63	.000	1.03	2.788	(1.588, 4.896)
	No	103(33.3%)	63(20.4%)			1		
Anti-diabetic medications	OAAs	130(42.1%)	65(21%)			1		
	Insulin + OAAs	31(10%)	4(1.3%)	3.88	.020	1.34	3.821	(1.236, 11.81)
	Insulin only	58(18.8%)	21(6.8%)	1.38	.296	.336	1.399	(.745, 2.626)
Level of education	Illiterate	68(22.0%)	17(5.5%)	2.77	.019	1.39	3.994	(1.260, 12.66)
	Can read & write	13(4.2%)	10(3.2%)	.90	.853	.125	1.134	(.301, 4.269)
	Grade 1-8	80(25.9%)	31(10.0%)	1.79	.052	1.02	2.777	(0.997, 7.652)
	Grade 9-12	32(10.4%)	14(4.5%)	1.58	.171	.696	2.006	(.741, 5.432)
	College/university	26(8.4%)	18(5.8%)			1		
Occupation	Unemployed	40(12.9%)	28(9.1%)			1		
	Employed	50(16.2%)	20(6.5%)	1.60	0.18	1.2	3.320	(0.810, 3.160)
	Merchant	6(1.9%)	23(7.4%)	2.68	.078	.98	2.673	(.896, 7.977)
	Farmer	20(6.5%)	76(24.6%)	2.66	.013	.97	2.644	(1.230, 5.685)
	Other	16(5.2%)	30(9.7%)	1.31	.178	.61	1.836	(.759, 4.439)

"1"= reference group, COR-crude odds ratio, AOR-adjusted odds ratio, CI- confidence interval
OAAs= Oral antidiabetic agents