Drug Use Profile and Mortality in Patients with Diabetes Mellitus

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Abstract: Objective: To analyze the medicine use by hospitalized patients with DM diagnosis and its association with mortality in one year follow up. Methods: Surveillance of all hospitalizations was conducted through the public health system in the mid-sized municipality of Minas Gerais, Brazil, for 18 weeks. Patients were interviewed regarding their socioeconomic, demographic, as well as medication use. Additionally, they were monitored regarding death outcomes. Deceased and survivors were compared using Multivariable analysis with Classification and Regression Tree. Results: During surveillance we identified 96 patients with DM diagnosis hospitalized, among these, 63 were interviewed regarding medication use. A total of 16 patients (28.1%) did reported difficulty in finding medication within the public health system, 22 (34.9%) did not use hypoglycemic drugs, and 25 (39.7%) had low medication adherence. We found high death outcomes during follow-up, when 32 patients had died (33.3%). The variables associated with death were: absence of information regarding the effects of discontinuing medication; dispensary location, polypharmacy; legal age of adulthood and number of children. Conclusions: This investigation describes problems related to the correct use of drugs by patients with DM who may be contributing to the frequent hospitalizations besides the high mortality rate in this population. These findings may prove useful in public policy planning for DM and may lead to a significant reduction in premature death.

Key words: Diabetes Mellitus, Primary Health Care, Mortality Rate, Brazilian Standardized Municipal Essential Medicines.

1. Introduction

Diabetes mellitus (DM) is one of the most common chronic diseases worldwide, and its incidence has increased steadily over the years. The number of adults living with diabetes having more than tripled over the past 20 years and in 2019, approximately 4.2 million adults die as a result of diabetes and its complications. In 2000, the global estimate of adults living with diabetes was 151 million. By 2009 it had grown by 88% to 285 million, 463 million adults (9.3%), between 20 to 79 years, are currently living with DM. One in eleven adults have DM and one in two adults are undiagnosed (232 million people), and at least USD 760 billion was spent on diabetes in 2019, corresponding to 10% of global health expenditure. IDF (International Diabetes Federation) estimates that there will be 578 million adults with diabetes by 2030, and 700 million by 2045 [1].

Brazil is in fifth place in the ranking of countries with the largest number of people with DM, being below only China, India, USA and Pakistan. In 2019 the number of people living with DM in this country was 16.8 million, with estimates of 21.5 million in 2030 and 26 million in 2045 [1]. Based in a national survey, the prevalence of DM increased from 5.5% in 2006 to 8.9% in 2016 [2]. The mortality rate associated with DM showed an 8% growth from 2000 to 2007. In 2010, it was responsible for 5.2% of all deaths, making it the third leading cause [3, 4].

The inadequate control of DM is associated with an
increased risk of developing acute and chronic complications, as well as with a reduction in the quality of life of the patient and a substantial increase in public healthcare spending [5]. In Brazil, in 2012, DM was responsible for 7.6% of the Brazilian Unified Health System’s (SUS) [4, 6] hospitalization costs, and during that same year nearly 8.0% of hospitalization expenses in the state of Minas Gerais were caused by DM [7].

When there is no effective to Primary Health Care (PHC) patient monitoring, hospitalizations (such as DM) due to Ambulatory Care Sensitive Conditions (ACSC) are more frequent [8]. The ACSC can be reduced and/or prevented if they are effectively diagnosed and treated in a timely outpatient manner [9]. For this reason, they have been utilized as indirect indicators for PHC access, coverage, and performance.

ACSC are conditions that could be effectively managed in the community with appropriate medical screening, monitoring, management and follow-up. Thus, if there is appropriate care within the community it is thought that patients with these conditions like DM should not be hospitalized. High ACSC rates due to DM could be associated with problems accessing and/or the use of medications to control the disease [10].

Drug use studies in patients diagnosed with DM and hospitalized by the ACSC have enabled us to assess drug use patterns and other factors that influence the effectiveness of drug treatment and contribute to the reduction of morbidity and mortality [11]. However, these studies are still rare among the national and international literature. Therefore, this study aimed at analyzing the medicine use by hospitalized patients with a DM diagnosis and its relationship with 1-year follow-up mortality.

2. Methods

2.1 Design Study, Population and Collection of Data

The present work was based on a prospective cohort study. All patients hospitalized due to ACSC with a DM diagnosis, in the prevalence study conducted by Cardoso [12], in Divinopolis municipality, were eligible for this cohort. Divinopolis is in the Midwest region of the State of Minas Gerais, Brazil. It has a population of 213,016 inhabitants and a human development index of 0.76. This municipality is a health care referral center in a region comprising 54 municipalities. It has two public hospitalization services, one hospital operating under an agreement with SUS and an immediate care unit.

Patients admitted due to ACSC were identified utilizing a screening form and a classification of admission (ACSC or not) defined by the Brazilian List [13]. In this list, all DM hospitalizations are considered CSAP. In this investigation, all hospitalizations performed and paid for by SUS during the study period (22 August 2011 to 23 November 2011) were documented based on patient medical charts and hospital records. The diagnoses reported in the screening records were validated by a community and family health professional. Methodological details can be found described elsewhere [12].

All DM patients identified were recruited for the cohort study and visited 12 months after their hospitalization to evaluate the effectiveness of the PHC in building the continued care after hospitalization event [14]. During this phase, death was assessed and utilized as a study endpoint. Baseline information was obtained during first ACSC hospitalization from June to October 2011, and the death outcome was assessed 12 months later. The data were collected through interviews conducted with the patient or a proxy by previously trained interviewers. All of the questionnaires used had been previously tested during pre-testing and a pilot study.

2.2 Study Variables

2.2.1 Outcome

Deaths were identified through telephone contact with relatives or at-home visits. This information was subsequently confirmed by the declarations of death.
2.2.2 Exposure Variables

(1) Sociodemographic and economic characteristics; 2) DM type and disease duration; 3) Health conditions: self-reported comorbidities and previous hospitalizations within the past year; 4) Medication: active ingredient; therapeutic class; number, duration, location of dispensing; difficulty acquiring; costs; information provided by a health professional regarding medication use; presence of medication in the Municipal Essential Medicines List (REUME); and the ability to self-administer medication independently.

All medications were coded according to the Anatomical Therapeutic Chemical-ATC at the second level [15]. Polypharmacy was defined as the use of five or more medications per day [16].

2.3 Statistical Analysis

Descriptive statistics with frequency distribution and central tendency measurements to characterize the population were used. Surviving patients were compared to deceased patients in relation to demographic, economic, and clinical characteristics, as well as medications. Among the 57 patients who said they used on use, using Mann-Whitney, Pearson, and Fisher’s Chi-squared tests [17].

Multivariate analysis was performed to evaluate the association between death and medicine profiles using the Classification and Regression Tree-CART method [18]. The objective was to establish a relationship between predictor variables and a single response variable. This method is well suited for use in small sample, besides presenting consistent results with traditional methods of statistical analysis, such as logistic regression [19]. The model included all explanatory variables that exhibited p-values < 0.20 in the bivariate analysis. The relative importance of the node was assessed by the decreased heterogeneity of the branch when compared with the node in the root provided by the improvement measure, utilizing the Gini 0.001 index. The analysis was conducted using the Statistical Package for the Social Sciences (SPSS) 19.0.

2.4 Compliance with Ethical Guidelines

This investigation was approved by the following Institutional Review Board: FUNEDI-Divinópolis number 58/2009 and the Federal University of São João del-Rei, number 258.574/2013.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All subjects were informed of the nature and purpose of the study, and gave written informed consent to participate before any screening procedures.

3. Results

3.1 Population and Mortality Rates

The prevalence study screened a total of 2,775 hospitalizations. The hospitalized patients were identified as ACSC (n = 860) and residents of the municipality of Divinópolis (n = 615). Of the 277 patients interviewed, 96 (34.7%) were hospitalized due to DM diagnose as ACSC.

Among the 96 patients followed in the cohort study, 32 (33.3%) died, and 11 (11.5%) could not be located for follow up. DM was registered as the underlying cause for 18.8% of death certificates, and DM as an associated cause in 25%. The majorities were female and white, and their median age was 63 years. With regard to education, 11% were illiterate, and nearly 78% had completed up to eight years of schooling. Most patients were married and widowed. Retirees accounted for 56.2% of all patients, with their median retirement wage being US $340.00, which was equivalent to the 2011 minimum wage and the median monthly family income was US $681.00. The most prevalent comorbidities were hypertension (87.3%), cardiovascular diseases (54%), and depression (34.9%). The leading type of self-reported DM was type 2. Of the patients, 36% had had this disease for
less than two years, and 38.7% had been hospitalized at other times during the previous year (Table 1).

Patients who died (n = 22) presented with significantly higher cardiovascular disease and hypertension incidence (p = 0.03) compared to survivors (n = 41). However, the group of survivors had more patients with DM as their primary diagnosis upon hospital admission.

3.2 Profile of Medication Use

A total of 63 (65.6%) were interviewed to assess the medication use profiles. Seven (7.3%) did not use any medication, 26 (27.0%) were discharged prior to the baseline interview. In the comparison between interviewed and non-interviewed patients, no difference was identified in the clinical variables (p > 0.05). Difference was observed only for civil status, predominantly singles among those not interviewed (p = 0.03).

Among the medications used by the population studied, six were illegible medical prescriptions, and three patients were unable to provide the names of the medications they used. In all, 303 medications were identified, and this corresponded to 33 therapeutic classes and 78 different drugs. Of these, 27 (34.6%) did not pertain to REMUME (data not shown). The most frequently used drug classes were: antihypertensive (87.7%), oral and/or insulin hypoglycemic agents (65.1%), and diuretics (54%), table 2.

The median daily number of medications used by patients was six, and 66.7% of the patients were polymedicated. The cost of medication was reported by 67.2% of patients, and the median expenditure was US $90.00 dollars (ranging from US $06.00 to US $614.00). Most of them had acquired their medications through SUS public pharmacies (84.5%), while 15.5% obtained their medication from privately owned pharmacies. Approximately 28% reported never or almost never finding their medications in the SUS pharmacy. The main problems reported regarding acquisition were unavailability of medication in the public SUS pharmacy (58%), high cost (20%), and difficulty finding the drugs in privately owned pharmacies (10%) (Data not show). Almost half (42.6%) of the patients reported needing help in order to take their medications. A significant number (24%) reported not receiving any information from their health professional regarding their medication, and a larger proportion of the patients who died (37.5% vs. 62.5%) declared not having received any information. The least reported information was what to do in case a dose is missed (Table 3).

Regarding the duration of use, 87.3% of patients had used all or a majority of their medications for a year or more. As proof of their medication use, 42.9% presented the prescriptions for all or most of their medications. Close to 40% stopped using some of their medications in the 15 days before the study. The reasons for doing so were negative side effects (23.9%) and forgetfulness (21.7%). Several (23.9%) stopped using some of their medications but could not give a reason as to why (data not shown).

Of the medications used by the study group, 34.6% were not prescribed in accordance with REMUME, and 28.1% were never or almost never found in SUS public pharmacies. The majority of medications the patients claimed they were unable to find in the SUS pharmacy did not belong to REMUME, and only 6.6% were not acquired because they were out of stock (data not shown).

Patients who died reported greater financials pending on medication, while the group who survived reported greater difficulty with finding medication in the SUS public pharmacy (p < 0.05). Approximately 35% of the patients did not use oral and/or insulin hypoglycemic agents. All the hypoglycemic agents utilized pertain to the biguanide and sulfonylurea categories. Among the biguanides, 500mg and 850mg of metformin were used. Among the sulfonylureas, glibenclamide, glimepiride, gliclazide, and
### Table 1  Comparison of patients hospitalized for ACSC in relation to death outcomes according to socioeconomic, demographic, and clinical profiles (n=63)

| Variable                        | Total n = 63 (%) | Death n = 22 (%) | No death n = 41 (%) | p value* |
|---------------------------------|------------------|------------------|---------------------|----------|
| **Gender**                      |                  |                  |                     |          |
| Female                          | 37 (58.7)        | 15 (40.5)        | 22 (59.5)           | 0.26     |
| Male                            | 26 (41.3)        | 07 (26.9)        | 19 (73.1)           |          |
| **Race #**                      |                  |                  |                     | 0.86     |
| White                           | 27 (42.9)        | 9 (33.3)         | 18 (66.7)           |          |
| Mixed                           | 24 (38.1)        | 8 (33.3)         | 16 (66.7)           |          |
| Other                           | 12 (19.0)        | 5 (41.7)         | 7 (58.3)            |          |
| **Age(years)** *                |                  |                  |                     | 0.16     |
| < 40                            | 3 (4.8)          | --               | 3 (100)             |          |
| Between 40 and 59               | 21 (33.9)        | 5 (23.8)         | 16 (76.2)           |          |
| > 60                            | 38 (61.3)        | 16 (42.1)        | 22 (57.9)           |          |
| **No paid work * **            |                  |                  |                     |          |
| 54 (85.7)                       | 20 (37.0)        | 34 (63.0)        | 0.32                |          |
| **Education(years) **           |                  |                  |                     | 0.25     |
| 0                               | 7 (11.1)         | 4 (57.1)         | 3 (42.9)            |          |
| 1 to 8                          | 49 (77.8)        | 14 (28.6)        | 35 (71.4)           |          |
| 9 to 11                         | 3 (4.8)          | 2 (66.7)         | 1 (33.3)            |          |
| >12                             | 4 (6.3)          | 2 (50.0)         | 2 (50.0)            |          |
| **Marital Status ##**          |                  |                  |                     | 0.46     |
| Widowed                         | 17 (27.0)        | 8 (47.1)         | 9 (52.9)            |          |
| Married                         | 32 (50.8)        | 10 (31.3)        | 22 (68.8)           |          |
| Other                           | 14 (22.2)        | 4 (28.6)         | 10 (71.4)           |          |
| **Number of Children** *        |                  |                  |                     | 0.10     |
| 1 to 3                          | 43 (44.8)        | 13 (44.8)        | 23 (50.0)           |          |
| 4 to 6                          | 23 (24.0)        | 13 (44.8)        | 10 (21.7)           |          |
| 7 or more                       | 18 (18.7)        | 3 (10.3)         | 13 (24.5)           |          |
| Hospitalization in the last year(yes)** | 12 (38.7) | 2 (16.7) | 10 (83.3) | 0.44 |
| **Self-reported type of DM**    |                  |                  |                     | 0.58     |
| Type 1                          | 16(29.1)         | 7 (43.8)         | 9(56.3)             |          |
| Type 2                          | 25(45.5)         | 7 (28.0)         | 15(72.0)            |          |
| Did not know                    | 14(25.5)         | 5 (35.7)         | 9 (64.3)            |          |
| **Length since DM diagnosis (year)** | 20 (36.4) | 7 (35.0) | 13 (65.0) | 0.71 |
| Less than 2                     | 18 (32.7)        | 5 (27.8)         | 13 (72.2)           |          |
| 3 to 10                         | 17 (30.9)        | 7 (41.2)         | 10 (58.8)           |          |
| More than 10                    |                  |                  |                     | 0.03     |
| 0                               | 4 (6.3)          | --               | 4 (100)             |          |
| 1                               | 20 (31.7)        | 3 (15.0)         | 17 (85.0)           |          |
| 2                               | 26 (41.3)        | 12 (46.2)        | 14 (53.8)           |          |
| 3                               | 13 (20.6)        | 7 (53.8)         | 6 (46.2)            |          |
| **Comorbidities**               |                  |                  |                     |          |
| Arterial systemic hypertension* | 55 (87.3)        | 22 (40.0)        | 33 (60.0)           | 0.03     |
| Cardiovascular disease          | 34 (54.0)        | 16 (47.1)        | 18 (52.9)           | 0.03     |
| Depression                      | 22 (34.9)        | 10 (45.5)        | 12 (54.5)           | 0.20     |
| **DM as the primary diagnosis for hospitalization** | 18 (28.6) | 2 (11.1) | 16 (88.9) | 0.01 |

#Races: black (n = 10), yellow (n = 2)
##Marital status: single (n = 8), divorced (n = 5), domestic partnership (n = 1). Tests used: *Pearson’s Chi-squared.*Fisher’s Chi-squared.
*Total n values other than 63: age = 62; hospitalization in the last year = 31; type of DM = 55; length of disease = 55.
Table 2  Distribution of drug classes for the study population.

| Drug class          | ATC (Level 2) | Frequency of total use n = 63 (%) | Deaths n = 22 (%) | No death n = 41 (%) |
|---------------------|--------------|----------------------------------|-------------------|---------------------|
| Antihypertensive    | C02, C07, C08, C09 | 54 (87.7)                       | 19 (35.2)         | 35 (64.8)           |
| Hypoglycemic        | A10          | 41 (65.1)                        | 15 (36.6)         | 26 (63.4)           |
| Diuretic            | C03          | 34 (54.0)                        | 13 (38.2)         | 21 (61.8)           |
| Hypolipidemic       | C04, C10     | 26 (41.3)                        | 10 (38.5)         | 16 (61.5)           |
| Antiplatelet        | B01          | 24 (38.1)                        | 8 (33.3)          | 16 (66.7)           |
| Antiepileptic       | N03, N05     | 15 (23.8)                        | 5 (33.3)          | 10 (66.7)           |
| Antulcer            | A02          | 10 (15.9)                        | 2 (20.0)          | 8 (80.0)            |
| Thyroid hormone     | H03          | 8 (12.7)                         | 3 (37.5)          | 5 (62.5)            |
| Antiasthmatic       | R01, R03     | 6 (9.5)                          | 2 (33.3)          | 4 (66.7)            |
| Anxiolytic          | N05          | 6 (9.5)                          | 2 (33.3)          | 4 (66.7)            |
| Anticoagulant       | B01          | 5 (7.9)                          | 2 (40.0)          | 3 (60.0)            |
| Glucocorticoid      | H02          | 5 (7.9)                          | 2 (40.0)          | 3 (60.0)            |
| Antipsychotic       | N05          | 4 (6.3)                          | 2 (50.0)          | 2 (50.0)            |
| Coronary Vasodilator| C01          | 3 (4.8)                          | 1 (33.3)          | 2 (66.7)            |
| Antidepressant      | N06, N07     | 3 (4.8)                          | 1 (33.3)          | 2 (66.7)            |
| Vitamin             | A02, A11, A12| 3 (4.8)                          | --                | 3 (100)             |
| Cardiac Glycoside   | C01          | 2 (3.2)                          | --                | 2 (100)             |
| Others*             | B03, C01, C02, C05, G04, J01, L02, M04, M05, N07, R06 | 54 (87.7) | 19 (35.2) | 35 (64.8) |

*Other classes: Vasodilator, Antiarrhythmic, Suppression of bone resorption, Anti Parkinson, Anti-anemic, Anti-vertigo, Vasculoprotective, Antianginal, Anti-vertigo/Antiemetic, Neuroleptic, Tranquilizer, Antifungal, Antibiotic, Alpha-adrenergic blocker, Antineoplastic, Antiandrogen; All with n = 1or 2. Statistical tests used: Pearson and Fisher Chi-squared (p value > 0.19).

chlorpropamide were used (data not shown). Of these, only glimepiride and chlorpropamide are not part of REMUME.

Only 21.4% of the patients used only one oral hypoglycemic agent, 26.2% used two associated oral hypoglycemic agents, 26.2% used one hypoglycemic agent associated with an insulin agent, 23.8% used only one insulin agent, and 2.4% used two different types of insulin agents. The majority of patients who were diagnosed within the previous two years used two hypoglycemic oral agents or one insulin agent. Patients who were diagnosed three to ten years previously more frequently used one hypoglycemic oral agent associated with one insulin agent, and patients who received the diagnosis more than ten years before used an insulin or a hypoglycemic oral agent. There was no statistically significant difference between the deceased and the survivors in terms of hypoglycemic agents (p > 0.05).

3.3 Factors Associated with Death

The results of the multivariate analysis are presented in the decision tree (Figure 1). The root node is presented with the total sample of patients (n = 63). The variable that best discriminated the group in relation to medication use profile, was reporting having received information regarding the effects of interrupting medication use, showing the separation of 2 groups in the decision tree. In the group that reported not receiving this information, 56.2% of the patients died. For the group that did receive this information, the variable location of prescription pick-up was important, considering almost 43% of the patients who died got their medication from a private pharmacy. For the patients who obtained their medications from SUS pharmacies, the polypharmacy was an associated variable, and 33% of these patients died. The model fit showed the tree correctly
Table 3  Comparison of patients hospitalized for ACSC in relation to death outcomes according to drug usage profiles.

| Variable                                      | Total n = 63 (%) | Death n = 22 (%) | No death n = 41 (%) | p value* |
|-----------------------------------------------|------------------|------------------|---------------------|----------|
| **Polypharmacy**                              | 42 (66.7)        | 17 (40.5)        | 25 (59.5)           | 0.19     |
| **Costs associated with medication** (yes)**  | 41 (67.2)        | 21 (51.2)        | 20 (48.8)           | **0.00** |
| **Pick-up location of medication**            | 0.17             |                  |                     |          |
| All or a majority in SUS pharmacy             | 49 (84.5)        | 16 (32.7)        | 33 (67.3)           | --       |
| All or a majority in privately-owned pharmacy | 9 (15.5)         | 5 (55.6)         | 4 (44.4)            | --       |
| **Availability of medications in SUS pharmacy** |                  |                  |                     | **0.05** |
| Never or almost never available               | 16 (28.1)        | 1 (6.3)          | 15 (93.8)           | --       |
| Many times or sometimes available             | 10 (17.5)        | 4 (40.0)         | 6 (60.0)            | --       |
| Always or almost always available             | 31 (54.4)        | 12 (38.7)        | 19 (61.3)           | --       |
| **Needs help to take medication**             |                  |                  |                     |          |
| Received information regarding medication from a medical professional: * | 40 (76.2)        | 18 (37.5)        | 30 (62.5)           | 0.33     |
| Quantity of each medication                   | 50 (100)         | 19 (38.0)        | 31 (62.0)           | --       |
| Medication administration time *              | 48 (96.0)        | 18 (37.5)        | 30 (62.5)           | 0.62     |
| Food with medication *                        | 43 (86.0)        | 16 (37.2)        | 27 (62.8)           | 0.54     |
| Name of medication *                          | 45 (90.0)        | 15 (33.3)        | 30 (66.7)           | 0.06     |
| Dosage, indication, and method of use         | 46 (73.0)        | 14 (30.4)        | 32 (69.6)           | 0.22     |
| Effects of interrupting medication            | 34 (68.0)        | 10 (29.4)        | 24 (70.6)           | 0.07     |
| Alcohol use                                   | 23 (46.0)        | 9 (39.1)         | 14 (60.9)           | 0.88     |
| What to do in case of missed dose             | 21 (42.0)        | 8 (38.1)         | 13 (61.9)           | 0.99     |
| Collateral effects/adverse effects            | 23 (46.0)        | 7 (30.4)         | 16 (69.6)           | 0.31     |
| **Length of time since beginning medication** |                  |                  |                     | 0.58     |
| All or the majority of for less than a year   | 8 (12.7)         | 3 (37.5)         | 5 (62.5)            | --       |
| All or the majority of for a year or more     | 55 (87.3)        | 19 (34.5)        | 36 (65.5)           | --       |
| **Proof of medication use**                   |                  |                  |                     | 0.40     |
| Prescription for all or most                  | 27 (42.9)        | 8 (29.6)         | 19 (70.4)           | --       |
| Package insert, box for all or most           | 14 (22.2)        | 7 (50.0)         | 7 (50.0)            | --       |
| None for all                                  | 22 (34.9)        | 7 (31.8)         | 15 (68.2)           | --       |
| **Stopped using a medication in the last 15 days** | 25 (39.7)        | 10 (40.0)        | 15 (60.0)           | 0.49     |

**Polypharmacy: using 5 or more medications per day.
• Test used: Pearson’s Chi-squared. *Test used: Fisher’s Chi-squared. •Total n values other than 63: prescription pick-up location = 58; costs associated with medication = 61; availability of medications in SUS = 57; and help to self-administer medications = 61.

classified 68% of the patients (risk: 0.32), which shows a good fit analysis for this study population.

4. Discussion

The main findings of this investigation were high mortality at one year follow-up and the high number of comorbidities associated with patients who died. There was no difference in drug classes between patients who died and survivors, but there was a difference in relation to drug expenditures and the difficulty in finding them in public pharmacies. In the multivariate analysis, the factors associated with death were the lack of information on the effects of drug discontinuation, location of dispensation and polypharmacy.

The present unprecedented study demonstrated an elevated mortality rate in the 12 months after admission, and DM was underreported in many cases. Studies showed the disease is not mentioned in 40% to 60% of the cases and is registered as an underlying cause among about 10% of death certificates [20, 21]. For 18.8% and 25% of the patients in our study, DM
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related to an increased incidence of metabolic disorder, disease complications, and death. On the other hand, patients who received this information used SUS public pharmacies as the main source of obtaining their medications utilized polypharmacy. Patients who used multiple medications may have insisted on acquiring them through the public health network, since the acquisition of the same medications from a privately owned pharmacy would be costly. Patients who acquired their drugs in private pharmacies presented higher rates of non-adherence. Costs associated with medications not appearing in essential drug lists that were acquired in private pharmacies may have contributed to non-adherence, leading to DM complications, hospitalizations, and deaths.

Polypharmacy among patients who use public health networks can result in the over-prescription of drugs, while under-utilization may occur for patients in private networks as a result of the difficulty obtaining medication due to its higher cost [23]. In addition, polypharmacy is often associated with increased side effects and non-compliance [24]. Many private pharmacies in Brazil still function part-time without the presence of a pharmacist. This scenario favors and encouraged patients to acquire unnecessary additional medications. Even with the presence of the pharmacist, a study reveals that fundamental information about DM medications is scarce or absent [25].

The proportion of patients who did not use any type of hypoglycemic agent for the treatment of DM (34.9%) was much higher than reported by similar studies (11%) [26, 27]. The use of a hypoglycemic oral agent associated with insulin was observed in both survivors and deceased (26.6% vs. 45.5%). The use of this drug association generally occurs in patients with disease duration of approximately nine years, when metabolic control typically becomes inadequate [28]. This association may serve as a marker of mortality rates among DM patients in studies of drug use.

Fig. 1  Classification and regression tree using the CART algorithm to evaluate the association between drug use profiles with death outcomes.

was registered as underlying and associated cause in the death certificates, respectively. This underreporting can occur when the physician diagnoses the patient and fills out the death certificate or when the health department staff performs the coding of the diagnosis and, when necessary, modifies the underlying cause based on defined rules, despite, in some situations, the presence of subjective criteria that could influence the decision [22].

Patients who did not receive information on the effects of interrupting medications use more often experienced fatal outcomes. This interruption may be
Many patients report that they cannot find their medications in the public pharmacy. However, we verified only a small portion of drugs (6.5%) were in fact unavailable in public pharmacies. This detail points to a pattern of prescriptions that do not adhere to the essential medications list provided by the Ministry of Health and/or the municipal health management, which does not appear to be a result of poor user access to medication.

The use of drugs not included on the official list is expected in situations of therapeutic failure, unavailability of certain medications, and special patient needs, and it should not occur when other therapeutic alternatives are present on the essential medications list. Poor adherence to official list of medications can be attributed, in part, to the prescribing habits of physicians, who are not aware of, or neglect the, REMUME. However, it may also be a result of the negligence of health management, which does not offer necessary training and information to health care professionals. A study conducted in another municipality of Minas Gerais also showed the majority (53.5%) of prescription drugs was not present on the municipal list [29]. The unavailability of medications in SUS, although it appeared to be low in our study, still represents a huge problem if these drugs are essential for the treatment of health conditions such as DM. Indeed, patients reported a lack of insulin in the city during the study period.

This study presents innovative results, but it has some limitations. First, the self-reported interviews may reflect socially acceptable responses, especially those related to DM treatment, considering the patients were hospitalized for complications relating to the disease at the time of the interview. In this sense, non-compliance could indicate personal responsibility for the DM complications requiring hospitalization. Additionally, ACSC may represent a reporting bias, because we could be evaluating the responses of users who are dissatisfied with not receiving timely and decisive care, which could have prevented unnecessary hospitalization.

5. Conclusions

This study evaluated the drug use profiles of patients hospitalized for DM as ACSC, verifying associations with the outcome of death. It shows us important findings related to the quality of pharmaceutical care within the APS in a Brazilian city of medium population size. It identified: i) a high percentage of patients who failed to take some of their medications within the previous 15 days, ii) unavailability of SUS medications, iii) non-adherence to the essential drugs list by healthcare professionals, and iv) drug expenditures. The government can take these results and use them to contribute to the future planning of DM health services, thus reducing unnecessary hospitalization and premature mortality rates. These findings deserve special attention and should be the subject of future investigations.

In conclusion, this investigation describes problems related to the correct use of drugs by patients diagnosed with Diabetes who may be contributing to the frequent hospitalizations besides the high mortality rate in this population.

Competing Interests

The authors declare that have no competing interests.

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