INTRODUCTION

Diabetes Mellitus (DM) is a non-communicable disease (NCD) that currently affects about 463 million people worldwide. According to the World Health Organization (WHO) in 2017, the DM incidence rate has shown a growth of 61.8% in recent years (Aquino et al., 2019; Ramos et al., 2016). Estimates point to around 700 million people affected by 2045 due to epidemiological and demographic transition (IDF, 2019). In Brazil, the prevalence of DM in 2014 was 8% in the population, mainly affecting the elderly and women.

NCDs have become the principal causes of morbidity and mortality in Brazil (Malta et al., 2020; Ramos et al., 2016). Therefore, patients with chronic diseases require not only continuous clinical care but also the development of public health policies (Aquino et al., 2019).

Despite the technological advances achieved in the treatment of DM and public policies that assure access to medicines and supplies, the glycemic control remains below ideal. Studies estimate that only 56.8% of the patients present the glycated hemoglobin (HbA1c) within the therapeutic goal. Therefore, health promotion is
essential for disease control and prevention of acute and chronic complications, especially those resulting from an ineffective therapy and an inadequate diet (Aquino et al., 2019; Borges, Lacerda, 2018; Silva et al., 2016).

Diabetic patients commonly present other comorbidities which leads to an increased prevalence of polypharmacy among them. Therefore, these patients become more vulnerable to non-desirable outcomes, such as failures in adherence and susceptibility to adverse effects. Pharmaceutical Care assumes a role to avoid these issues through strategies such as the promotion of the rational use of medicines, taking into consideration individual health needs (Aguirre et al., 2017; Costa et al., 2017; Ramos et al., 2016).

Pharmaceutical Care comprehends a variety of pharmaceutical services provided to the patient, the family, and the community; one of these services is the pharmacotherapeutic management. The prevention and resolution of pharmacotherapy problems, the rational use of medicines, promotion, protection, and recovery of health, as well as prevention of diseases and health issues are its goals (CFF, 2016). Thus, the pharmaceutical professional composes the multidisciplinary team, contributing to attend the health demands of society and promote comprehensive care in the health system (Santos, Silva, Tavares, 2018).

This study highlights the pharmacist’s role in optimizing pharmacotherapy management, reducing morbidity and mortality, and achieving better clinical outcomes by presenting the Drug-therapy Problems (DTPs) profile and interventions made by this professional in a community pharmacy.

The implementation of Pharmaceutical Care in the Public Health System has occurred in some cities in Brazil. However, there is still a lack of indicators from this process of pharmacotherapeutic management. These data are essential to contribute to the delineation of more consistent and robust models, the consolidation of guidelines, and the promotion of homogenous actions (Brasil, 2015).

Therefore, this study aimed to evaluate the Drug-therapy Problems (DTPs) profile and Pharmacist Interventions (PIs) of a pharmacotherapeutic management model in patients with Type 2 Diabetes Mellitus (T2DM) from a Pharmaceutical Care Program within the Primary Health Care (PHC) in Juiz de Fora (Minas Gerais State, Brazil).

**MATERIAL AND METHODS**

**Study design and participants**

This is a cross-sectional, quantitative, descriptive, and retrospective epidemiological study based on the analysis of patients’ records. The study’s scenario was the University Pharmacy (UP), located inside the campus of Federal University of Juiz de Fora (UFJF), Minas Gerais state, Brazil. Sample number was stipulated by convenience sampling. Patients from the West Health District area in Juiz de Fora-MG were selected according to the UP’s service offer.

Inclusion criteria were patients above 18 with T2DM, with or without comorbidities, who attended at least three pharmaceutical consultations between July 2016 (implementation of the Pharmaceutical Care Program) and October 2018, and patients who presented at least two laboratory tests with values of glycated hemoglobin. We obtained a sample composed of 17 patients according to the selected criteria. The data collection comprehends all pharmaceutical consultations performed within the study period.

**Pharmacotherapeutic management model**

Pharmacotherapeutic follow-up methods usually apply tools and strategies from different models, this building process needs to consider the service structure, its particularities, the professional’s qualification, and their experience (Correr, Noblat, Castro, 2016). Therefore, the Pharmaceutical Care Program in UP/UFJF adopts data collection forms, including the classification of DTPs and PIs, according to Brasil (2015), which presents the process of implantation of pharmaceutical clinical services in the PHC of Curitiba, Brazil. Additionally, Dadér Program composes the assessment and follow-up methods (Hernandez, Castro, Dadér, 2007). The pharmacists use the SOAP acronym (Subjective,
Objective, Assessment, and Plan) to register patient’s clinical evolution after each consultation (Brasil, 2015).

Setting

In April 2016, a cooperation agreement signed between UFJF and the Municipal Health Secretariat of Juiz de Fora established the Western Regional Pharmacy which takes place at the facilities of the UP/UFJF. Since then, the population from São Pedro, a neighborhood of the west zone of the city, has free access to medicines provided by the Brazilian Public Health System and listed in the Municipal List of Essential Medicines (in Portuguese: Relação Municipal de Medicamentos Essenciais – REMUME). Besides the medication dispensing, the UP offers free pharmaceutical services through a Pharmaceutical Care Program.

Clinical services provided by the UP/UFJF include pharmacotherapeutic follow-up, medication review, medication reconciliation and health education. The UP serves as a scenario for residents engaged in the Multiprofessional and Pharmacy Programs. Thus, during the study period, 12 residents have worked in the Pharmaceutical Care Program on a rotating basis, performing the consultations in pairs.

After the first consultation pharmacists start the study phase, aiming to identify the DTPs and plan the PIs. Subsequent appointments are called inter-consultations. The description of the clinical evolution of patients, including the DTPs identified by the pharmacists and the PIs to address them, as well as medical prescriptions, laboratory exams, and other documents, compose the pharmacotherapeutic records. These files consist of an instrument to outline the patient pharmacotherapeutic profile and served as the source to obtain the data of this study.

Data analysis

Patients were identified by numeric codes and descriptive statistics were carried out to analyze the data through Microsoft Excel® and GraphPad Prism®. The drug utilization study allowed the determination of the pharmacoepidemiological profile. The Anatomical Therapeutic Chemical (ATC) code, recommended in 2006 by the WHO, was applied as a tool for the classification of the therapeutic molecules.

The DTPs identified were grouped into nine categories: problems involving selection and prescription, administration and patient adherence to treatment, dispensing errors, medication discrepancies (between different levels of health care), medication quality problems, monitoring, ineffective treatment, adverse drug reaction, and drug intoxication. As for the PIs, there are five types: information and counseling, provision of materials, monitoring, pharmacotherapy suggestions (alterations with prescriber’s agreement), and referral (Brasil, 2015). Analysis of all PIs allowed classifying the respective DTP as resolved or not to determine whether PIs were effective.

Ethical aspects

The Human Research Ethics Committee of the Federal University of Juiz de Fora approved this research (CEP number: 2.456.597/2017). The study protocol complied with Brazilian National Health Council regulations (Directive CNS 466/2012) governing human research.

RESULTS AND DISCUSSION

We obtained a study sample of 17 T2DM patients from a total of 94 individuals included in the Pharmaceutical Care Program. The pharmacists performed a total of 238 consultations, an average of 14 ± 8 consultations per patient, in the pharmacotherapeutic management model provided by UP of UFJF during analysis period.

Table I presents the patients’ sociodemographic, behavioral, and drug utilization characteristics variables.
Following a worldwide trend, in Brazil, the population is going through an aging process, expressed by the increase of individuals over 60 years. As a result of this demographic transition, chronic non-communicable diseases became more prevalent, a fact exemplified by the significant percentage of elderly (76%) in the group of patients (Ramos et al., 2016; WHO, 2015).

The level of education is a factor that influences the individual’s abilities to self-care. The majority of the study population has not completed elementary school, and the group also includes unlettered. Authors highlight the low education level among patients with diabetes as a socioeconomic indicator that impacts access to health services and the practice of self-care. In this sense, strategies for patient empowerment like those provided by this pharmacotherapeutic management model are strongly indicated (Cazarim et al., 2016; Malta et al., 2020).

The Ministry of Health developed a significant initiative in the field of Pharmaceutical Assistance with the National Survey on Access, Use, and Promotion of Rational Use of Medicines (in Portuguese: Pesquisa Nacional sobre Acesso, Utilização e Promoção do Uso Racional de Medicamentos no Brasil - PNAUM). The strategy aimed to characterize the organization of Primary Care services from the perspective of access
and promotion of rational use of medicines as well as identifying and discussing factors that interfere in the consolidation of Pharmaceutical Assistance in Brazil. PNAUM was the first population study with sampling from the five regions of the country which evaluated the sociodemographic profile, the health conditions, the prevalence of NCDs, and the medication use (Alvares et al., 2017; Ramos et al., 2016).

Ascef et al. (2017), through PNAUM, point out that only 26.1% of the Brazilian population practice physical activity which is in line with what we observed in this study – where only 24% were not in sedentary condition. Lifestyle directly influences the control and progression of diabetes. According to Silva et al. (2016), there is a strong association of T2DM with overweight and obesity. It highlights the metabolic changes in those patients, especially when they do not practice physical activity.

The body mass index (BMI) is a parameter calculated with the patient’s weight and height and classified among the following ranges: recommended (18.5 to 24.9 kg/m²), overweight (25 to 29.9 kg/m²) and obesity (equal to or above 30 kg/m²). The results showed 12% (n = 2) of the patients within the recommended range, 35% (n = 6) as overweight and 53% (n = 9) as obesity. Excessive fat accumulation impairs diabetes control and represents a risk factor for the occurrence of cardiovascular events, especially in a population whose main associated comorbidity was hypertension (100%) (Lade et al., 2016).

An effective structuring of Pharmaceutical Assistance through Health Care Networks is necessary to qualify the health care provided to the population and expand access to medicines (Araújo et al., 2017), meeting the integrality principle of the Brazilian Public Health System (BPHS), the Unified Health System named (Sistema Único de Saúde – SUS). The study evidenced that the preferential way of acquiring drugs is through the public health system, with the private pharmacies representing an alternative way of acquisition, when there is a shortage of standardized medicines or when the prescription presents drugs not included in the list of REMUME. Moreover, a third way to obtain medication is through the Popular Pharmacy, a program developed by the federal government in which the accredited pharmacies provide drugs at low cost to the population.

Another aspect investigated was the presence of polypharmacy which refers to the use of multiple medications by the same patient. Despite the lack of a universal consensus, the concomitant use of five drugs or more is already considered polypharmacy (Nascimento et al., 2017; Ramos et al., 2016). According to this classification, the present study showed that 94% of individuals are polymedicated with an average of 9 drugs per patient. Polypharmacy has a potential impact in the field of public health because polymedicated individuals present increased chances of low adherence, adverse reactions, drug interactions, and hospitalization (Huszcz, Sato, Santiago, 2018; Tavares et al., 2016).

Table II shows the ten medications most used by patients in this study. In all, there were 52 different drugs on the group’s use list.

### Table II - Most prescribed drugs for study patients

<table>
<thead>
<tr>
<th>Drug</th>
<th>Therapeutic Class</th>
<th>ATC Code</th>
<th>% of patients using</th>
</tr>
</thead>
<tbody>
<tr>
<td>Losartan</td>
<td>Angiotensin II Receptor Blockers</td>
<td>C09CA01</td>
<td>70</td>
</tr>
<tr>
<td>Metformin XR</td>
<td>Biguanides</td>
<td>A10BA02</td>
<td>59</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>Statins</td>
<td>C10AA01</td>
<td>59</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
<td>Salicylates</td>
<td>B01AC06</td>
<td>59</td>
</tr>
<tr>
<td>Insulin NPH</td>
<td>Hormone</td>
<td>A10AC01</td>
<td>47</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>Proton-pump Inhibitors</td>
<td>A02BC01</td>
<td>47</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>Thiazide Diuretics</td>
<td>C03AA03</td>
<td>47</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>Calcium Channel Blockers</td>
<td>C08CA01</td>
<td>41</td>
</tr>
</tbody>
</table>
Biguanides and sulfonylureas remain as main options for the treatment of T2DM. Among the biguanides, the first choice is metformin, an oral antidiabetic drug that appears in 59% of the prescriptions in this study with emphasis on the presentation metformin XR 500 mg. The extended-release presentation or XR is available in the Popular Pharmacy program and its main advantage is to cause fewer adverse gastrointestinal effects – mainly diarrhea, nausea, and vomiting – than those commonly caused by the immediate release presentation (Conceição, Silva, Barbosa, 2017).

Insulin therapy is the gold standard in the treatment of type 1 diabetes, providing an adequate supply of the hormone in the basal and fed states. Additionally, it is an alternative in cases of T2DM refractory to treatment with oral hypoglycemic agents and/or associated complications. Among the T2DM patients evaluated, 58.8% used some variety of insulin.

Concerning laboratory monitoring, value of glycated hemoglobin (HbA1c) in comparison with appropriate fasting or postprandial blood glucose parameters offers an advantage of reflecting glycemic control from the last 3 to 4 months, being therefore, a more reliable indicator of disease control (SBD, 2019). Due to the heterogeneity in the HbA1c measurement intervals verified among the patients, it was not possible to estimate the improvement in glycemic control since their engagement in the Pharmaceutical Care Program, characterizing a limitation for accessing the pharmacotherapeutic management impact on T2DM. It is worth mentioning that the non-compliance with the deadline recommended by the Brazilian Diabetes Society compromises the offer of a comprehensive treatment by the public health system as well as the prevention of future complications (SBD, 2019).

DTPs identified during the pharmacotherapeutic follow-up of T2DM patients were classified by categories and frequency (Figure 1).

### TABLE II - Most prescribed drugs for study patients

<table>
<thead>
<tr>
<th>Drug</th>
<th>Therapeutic Class</th>
<th>ATC Code</th>
<th>% of patients using</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gliclazide</td>
<td>Sulfonylurea</td>
<td>A10BB09</td>
<td>35</td>
</tr>
<tr>
<td>Atenolol</td>
<td>Beta Blockers</td>
<td>C07AB03</td>
<td>30</td>
</tr>
</tbody>
</table>

**FIGURE 1** - Analysis of DTPs by category (n=115).
Results show that the most common DTPs were as follows: administration and patient adherence to treatment (46%), monitoring (23%), and problems involving selection and prescription (11%). These same categories were also the most common among patients attended at the public health service in Curitiba/PR, when the population affected NCDs in the region was evaluated (Brasil, 2014; Brasil, 2015).

The WHO points out that more than half of the medications are improperly prescribed or dispensed to users. Additionally, about 50% of them misuse medicines contributing to the increase in morbidity and mortality rates (WHO, 2006). DTPs occurrences totaled 115 with at least 3 DTPs per person and an average of 6.7. Similar data were found in a survey carried out in the city of Curitiba in 2015, which presented an average of 5.6 DTPs per individual (Brasil, 2014; Brasil, 2015).

The selection of drugs that will be part of the prescription configures a crucial step that directly impacts the treatment’s effectiveness. A common issue occurs when the prescriber opts for a medication not included in REMUME or any other free access routes (for example, Popular Pharmacy). The selection of non-standard drugs creates a favorable situation for noncompliance due to financial difficulties, contributing to ineffective treatment consequently. We observed cases as explained when prescriptions contained the following medicines: dapagliflozin, acarbose, and alogliptin.

Aquino et al. (2019) performed research with diabetic patients assisted in BPHS, revealing that 50% of DTPs are related to adherence which is similar to this study (46%). On the other hand, studies comprehended in PNAUM, carried out by Tavares et al. (2016), showed that low adherence to pharmacological treatment of chronic diseases in Brazil was 30.8% with prevalence among patients with low education. Also, patients assisted by two or more doctors have a 47% higher probability of low adherence to pharmacotherapy than patients treated by a single doctor. This data suggests flaws in the integrality of healthcare. Pharmacists applied reconciliation twice, corresponding to 3% of the total DTPs. Both interventions proved to be resolutive.

Non-adherence to drug therapy is a problem frequently identified among patients, especially among those with chronic conditions and those who need to administer medications more than once a day (Huszcz, Sato, Santiago, 2018). According to Ruppar and Conn (2011), problems related to adherence are multifactorial and involve the health system, the health policies, the family, the community, the health professionals, and the patients. Untreated diabetes can be disabling and may prevent the individual from continuing to work and perform daily tasks due to the chronic complications that may arise, such as retinopathies, neuropathies, and renal failure (Nicoletti, Kubota, 2017).

Pharmaceutical Care stands out as a way to promote better control of diabetes. Through this practice, the patient can acquire more knowledge and understanding about the treatment and health problem, obtaining relevant information that stimulates pharmacotherapy adherence, in addition to improving communication with the pharmacist (Nicoletti, Kubota, 2017). Pharmacotherapeutic follow-up helps to modify the patient’s perceptions about treatment. For instance, patients with diabetes receive instructions about the correct use of medications and handling of insulin, regarding the places of application, storage, use of the glucometer, and the disposal of generated health waste, characterizing a continuous and integral health education process (Cunha et al., 2017). Thus, therapeutic goals can be achieved with the prospect of reducing administration errors and adverse reactions, encouraging habits that benefit glycemic control and the rational use of medications (Nicoletti, Kubota, 2017).

Based on the prevalence of the category of administration and patient adherence to treatment, comprising 46% of the total DTPs identified, Figure 2 expresses the distribution of these DTPs among their subcategories. Results show that the main DTPs related to administration and patient adherence are omission of doses (underdosing) by the patient (24%) and incorrect frequency or administration time (19%).
The findings were similar to the study in Curitiba/PR, where 82% of patients with NCDs presented DTPs related to adherence and medication administration, mainly omission of doses (54%) and incorrect frequency or administration time (32.8%) (Brasil, 2015). Santos, Silva and Tavares (2018) analyzed the implementation of a clinical pharmaceutical service in a region of São Paulo, detecting non-adherence to pharmacotherapy as the main problem (58.4%). The most common DTPs were related to missed doses and incorrect frequency of administration as the prevalent subcategories in this study.

PIs performed were classified in categories expressed in Figure 3, which points out the prevalence of actions developed to solve the identified DTPs.
Analyzing the PIs by category, results show that 60% of the interventions comprehend information and counseling, followed by the provision of materials (18%), and monitoring (15%). A total of 437 interventions were performed, generating an average of 25 PIs per patient. According to Brasil (2015), interventions were carried out in 97.7% of patients, obtaining an average of 6.6 per patient. The information and counseling category was the most frequent finding (60%), data similar to reports from Huszcz, Sato and Santiago (2018) which points out 46.5% of the actions developed by pharmacists belonging to this category. On the other hand, Provin et al. (2010) reported that communication between the pharmacist and the physician was the principal intervention to solve problems of therapeutic inefficacy.

A possible hypothesis for this finding is related to the different levels of health care.

The provision of materials in the care process is sometimes a valuable resource in the consolidation of pharmacotherapy. This kind of intervention allows the professional to exercise the art of care through didactic and accessible tools. In the Pharmaceutical Care Program, patients receive an individualized care plan as well as a capillary blood glucose monitoring diary. A useful tool is the daily medication schedule (Figure 4A) for patients who have difficulties with adherence to pharmacotherapy, especially unlettered. Another strategy is to supply a medicine organizer box (Figure 4B) when the patient demonstrates some difficulty in organizing, storing, and handling medications.

FIGURE 4 - Examples of educational materials provided to patients by the Pharmaceutical Care Program.
Legend: Daily Medication Schedule (A); Medicine Organizer Box (B).

Among study patients, eight received a daily medication schedule and four of them additionally received the medicine organizer box. Patients with low education levels usually require tools complementary to verbal communication and when well instructed can build autonomy and favor adherence to treatments.

The definition of resolvability is associated with the final resolution of problems brought by patients and identified in the service, including also patient satisfaction. Therefore, resolvability implies a satisfactory answer that the service provides to the user when seeking the health need. It is worth mentioning that this response does not exclusively comprise the cure of diseases but also the relief or minimization of suffering, promotion and maintenance of health (Costa et al., 2014).

In this study was identified and recorded a total of 115 DTPs in patient’s files – 77 in the first consultations and 38 during the pharmaceutical care process. The service achieved resolution of 91 (79%) of DTPS identified, especially those related to monitoring (29%),
administration and adherence (29%), and problems involving selection and prescription (21%).

After identifying a DTP, the pharmacist mobilizes efforts in an attempt to resolve it. In this sense, results are very expressive, demonstrating a resolvability generated by the pharmacotherapeutic management model, mainly concerning actions directly related to the professional’s duties. Some factors justify limitations to reach the totality of the resolvability parameter. For example, situations that require interventions from other health professionals and also patients who still have not assumed responsibility for their self-care. Permanence in the pharmacotherapeutic follow-up is necessary since new DTPs appear during the follow-up through changes in health conditions, drug therapy, remissions, and confessions about the conducts performed by patients (Araújo et al., 2017; Huszcz, Sato, Santiago, 2018).

Another limitation observed during the study was a lack of integration with other health professionals since the UP is not located within the PHC unit, interfering in the performance of a more robust statistical analysis. Results of the resolvability were computed based on the reports present in the patients’ files which contain the outcomes related to each DTP identified and patients’ perceptions.

In Brazil, although the pharmaceutical care scenario has been strengthening recently, this practice still faces problems and challenges for its implementation, mainly within the BPHS in which the assurance of access to medicines also configures a challenge to managers. The performance of clinical activities by the pharmacist in health units and not only administrative ones is a barrier to be overcome to optimize health promotion (Huszcz, Sato, Santiago, 2018; Nicoletti, Kubota, 2017) and guarantee integrality right in health, regarding a perspective of an expanded concept of health.

The engagement of professionals in multidisciplinary health teams, along with validation of their social role, can promote the consolidation of pharmaceutical care as a tool not only to support the rational use of medicines but also to contribute to health promotion and reduction of morbidity and mortality related to drugs (Ascef et al., 2017; Nicoletti, Kubota, 2017).

Despite the limitation of this study, regarding its design for results extrapolation, its importance relies on generating hypotheses for clinical trials and other more robust studies. The lack of studies demonstrating the profile of PIs reinforces the relevance of this work. More research in this field is required to corroborate the implementation of Pharmaceutical Care in the different types of health services, mainly in Brazil and other low-middle income countries. Pharmaceutical Care contributes to the management of complex chronic diseases like diabetes and the reduction of damages caused by the inappropriate use of medicines, becoming especially important in health systems that have the primary care as the basis and coordinator of the system.

CONCLUSION

Regarding DTPs, the most prevalent ones were those associated with administration and adherence of patients to treatment. The majority of PIs were related to information, counseling and management of pharmacotherapy.

Results show that pharmacotherapeutic management in PHC accomplishes high resolvability of DTPs through accessible interventions. These findings reinforce the hypothesis that valorization of pharmacists at clinical practice and their insertion in the multidisciplinary team can improve the care of chronic diseases such as diabetes, the communication among health care professionals and the adherence to therapy, also contributing to achievement of a comprehensive Public Health System.

ACKNOWLEDGEMENTS

We thank Débora Rafael de Almeida (deboralmeida1510@gmail.com) from Juiz de Fora-MG, Brazil, for proofreading the translation of this manuscript. We are also thankful to all professors, pharmacists, residents, and collaborators of the University Pharmacy (UP) from the Federal University of Juiz de Fora (UFJF).

REFERENCES


Received for publication on 28th October 2020
Accepted for publication on 04th July 2021