Identification and resolution of drug-related problems among diabetic patients attending a referral hospital: a prospective observational study

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Abstract

Background: People living with diabetes are more vulnerable to drug-related problems due to the presence of multiple diseases. This study aimed to identify drug-related problems and contributing factors among diabetic patients.

Methods: This study used a prospective observational study design. The study was conducted among diabetic patients during follow-up at Mettu Karl Referral Hospital from 15 April to 09 August 2019. The consecutive sampling was utilized to collect data. The identification of drug-related problems was performed using the Pharmaceutical Care Network Europe version 8.03. Following data collection, data were entered into Epidata manager version 4.4.2 and exported to the SPSS version 24.0 for analysis. Multivariable logistic regression analysis was done to identify predictors of drug-related problems.

Results: A total of 330 people with diabetes were included in the study, among whom 279 (84.5%) had at least one drug-related problem. A total of 455 drug-related problems were identified. Effects of drug treatment not being optimal (52.7%) and untreated symptoms or indications (30.1%) were the most commonly identified drug-related problems. About 865 interventions were provided for identified drug-related problems and 79.8% was accepted. Diabetes duration $\geq$ 7 years [AOR = 2.02; 95% CI (1.06, 3.85); $p = 0.033$] and the presence of comorbidity [AOR: 2.33; 95% CI (1.18, 4.60); $p = 0.015$] were factors identified as predictors of drug-related problems.

Conclusion: The present study identified that drug-related problems are common among diabetic patients. Effects of drug treatment not being optimal and untreated symptoms or indications were the most commonly identified drug-related problems. Longer diabetes duration and the presence of comorbidities were predictors of drug-related problems.

Keywords: Diabetes, Drug-related problems, Ethiopia

Background

Diabetes is a metabolic disorder characterized by hyperglycemia due to defects in insulin secretion and/or action [1]. Its prevalence has been steadily increasing throughout the world [2]. In 2019, the International Diabetes Federation (IDF) estimated 463 million adult people with diabetes worldwide. The IDF also estimated 19.4 million adults living with diabetes in Africa [3]. In Ethiopia, there are large numbers of people living with diabetes with an estimated 2.6 million [4]. Diabetes is a global health problem and an economic burden worldwide [2]. Diabetes-related global healthcare expenditure...
was 850 billion USD in 2017. Globally, diabetes contributed about 5 million deaths among the adult population in 2017. Similarly, it resulted 6% of all-cause mortality in the Africa region [5].

Although pharmacotherapy plays a major role in the cure, prevent, or diagnose diseases, it can expose patients to drug-related problems (DRPs) [6]. According to the Pharmaceutical Care Network Europe (PCNE) classification of DRPs volume 8.03, DRP is defined as “an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes” and it classifies them into three primary domains, including treatment effectiveness problem, treatment safety and others [7]. Drug therapy problems are a consequence of a patient’s drug-related needs that have gone unmet. They are central to pharmaceutical care practice [8].

Different studies were conducted to identify drug therapy problems among people living with diabetes. For example; a study done in Jordan identified that 81.2% of study participants had at least one DRP [9]. A study from Malaysia indicated that 91.8% of diabetic patients had at least one DRP [10]. Averaging 2.1 drug therapy problems per patient were identified by Ogbonna et al. in Nigeria [11]. In Ethiopia, some studies were conducted to identify DRPs among diabetic patients. Accordingly, a study conducted in Addis Ababa showed that 45.9% of participants experienced drug therapy problems [12]. The presence of DRPs in Wolaita Soddo and Jimma was 83.1% and 88%, respectively [13, 14].

The consequences of DRPs can be increased hospitalizations, emergency department visits, additional physician office visits, and additional prescriptions [6]. DRPs interfere with patient optimal therapeutic outcomes and may be associated with higher morbidity, mortality, and healthcare cost [15]. It is identified that cost-related morbidity and mortality due to drug therapy problems exceed the cost of the medications themselves [16]. A study showed that the economic burden due to drug-related morbidity and mortality in the United States (U.S) was $177.4 billion annually [6].

Several factors could contribute to drug therapy problems occurrence. Diabetes, its complications, and comorbid conditions cause patients to require multiple drug therapy. This results in diabetic patients more vulnerable to drug-related problems [1, 2]. Multiple drug therapy has been identified as a risk of occurrence of drug therapy problems [17]. A study revealed that liver or renal dysfunction can cause drug therapy problems through the alteration of the pharmacokinetics of diabetic medications [10]. It is also observed that older age, the presence of comorbidities, polypharmacy, and history of hospitalization are significantly associated with the occurrence of drug therapy problems [13]. DRPs can occur at any stage of medication use processes. However, lack of proper follow-up and reassessment of medical treatment by the physician is also a major problem [6].

The purpose of identifying DRPs is to help patients achieve their goals of therapy and realize the best possible outcomes from drug therapy. If not resolved, drug therapy problems have clinical consequences [8]. Clinical pharmacists play a crucial role in healthcare settings by identifying and resolving DRPs. The active role of the clinical pharmacists in healthcare settings has promoted improvement in medication use, thus maximizing the desired clinical outcomes while avoiding the unwanted effects of medication therapy with reduced cost [18]. Clinical pharmacists can effectively identify and prevent clinically significant DRPs [19].

With the advances in pharmacotherapy worldwide, understanding the nature of DRPs as well as the role of clinical pharmacists in identifying, preventing, and resolving of DRP is useful in preparing interventional strategies to reduce DRPs. The studies on DRPs among diabetic patients in sub-Saharan Africa particularly in Ethiopia were mainly focused on type 2 diabetes. And also the majority of studies conducted in Ethiopia were cross-sectional studies. The present study includes both type 1 and 2 diabetes and it was a prospective observational study. Additionally, Mettu Karl referral hospital provides services for about 2.5 million people from the catchment area. Due to its location, the hospital is serving the population from three different regions of the country, unlike most of other hospitals which service mainly population from a single region. Despite such a large hospital which services huge number population, there was no study conducted to identify and resolve DRPs. Hence, this study aimed to identify DRPs and predictors among people living with diabetes.

**Materials and methods**

**Study design, setting and population**

Hospital-based prospective observational study was conducted from April 15 to August 09, 2019. It was conducted at the ambulatory clinic of Mettu Karl Referral Hospital. The hospital is found in Mettu town of Oromia region in Southwest Ethiopia at 600 km from Addis Ababa, the capital city of Ethiopia. It serves about 2.5 million people from different regions of the country. The hospital health service covers the outpatient department, inpatient services, critical care, and emergency intervention unit. It provides health services for approximately 13,453 inpatient and 80,000 outpatient attendances a year.

The source population was all diabetic patients on follow-up at Mettu Karl Referral Hospital. The study population was all adult diabetic patients who visited Mettu
Karl Referral Hospital during the data collection period and fulfilled the inclusion criteria. Type 1 and type 2 diabetic patients with age ≥ 18 years and who started taking antidiabetic medications were included. The 1-month follow-up schedule was used for data collection as the majority of patients revisit the hospital every 1 month. Diabetic patients who were not willing to participate in the study and who were not fasting were excluded.

This work was done alongside our recently published paper on glycemic control by Sheleme et al. [20]. Primarily, the study had glycemic control and drug-related problems as primary outcomes. The sample size calculation was done considering both outcomes and glycemic control provided us the maximum sample size. Thus, the proportion of poor glycemic control (59.4%) which reported from a study conducted in Jimma University Medical Center was used. The other parameters were 95% confidence interval (CI), 5% margin of error, and 10% nonresponse rate. The total number of diabetic patients with follow-up at Mettu Karl Referral Hospital was 1560. The required sample size was estimated using the single population formula and 330 was obtained after considering the correction formula. A consecutive sampling technique was used to collect data from patients who fulfilled the inclusion criteria.

**Study variables**
The dependent variable was the presence of drug-related problems. The independent variables included sociodemographic variables (age, sex, education status, occupation, and residence), family history diabetes, duration of diabetes, comorbidities, diabetes-related complications, glycemic control status, and type of medications used.

**Data collection tool and procedure**
The data collection was performed using a structured questionnaire and abstraction format. The questionnaire and data extraction format included patient details, investigations, medications, and clinical characteristics. The data abstraction format was used to collect the current medications a patient was taking, and disease-related data. The questionnaire was translated into Afan Oromo and Amharic languages to interview the patients. Data were collected by one nurse, one pharmacist and two clinical pharmacists. The two formers (nurse and pharmacist) interviewed the patients to get their sociodemographic characteristics and collected necessary data from patients’ medical records. The clinical pharmacists evaluated DRPs and forwarded recommendations for attending physician in order to resolve identified DRPs. Another two clinical pharmacists supervised the study alongside principal investigator to ensure the quality of data collection.

Fasting blood sugar (FBS) was measured at baseline, month-1, month-2 and month-3 of the study period. The baseline FBS was obtained on the 1st day of the patient visited hospital during the study period. The month-1 FBS was taken on the next month of the initial visit in the study period. The month-2 and month-3 FBS were obtained on the 2nd and 3rd month of the initial visit of the study period, respectively. The average of FBS measurements of 3 consecutive months was taken to categorize the diabetic patient’s blood glucose control as achieved or not achieved.

**Identification of DRPs**
DRP was the primary outcome of the study. The classification of DRPs and their causes was done according to PCNE classification of DRPs volume 8.03. It classifies them into three primary domains including treatment effectiveness, treatment safety, and others (cost-effectiveness of the treatment, unnecessary drug treatment and unclear problem/complaint [7]. The identification of DRPs was performed by independent clinical pharmacists. The DRPs were assessed at baseline and then every month for 3 months of the study period. For identified DRPs, clinical pharmacists provided recommendations to a physician for adjustment, suggested a need to further investigate a patient’s condition, gave counseling to patients, and caregivers and encouraged the patients for drug adherence.

**Data quality assurance**
The questionnaire was pretested on 17 diabetics at the ambulatory clinic of Jimma University Medical Center to check its consistency, applicability, and understandability. Four data collectors and two supervisors were trained for 2 days. Unclear and misunderstood questions were modified before data collection. All completed data collection forms were checked for their completeness, consistency, clarity, and accuracy by the principal investigator on daily basis.

**Data processing and statistical analysis**
Data were first coded and edited properly by the principal investigator. Then, the data were entered into Epidata Manager version 4.4.2 and double entry verification was made. Data were exported to Statistical Package for Social Science (SPSS) version 24.0 for analysis. A multi-variable logistic regression model was done to identify predictors of DRPs. The variables were considered as predictors if statistically significant at p-value < 0.05.
Definition of terms
DRP is an event involving drug therapy that actually or potentially interferes with desired health outcomes [7]. The clinical pharmacists’ intervention outcomes were categorized using PCNE version 8.03 as the DRPs were ‘solved,’ ‘partially solved,’ or ‘not solved’ [7].

Results
Socio-demographic and clinical characteristics of the study participants
A total of 330 adult diabetic patients were included in this study. One hundred ninety-eight (60.0%) participants were males. The age of 156 (47.3%) study participants was found within the range of 41 to 60 years. The educational status of the study population showed that 114 (34.5%) had attained primary school education. In terms of occupation, 113 (34.2%) study participants were farmers. More than half (53.6%) of the respondents were urban residents. The mean ± SD diabetes duration of participants was 7.72 ± 5.91 years and 47.6% had a duration of 7 or more years. Comorbid diseases and diabetes complications were identified in 43.3% and 38.5%, respectively. On assessing the glycemic control status, 72.7% of participants did not achieve the recommended goals of glycemic control (Table 1).

Medication usage patterns among study population
The combination metformin and glibenclamide was prescribed to 27.6% of participants. Insulin injection (40.3%) was the most frequently used monotherapy. Oral antidiabetic medications with insulin were given in 14.2% of the study participants. Cardiovascular drugs were the most commonly co-prescribed medications, of which 26.4% were angiotensin converting enzyme inhibitors (Table 2).

Types, causes of DRPs and interventions
A total of 455 DRPs were identified. Among the 330 study participants, 279 (84.5%) had at least one DRP and the mean number of DRPs per patient was 1.38 ± 0.85. Problems regarding treatment effectiveness were the most common DRPs encountered, with the effect of drug treatment not optimal being the most frequent problem (52.7%), followed by untreated symptoms or indications which counted for 30.1% (Table 3).

There were about 527 identified causes of DRPs. The most common causes of DRPs were related to drug selection (32.3%) with no or incomplete drug treatment in spite of existing indications being the most common cause (26.0%). Patient-related problems (30.2%) were the second most common cause of DRPs (Table 3).

A total of 865 interventions were provided. Most of the interventions were given at the prescriber level (40.6%), followed by at the drug level (35.8%) and at the patient level (23.6%). The acceptance rate of the provided interventions was 79.8%. Among the identified DRPs, about 322 (70.8%) was fully resolved. On the other hand, 44 (9.7%) DRPs were partially resolved (Table 3, and Fig. 1).

Predictors of DRPs among study population
The multivariable analysis indicated that longer duration of diabetes and the presence of comorbidities were predictors of DRPs. Study participants who have lived with diabetes for 7 years or more were about two times more likely to have DRPs when compared to those who have lived with diabetes for less than 7 years [AOR = 2.02; 95% CI (1.06, 3.85); p = 0.033]. The participants who had comorbidity were 2.3 times more likely to have DRPs [AOR: 2.33; 95% CI (1.18, 4.60); p = 0.015] compared to those who had no comorbidity (Table 4).

Discussion
DRPs are considered as serious, expensive, and complicate the health-care system. They are common among people living with chronic illness like diabetic patients [9]. If drug therapy problems are not addressed, they can lead to clinical complications [21]. Detecting and resolving DRPs is important to ensure that patients achieve the optimal therapeutic goals [21].

Overall, the current study showed that 84.5% of the study participants had at least one DRP. This result is similar to previously conducted studies, including a study conducted in Jordan (81.2%) and in Ethiopia (88%) [9, 14]. However, it is higher than the finding of another study previously conducted in Ethiopia, which reported 64.2% of DRPs among diabetic patients attending follow-up [22]. The discrepancy may be due to the difference in the method used to assess and classify DRPs. In our study, PCNE classification of DRPs was used, while the previous study utilized Cipolle’s method of DRPs classification system.

The present study showed that treatment effectiveness (86.4%) was the main category of DRP identified and treatment safety (9.2%) was the second most commonly encountered. The effects of drug treatment not being optimal (52.7%) and untreated symptoms or indications (30.1%) were the most frequently observed treatment effectiveness problem. Drug selection (32.3%) and dose selection (15.2%) were the main causes of DRPs. Our study findings are consistent with a previous study done in Ethiopia which showed that the effect of drug treatment not being optimal (49.2%), and untreated indication and symptoms (21.1%) were the most common type of identified DRPs [23]. It is also consistent with a study conducted in China, which reported that treatment effectiveness (53.71%) and treatment safety (33.90%) were the most common DRPs encountered. The study also showed...
that drug selection (71.43%) and dose selection (20.57%) were the main causes of DRPs [24].

Following the identification of DRPs, interventions were provided by the clinical pharmacists. Interventions were given at different levels including at the prescriber level, at the drug level and at the patient level. The acceptance rate of the clinical pharmacists’ recommendations was 79.8%. This is in line with a study conducted by Argaw et al. [14], which revealed that the acceptance rate of clinical pharmacist’s recommendations was 72.6%. The identification and intervention by clinical pharmacists with clinically significant

| Table 1 Socio-demographic and clinical characteristics of participants on follow-up at Mettu Karl Referral Hospital, Southwest Ethiopia, 2019 |
| Variables | Categories | Type 1 DM | Type 2 DM | Total |
|-----------|------------|-----------|-----------|-------|
|-----------|------------|-----------|-----------|-------|
| Sex       | Male       | 87 (43.9) | 111 (56.1)| 198 (60.0) |
|           | Female     | 41 (31.1) | 91 (68.9) | 132 (40.0) |
| Age (years) | 18–40     | 70 (72.9) | 26 (27.1) | 96 (29.1)   |
|           | 41–60      | 45 (28.8) | 111 (71.2)| 156 (47.3) |
|           | > 60       | 13 (16.7) | 65 (83.3) | 78 (23.6)   |
| Educational status | No formal education | 31 (43.7) | 40 (56.3) | 71 (21.5)   |
|           | Primary education | 47 (41.2) | 67 (58.8) | 114 (34.5) |
|           | Secondary education | 32 (49.2) | 33 (50.8) | 65 (19.7)   |
|           | Tertiary education | 18 (22.5) | 62 (77.5) | 80 (24.2)   |
| Occupation | Farmers    | 55 (48.7) | 58 (51.3) | 113 (34.2) |
|           | Merchants  | 43 (44.3) | 54 (55.7) | 97 (29.4)   |
|           | Employees  | 12 (26.7) | 33 (73.3) | 45 (13.6)   |
|           | House wives | 6 (14.6)  | 35 (85.4) | 41 (12.4)   |
|           | Retired    | 5 (20.0)  | 20 (80.0) | 25 (7.6)    |
|           | Others a   | 7 (77.8)  | 2 (22.2)  | 9 (2.7)     |
| Residence | Urban      | 55 (31.1) | 122 (68.9)| 177 (53.6) |
|           | Rural      | 73 (47.7) | 80 (52.3) | 153 (46.4) |
| Family history of DM | Yes | 20 (21.1) | 75 (78.9) | 95 (28.8)   |
|           | No         | 108 (46.0)| 127 (54.0)| 235 (71.2) |
| Duration of DM (years) | < 7 | 59 (17.9) | 114 (34.5)| 173 (52.4) |
|           | ≥ 7        | 69 (20.9) | 88 (26.7) | 157 (47.6) |
| Presence of comorbidities | Yes | 48 (33.6) | 95 (66.4) | 143 (43.3) |
|           | No         | 80 (42.8) | 107 (57.2)| 187 (56.7) |
| Type of comorbidities | Hypertension | 43 (33.3) | 86 (66.7)| 129 (39.1) |
|           | Heart failure | 4 (20.0)  | 16 (80.0) | 20 (6.1)    |
|           | Asthma     | 4 (50.0)  | 4 (50.0)  | 8 (2.4)     |
|           | Ischemic heart disease | 0 (0.0) | 7 (100.0) | 7 (2.1)     |
|           | Others b   | 2 (25.0)  | 6 (75.0)  | 8 (2.4)     |
| Presence of complications | Yes | 35 (27.6) | 92 (72.4) | 127 (38.5) |
|           | No         | 93 (45.8) | 110 (54.2)| 203 (61.5) |
| Type of complications | Neuropathy | 14 (17.7) | 65 (82.3)| 79 (23.9)   |
|           | Retinopathy | 16 (39.0) | 25 (61.0)| 41 (12.4)   |
|           | Nephropathy | 6 (18.8)  | 26 (81.2)| 32 (9.7)    |
|           | Others c   | 1 (16.7)  | 5 (83.3)  | 6 (1.8)     |
| Glycemic control | Achieved (80–130 mg/dl) | 24 (7.3)  | 66 (20.0)| 90 (27.3)   |
|           | Unachieved (> 130 mg/dl) | 104 (31.5)| 136 (41.2)| 240 (72.7)  |

DM diabetes mellitus

a Daily laborers, drivers and students

b Stroke, toxic goiter and human immunodeficiency virus (HIV)

c Impotency and foot ulcer
DRPs, and further, the acceptance of interventions by prescribers, are evidence of the major contribution of clinical pharmacists in minimizing the occurrence of DRPs, thus implying better drug therapy for the patient [19].

In this study, multivariable analysis showed that longer diabetes duration was an independent predictor of DRPs. Study participants who have lived with diabetes for 7 years or more had more DRPs when compared to those who have lived for less than 7 years. This finding is similar with a study done in India, which reported that duration of diabetes was associated with DRPs [6]. This may be because patients with longer diabetes duration are at higher risk of developing diabetes complications, and likely to have comorbid conditions which contribute to multiple drug therapy which in turn increases the chance of drug–drug interactions, adverse drug events and non-adherence to drugs.

This study observed that the presence of comorbidity was another independent predictor of DRPs. It is similar with previous studies conducted in Ethiopia [13, 16]. A study conducted by Amit Sharma et al. [6] also reported that the presence of comorbidities were significantly associated with DRPs. In the presence of multiple medical conditions, medications are required to be initiated for those medical conditions causing the prescription of multiple drugs. The multiple drugs utilization can cause drug–drug interaction and a complex drug schedule. The frequent daily medication use and increased pill numbers may contribute to drug therapy problems.

**Strength and limitation of the study**

The strength of this study was that DRPs were identified prospectively using the standardized tool PCNE version 8.03. One of the limitations of the present study was that the severity of DRPs was not determined. The second limitation was the use of FBS to assess glycemic control level since the HbA1c test was not available in the study area. The third limitation of the study was using of consecutive sampling technique which might weaken the generalization of the findings. Another limitation of the study was that some data were obtained from the patients’ medical record which might affect the quality of data.

**Conclusion**

The present study identified that DRPs are common among diabetic patients attending follow-up. Patients with longer duration of diabetes and comorbidities had a higher chance of developing DRPs. Effect of drug treatment not being optimal and untreated symptoms or indications were the most commonly identified DRPs. Most of the recommendations suggested by clinical pharmacists to solve DRPs were accepted. Clinical pharmacists play a major role in identifying and resolving DRPs, and therefore it is important to strengthen clinical pharmacists’ services in health-care system.
Table 3  Drug-related problems among participants at Mettu Karl Referral Hospital, 2019

| Code | Detailed classification | n (%) |
|------|-------------------------|-------|
| P    | Problem                 | 455 (100) |
| P1   | Treatment effectiveness | 393 (86.4) |
| P1.1 | No effect of drug treatment | 16 (3.5) |
| P1.2 | Effect of drug treatment not optimal | 240 (52.7) |
| P1.3 | Untreated symptoms or indication | 137 (30.1) |
| P2   | Treatment safety        | 42 (9.2) |
| P2.1 | Adverse drug event (possibly) occurring | 42 (9.2) |
| P3   | Other                   | 20 (4.4) |
| P3.1 | Problem with cost-effectiveness of the treatment | 12 (2.6) |
| P3.2 | Unnecessary drug treatment | 8 (1.8) |
| C    | Cause                   | 527 (100) |
| C1   | Drug selection          | 170 (32.3) |
| C1.1 | Inappropriate drug according to guidelines/formulary | 12 (2.3) |
| C1.2 | Inappropriate drug (within guidelines but otherwise contra-indicated) | 4 (0.8) |
| C1.3 | No indication for drug  | 8 (1.5) |
| C1.4 | Inappropriate combination of drugs | 6 (1.1) |
| C1.5 | Inappropriate duplication of therapeutic group or active ingredient | 3 (0.6) |
| C1.6 | No or incomplete drug treatment in spite of existing indication | 137 (26.0) |
| C2   | Drug form               | 0 (0.0) |
| C3   | Dose selection          | 80 (15.2) |
| C3.1 | Drug dose too low       | 28 (5.3) |
| C3.2 | Drug dose too high      | 18 (3.4) |
| C3.3 | Dosage regimen not frequent enough | 7 (1.3) |
| C3.4 | Dosage regimen too frequent | 11 (2.1) |
| C3.5 | Dose timing instructions wrong, unclear or missing | 16 (3.0) |
| C4   | Treatment duration      | 15 (2.8) |
| C4.1 | Duration of treatment too short | 9 (1.7) |
| C4.2 | Duration of treatment too long | 6 (1.1) |
| C5   | Dispensing              | 45 (8.5) |
| C5.1 | Prescribed drug not available | 10 (1.9) |
| C5.2 | Necessary information not provided | 35 (6.6) |
| C6   | Drug use process        | 58 (11.0) |
| C6.1 | Inappropriate timing of administration or dosing intervals | 27 (5.1) |
| C6.2 | Drug under-administered | 17 (3.2) |
| C6.3 | Drug over-administered  | 3 (0.6) |
| C6.4 | Drug not administered at all | 11 (2.1) |
| C7   | Patient related         | 159 (30.2) |
| C7.1 | Patient uses/takes less drug than prescribed or does not take the drug at all | 25 (4.7) |
| C7.2 | Patient uses/takes more drug than prescribed | 4 (0.8) |
| C7.4 | Patient uses unnecessary drug | 3 (0.6) |
| C7.6 | Patient stores drug inappropriately | 71 (13.5) |
| C7.7 | Inappropriate timing or dosing intervals | 29 (5.5) |
| C7.8 | Patient administers/uses the drug in a wrong way | 5 (0.9) |
| C7.9 | Patient unable to use drug/form as directed | 22 (4.2) |
| I    | Interventions           | 865 (100.0) |
| I1   | At prescriber level     | 351 (40.6) |
| I1.1 | Prescriber informed only | 43 (5.0) |
| I1.2 | Prescriber asked for information | 22 (2.5) |
| I1.3 | Intervention proposed to prescriber | 71 (8.2) |
Table 3 (continued)

| Code  | Detailed classification                                      | n (%)  |
|-------|-------------------------------------------------------------|--------|
| I1.4  | Intervention discussed with prescriber                      | 215 (24.9) |
| I2    | At patient level                                            | 204 (23.6) |
| I2.1  | Patient (drug) counseling                                   | 161 (18.6) |
| I2.3  | Patient referred to prescriber                               | 32 (3.7)  |
| I2.4  | Spoken to family member/caregiver                           | 11 (1.3)  |
| I3    | At drug level                                               | 310 (35.8) |
| I3.1  | Drug change                                                 | 25 (2.9)  |
| I3.2  | Dosage change                                               | 84 (9.7)  |
| I3.4  | Instructions for use change                                 | 43 (5.0)  |
| I3.5  | Drug pause or stop                                          | 21 (2.4)  |
| I3.6  | Drug start                                                  | 137 (15.8) |
| A1    | Intervention acceptance                                     | 690 (79.8) |
| A1.1  | Intervention accepted and fully implemented                 | 608 (88.1) |
| A1.2  | Intervention accepted, partially implemented                | 64 (9.3)  |
| A1.3  | Intervention accepted but not implemented                   | 18 (2.6)  |
| A2    | Intervention not accepted                                   | 175 (20.2) |
| A2.1  | Intervention not accepted: not feasible                     | 8 (4.6)   |
| A2.2  | Intervention not accepted: no agreement                     | 167 (95.4) |
| O     | Outcome of intervention                                     |        |
| O1.1  | Problem totally solved                                      | 322 (70.8) |
| O2.1  | Problem partially solved                                    | 44 (9.7)  |
| O3.2  | Problem not solved, lack of cooperation of prescriber       | 85 (18.7) |
| O3.4  | No need or possibility to solve problem                     | 4 (0.9)   |

P problem, C cause, I intervention, A acceptance; O outcome

Number of diabetic patients included in the study to evaluate DRPs = 330

Evaluation of DRPs by clinical pharmacists

Total number of identified and intervened DRPs = 455

Total number of recommendations provided by clinical pharmacists to resolve DRPs = 865

Number of recommendations accepted = 690

Number of recommendations not accepted = 175

Number of DRPs totally solved = 322

Number of DRPs partially solved = 44

Number of DRPs not solved = 89

Fig. 1 DRPs evaluation flowchart
Table 4  Multivariable analysis results for the variables associated with DRPs

| Variable                  | Category | DRP | No | Yes | AOR (95% CI) | p-value |
|---------------------------|----------|-----|----|-----|--------------|---------|
| Diabetes duration (years) | < 7      | 35  | 138| 1   |              |         |
|                          | ≥ 7      | 16  | 141| 1   | 2.019 (1.059, 3.850) | 0.033*  |
| Comorbidity               | No       | 13  | 130| 1   |              |         |
|                          | Yes      | 38  | 149| 1   | 2.333 (1.182, 4.604) | 0.015*  |
| Age (years)               | 18–40    | 22  | 74 | 1   |              |         |
|                          | 41–60    | 23  | 133| 1   | 1.385 (0.705, 2.721) | 0.344   |
|                          | > 60     | 6   | 72 | 1   | 2.381 (0.872, 6.504) | 0.091   |
| Educational status        | No formal education | 7   | 64 | 1   | 2.207 (0.816, 5.965) | 0.119   |
|                          | Primary education | 14  | 100| 1   | 2.477 (1.068, 5.746) | 0.058   |
|                          | Secondary education | 14  | 51 | 1   | 1.319 (0.552, 3.154) | 0.534   |
|                          | Tertiary education | 16  | 64 | 1   |              |         |

AOR adjusted odds ratio, DRP drug-related problem

* Statically significant at p-value less than 0.05
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