INTRODUCTION

Diabetes mellitus (DM) has been a health burden worldwide, including Indonesia. Type 2 diabetes mellitus (T2DM) is the most common type of DM characterized by insulin resistance\(^1\). In 2019, it was estimated that 463 million (9.3\%) adults worldwide suffered from DM. This number is predicted to increase to 578 million in 2030. It is also estimated that 4.2 million people lost their lives due to DM and its complications. Meanwhile, over 700,000 people over 15 in Indonesia suffer from DM, while more than 13,000 originated from West Sumatra\(^2,3\).

Persistent hyperglycemic conditions in uncontrolled DM can cause acute or chronic complications. Among acute complications were diabetic ketoacidosis and diabetic coma. Meanwhile, the chronic complications of DM are nephropathy, neuropathy, and cerebrovascular disease\(^4\).

Blood glucose control is essential to prevent those complications, observed through several parameters such as fasting blood glucose, postprandial blood glucose, and glycated hemoglobin\(^5\). Blood glucose control is influenced by several factors, such as demographic and clinical characteristics. However, it was also well understood that patients who take antidiabetic medications as instructed are likely to have lower glycated hemoglobin levels and better control of DM-related
Nevertheless, T2DM therapy needs a long and complex process, often not favored by patients. Several interventions can improve patients' understanding and behavior related to their medications, for example, educational video and smartphone-based education. However, in Indonesia, patients may not always have adequate access to technology. Thus, there is a need to develop a simple approach to implement in Indonesia's primary health care setting.

Drug information service is one of the pharmaceutical services that can improve clinical outcomes in T2DM. Drug information service is a part of pharmaceutical care delivered in public health centers and other settings like hospitals or pharmacies. Drug information service is defined as a service by pharmacists to provide accurate, precise, and up-to-date information to doctors, pharmacists, other health professionals, and patients. This service includes providing and disseminating information to consumers, both actively and passively, answering questions from patients and health professionals, and creating media of information such as leaflets, drug labels, posters, and newsletters.

Few studies have examined the impact of drug information on patient outcomes. A review by Rutter et al. from 20 studies concluded that drug information service affects patient outcomes positively. Previous studies and a review article also shows that pharmaceutical care intervention, which includes providing medication information to patients with T2DM, had a positive impact on clinical outcome. A study in France shows that tailored information about the disease, diet, and drug treatment improved patients' HbA1c levels. However, studies that reported the effect of drug information services on clinical outcomes in T2DM patients are relatively rare. Thus, we conduct a quasi-experimental study to understand the effect of drug information service provision on the clinical outcome of T2DM patients at Andalas Public Health Center in Padang, Indonesia.

MATERIALS AND METHODS

Materials

This study was conducted at Andalas Public Health Center in Padang, West Sumatra, Indonesia, from August to October 2021. The tools used in this study were data collection forms, stationery, and laptops. Meanwhile, the materials used were drug information sheets and patients' data compiled by the public health center.

Methods

Study design

This quasi-experimental study was conducted using one group pre-post-test design. All participants in this study were given a drug information service. The fasting blood glucose level was measured before and after the intervention. The staff at the public health center performed the blood glucose level measurement.

Population and sampling

The population of this study was the patients with T2DM who were registered in a Chronic Disease Management Program (Program Pengelolaan Penyakit Kronis/PROLANIS) at Andalas Public Health Center in Padang, West Sumatra, Indonesia. The sample was chosen according to the inclusion criteria and exclusion criteria. The inclusion criteria were adult T2DM patients ≥18 years who received oral antidiabetic medication and consented to participate. The exclusion criteria were the patients who dropped out from the study or were referred to other healthcare facilities.

Intervention

A drug information service was provided through direct explanation to the patients. The drug information in this study consisted of the medication indication, instruction on medication use, and the side effects of each medication. A drug information guide (https://doi.org/10.5281/zenodo.6496273) was developed for oral antidiabetic agents that were commonly used in the public health center. Patients were also reminded to take their medications as instructed and to return 30 days later for a follow-up period.
Data analysis

Sociodemographic data were analyzed descriptively. The data distribution of fasting blood glucose was analyzed using the Shapiro-Wilk test. The association between patients' gender, age group, and the number of medications with fasting blood glucose levels were measured using the independent t-test method. Meanwhile, the difference between types of comorbidities with blood glucose levels was measured by one-way ANOVA. A Pearson correlation test was also performed to analyze the correlation between the duration of DM and patients' blood glucose levels. The difference in fasting blood glucose before and after the intervention was assessed using Wilcoxon signed-rank test because the data on blood glucose levels after intervention were not normally distributed.

Ethical approval

This study had obtained ethical approval from the Research Ethics Committee, Faculty of Medicine Universitas Andalas, and registered under No. 391/UN.16.2/KEP-FK/2021.

RESULTS AND DISCUSSION

From August to October 2021, 73 patients were recruited for this study. Six patients did not attend the follow-up, four moved to other healthcare facilities for control or medical treatment, while 23 did not attend the healthcare center on time (30 days after the previous visit). Thus, only the data from 40 patients were included for further analysis. Most participants were female (N=34; 85%) and did not work, either homemakers or pensionary (N=35; 90%), as seen in Table I. Table II shows that most patients also had T2DM for 1 to 5 years (N=36; 90%). Besides, most patients (N=29, 72.5%) also had comorbidities, mostly hypertension (N=17, 42.5%), although other comorbidities such as hypercholesterolemia were also found.

| Table I. Sociodemographic characteristics of participants |
|-----------------------------------------------------------|
| **Characteristics**                  | Number of subjects (N=40) | Percentage (%) |
|--------------------------------------|---------------------------|----------------|
| **Gender**                           |                           |                |
| Male                                 | 6                         | 15             |
| Female                               | 34                        | 85             |
| **Age (years)**                      |                           |                |
| 18-59                                | 20                        | 50             |
| ≥60                                  | 20                        | 50             |
| **Last education**                   |                           |                |
| Elementary school                    | 15                        | 37.5           |
| Junior high school                   | 9                         | 22.5           |
| Senior high school                   | 12                        | 30             |
| Diploma/bachelor degree              | 5                         | 10             |
| **Occupation**                       |                           |                |
| Worked                               | 5                         | 10             |
| Not worked                           | 35                        | 90             |

| Table II. Clinical characteristics of participants |
|-----------------------------------------------------|
| **Characteristics**                                 | Number of subjects (N=40) | Percentage (%) |
| Duration of T2DM                                     |                           |                |
| < 1 year                                            | 4                         | 10             |
| 1-5 years                                           | 36                        | 90             |
| **Number of comorbidities**                         |                           |                |
| 0                                                   | 11                        | 27.5           |
| 1                                                   | 20                        | 50             |
| 2-3                                                 | 9                         | 22.5           |
| **Type of comorbidities**                           |                           |                |
| Hypertension                                        | 17                        | 42.5           |
| Hypercholesterolemia                                | 3                         | 7.5            |
| Hypertension + hypercholesterolemia                 | 6                         | 15             |
| Other                                               | 3                         | 7.5            |
Generally, most participants received the combination of two oral antidiabetic drugs from biguanide (metformin) and sulfonylurea class of therapy (N=29; 72.5%), as shown in Table III. The most common sulfonylurea drugs administered to the patients were glimepiride, used by 31 participants (77.5%). According to the T2DM management guideline in Indonesia, the first-line medication for T2DM is metformin due to its good effectiveness, low hypoglycemia risk, neutral effect on body weight, improved cardiovascular outcome, and low cost. Meanwhile, sulfonylurea monotherapy could cause side effects such as hypoglycemia and body weight gain. Combined antidiabetic therapy is recommended when the glycemic target is not reached. Hence, the high percentage of combination therapy in this study implies that the patients may need more than one antidiabetic medication to achieve the glycemic target.

Table III. Participants’ medication profile

| Characteristics          | Number of subjects (N=40) | Percentage (%) |
|--------------------------|---------------------------|----------------|
| Number of medication     |                           |                |
| 1 oral antidiabetic agent| 8                         | 20             |
| 2 oral antidiabetic agents| 32                        | 80             |
| Type of antidiabetics    |                           |                |
| Metformin                | 5                         | 12.5           |
| Glimepiride              | 2                         | 5              |
| Gliquidone               | 1                         | 2.5            |
| Metformin+glimepiride    | 29                        | 72.5           |
| Metformin+glibenclamide  | 2                         | 5              |
| Glimepiride+gliquidone   | 1                         | 2.5            |

Indonesian National Formulary has a set of criteria that manage the administration and restrictions of the different antidiabetic drug classes. Metformin and specific sulfonylurea agents (glibenclamide, glimepiride, and glipizide) can be administered in primary health care facilities. The availability of these drugs on the national formulary may explain why participants received these drug classes for antidiabetics. Although gliquidone is not listed as the medication for patients in primary health care, it can be administered for the back-referral program. A back-referral program is a health service that provides treatments and medications based on the recommendation of a specialist physician for patients with chronic diseases in primary health care.

Due to the restrictions at the time of the study and the high cases of COVID-19 in the area, we could obtain fasting blood glucose data as the clinical outcome. Besides HbA1c, fasting blood glucose is also one of the monitoring parameters useful in T2DM patients. Compared to HbA1c, fasting blood glucose is a direct, widely accepted, and inexpensive measure. For patients taking oral antidiabetics, blood glucose monitoring also can be considered to assess changes in blood glucose control, monitor the effect of foods on postprandial blood glucose, and changes in blood glucose levels during illness. Before the intervention, participants’ fasting blood glucose levels ranged from 95-295 mg/dL. An analysis of the difference in blood glucose levels across different comorbidities and medications was also conducted (Table IV) to check for any significant differences. However, no characteristics were associated with patients’ blood glucose levels before intervention (p >0.05). It showed that the pre-intervention blood glucose levels were not different among participants of different gender, ages, duration of T2DM, type of comorbidities, and a number of medications. In other words, this means that patients had no difference in baseline blood glucose levels. In contrast, other studies reported otherwise. A study in China suggested that older age and fewer than 12 years of education were associated with poor glycemic control. Meanwhile, another study in Ethiopia found that comorbidities, disease duration (more than seven years), and combination therapy that included insulin were predictors of poor glycemic control in patients with T2DM.

Thirty days after the intervention, patients’ fasting blood glucose levels ranged from 113-364 mg/dL (Table V). This data showed that not all participants successfully achieved the target of blood glucose control. Guidelines released by the American Diabetes Association and the Indonesian Association of Endocrinology (Perhimpunan Endokrinologi Indonesia/PERKENI) recommend that adults with diabetes achieve pre-prandial capillary plasma glucose of 80-130 mg/dL.
Despite an increase in both minimum and maximum levels of fasting blood glucose post-intervention, patients’ fasting blood glucose levels under 130 mg/dL increased from 12.5% to 25% (Table V). The mean and median of this parameter also decreased slightly. However, there was no significant difference between fasting blood glucose levels pre-intervention and post-intervention (p >0.05). Although post-interventional blood glucose was not significantly different from the baseline level, the slight decrease in the mean and median in this study might be worth exploring further. This finding differs from previous studies that documented pharmacists-led interventions could improve patients’ blood glucose control.

In a study in Pakistan\(^3\), the intervention involved pictorial charts and verbal communication related to diabetes management. The patients were followed up one month after the baseline. Meanwhile, in a study in Nigeria\(^3\), the intervention was given in two consecutive face-to-face interviews and educational sessions, with a three-month follow-up period. Other studies in Indonesia suggested that educational videos, patient counseling, and drug information provided by pharmacists could improve patients’ HbA1c\(^34\),\(^35\). However, another study in Indonesia also did not find a significant effect of drug information service on blood glucose levels, despite lower blood glucose levels observed in the intervention group\(^36\). These studies suggested the advantages of using a multimodal educational method for patients, not only relying on direct explanation to significantly affect patients’ blood glucose control. Moreover, glycemic control was also influenced by multiple factors which are not always related to medications, such as dietary control\(^37\), and other physical-related factors, such as BMI and central obesity\(^38\). This study was conducted when the COVID-19 cases were still high in Indonesia, which made more intensive and comprehensive educational provision to patients impossible. Besides, the fasting blood glucose monitoring needs to be accompanied by other glucose monitoring parameters such as HbA1c, as it reflects blood glucose control in the longer term. The sample of this study is also relatively small, which may not be representative of T2DM patients who received care at primary health care facilities in Indonesia. Further studies involving more patients and control groups are needed to examine drug information’s effect in a more robust study design.

**CONCLUSION**

It is concluded that the provision of drug information results in lower blood glucose levels of T2DM patients at Andalas Public Health Center, Padang, Indonesia, even though the effect is not statistically significant.

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AUTHORS' CONTRIBUTION

Lailaturrahmi: conceptualization, methodology, formal analysis, writing – original draft, writing – review & editing, project administration, funding acquisition. Fuji Araswati: investigation, formal analysis, writing – original draft. Armenia: conceptualization, methodology, supervision. Rahmi Yosmar: conceptualization, methodology, writing – review & editing, supervision, funding acquisition.

DATA AVAILABILITY

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Wu Y, Ding Y, Tanaka Y, Zhang W. Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. Int J Med Sci. 2014;11(11):1185-200. doi:10.7150/ijms.10001

2. Soewondo P, Ferrario A, Tahapary DL. Challenges in diabetes management in Indonesia: a literature review. Global Health. 2013;9:63. doi:10.1186/1744-8603-9-63

3. Badan Penelitian dan Pengembangan Kesehatan. Laporan Nasional RISKESDAS 2018. Jakarta: Lembaga Penerbit Badan Penelitian dan Pengembangan Kesehatan; 2018. 198 p.

4. Chentli F, Azzoug S, Mahgoun S. Diabetes mellitus in elderly. Indian J Endocrinol Metab. 2015;19(6):744-52. doi:10.4103/2230-8210.167553

5. Hershon KS, Hirsch BR, Odugbesan O. Importance of Postprandial Glucose in Relation to A1C and Cardiovascular Disease. Clin Diabetes. 2019;37(3):250-9. doi:10.2337/cd18-0040

6. Chaudhury A, Duvoor C, Dendi VSR, Kraleti S, Chada A, Ravilla R, et al. Clinical Review of Antidiabetic Drugs: Implications for Type 2 Diabetes Mellitus Management. Front Endocrinol. 2017;8:6. doi:10.3389/fendo.2017.00006

7. Marín-Peñalver JJ, Martín-Timón I, Sevillano-Collantes C, Cañizo-Gómez FJD. Update on the treatment of type 2 diabetes mellitus. World J Diabetes. 2016;7(17):354-95. doi:10.4239/wjd.v7.i17.354

8. Alqarni AM, Alrahbeni T, Al Qarni A, Al Qarni HM. Adherence to diabetes medication among diabetic patients in the Bisha governorate of Saudi Arabia - a cross-sectional survey. Patient Prefer Adherence. 2018;13:63-71. doi:10.2147/ppa.s176385

9. Aloudah NM, Scott NW, Aljadhay HS, Araujo-Soares V, Alrubaan KA, Watson MC. Medication adherence among patients with Type 2 diabetes: A mixed methods study. PLoS One. 2018;13(12):e0207583. doi:10.1371/journal.pone.0207583

10. Polonsky WH, Henry RR. Poor medication adherence in type 2 diabetes: recognizing the scope of the problem and its key contributors. Patient Prefer Adherence. 2016;10:1299-307. doi:10.2147/ppa.s106821
11. Verville L, Côté P, Grondin D, Mior S, Moodley K, Kay R, et al. Using technology-based educational interventions to improve knowledge about clinical practice guidelines. J Chiropr Educ. 2021;35(1):149-57. doi:10.7899/jce-19-17

12. Alexandra S, Handayani PW, Azzahro F. Indonesian hospital telemedicine acceptance model: the influence of user behavior and technological dimensions. Helyon. 2021;7(12):e8599. doi:10.1016/j.helyon.2021.e8599

13. Shrestha S, Shrestha R, Ahmed A, Sapkota B, Khattiwada AP, Christopher CM, et al. Impact of pharmacist services on economic, clinical, and humanistic outcome (ECHO) of South Asian patients: a systematic review. J Pharm Policy Pract. 2022;15(1):37. doi:10.1186/s40545-022-00431-1

14. Alamri SA, Al Jaizani RA, Naqvi AA, Al Ghamdi MS. Assessment of Drug Information Service in Public and Private Sector Tertiary Care Hospitals in the Eastern Province of Saudi Arabia. Pharmacy. 2017;5(3):37. doi:10.3390/pharmacy5030037

15. Rutter J, Rutter P. Impact of pharmacy medicine information service advice on clinician and patient outcomes: an overview. Health Info Libr J. 2019;36(4):299–317. doi: https://doi.org/10.1111/hir.12270

16. Gatwood JD, Chisholm-Burns M, Davis R, Thomas F, Potukuchi P, Hung A, et al. Impact of pharmacy services on initial clinical outcomes and medication adherence among veterans with uncontrolled diabetes. BMC Health Serv Res. 2018;18(1):855. doi:10.1186/s12913-018-3665-x

17. Negash Z, Berha AB, Shibeshi W, Ahmed A, Woldu MA, Engidawork E. Impact of medication therapy management service on selected clinical and humanistic outcomes in the ambulatory diabetes patients of Tikur Anbessa Specialist Hospital, Addis Ababa, Ethiopia. PLoS One. 2021;16(6):e0251709. doi:10.1371/journal.pone.0251709

18. Coutureau C, Slimano F, Mongaret C, Kanagaratnam L. Impact of Pharmacists-Led Interventions in Primary Care for Adults with Type 2 Diabetes on HbA1c Levels: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2022;19(6):3156. doi:10.3390/ijerph19063156

19. Michiels Y, Bugnon O, Chicoye A, Dejager S, Moisan C, Allaert FA, et al. Impact of a Community Pharmacist-Delivered Information Program on the Follow-up of Type-2 Diabetic Patients: A Cluster Randomized Controlled Study. Adv Ther. 2019;36(6):1291–303. doi:10.1007/s12325-019-00957-y

20. Baker C, Retzik-Stahr C, Singh V, Plomondon R, Anderson V, Rasouli N. Should metformin remain the first-line therapy for treatment of type 2 diabetes? Ther Adv Endocrinol Metab. 2021;12:2042018820980225. doi:10.1177/2042018820980225

21. Kalra S, Das AK, Priya G, Ghosh S, Mehrotra RN, Das S, et al. Fixed-dose combination in management of type 2 diabetes mellitus: Expert opinion from an international panel. J Family Med Prim Care. 2020;9(11):5450-7. doi:10.4103/jfmpc.jfmpc_843_20

22. Ministry of Health Republic of Indonesia. Formularium Nasional. Jakarta: Ministry of Health Republic of Indonesia; 2017.

23. BPJS Kesehatan. Panduan Praktis Program Rujuk Balik Bagi Peserta JKN. Jakarta: BPJS Kesehatan; 2014.

24. Esti AB, Sandra C, Witcahyo E. Back-Referral Program in the Era of National Health Insurance at Balung District General Hospital of Jember in 2017. J Administrasi Kesehat Indonesia. 2019;7(1):33-9. doi:10.20473/jaki.v7i1.2019.33-39

25. Chen J, Wu C, Wang X, Yu J, Sun Z. The Impact of COVID-19 on Blood Glucose: A Systematic Review and Meta-Analysis. Front Endocrinol. 2020;11:574541. doi:10.3389/fendo.2020.574541

26. d’Emden M, McLeod D, Ungerer J, Appleton C, Kanowski D. Development of a fasting blood glucose-based strategy to diagnose women with gestational diabetes mellitus at increased risk of adverse outcomes in a COVID-19 environment. PLoS One. 2020;15(12):e0243192. doi:10.1371/journal.pone.0243192
27. Parrinello CM, Selvin E. Beyond HbA1c and glucose: the role of nontraditional glycemic markers in diabetes diagnosis, prognosis, and management. Curr Diab Rep. 2014;14(11):548. doi:10.1007/s11892-014-0548-3

28. Czupryniak L, Barkai L, Bolgarska S, Bronisz A, Broz J, Cypryk K, et al. Self-monitoring of blood glucose in diabetes: from evidence to clinical reality in Central and Eastern Europe—recommendations from the international Central-Eastern European expert group. Diabetes Technol Ther. 2014;16(7):460-75. doi:10.1089/dia.2013.0302

29. Tao J, Gao L, Liu Q, Dong K, Huang J, Peng X, et al. Factors contributing to glycemic control in diabetes mellitus patients complying with home quarantine during the coronavirus disease 2019 (COVID-19) epidemic. Diabetes Res Clin Pract. 2020;170:108514. doi:10.1016/j.diabres.2020.108514

30. Mamo Y, Bekele F, Nigussie T, Zevudie A. Determinants of poor glycemic control among adult patients with type 2 diabetes mellitus in Jimma University Medical Center, Jimma zone, south west Ethiopia: a case control study. BMC Endocr Disord. 2019;19(1):91. doi:10.1186/s12902-019-0421-0

31. American Diabetes Association. 6. Glycemic Targets: Standards of Medical Care in Diabetes—2019. Diabetes Care. 2019;42(Suppl 1):S61-70. doi:10.2337/dc19-s006

32. Abubakar M, Atif M. Impact of Pharmacist-Led Interventions on Diabetes Management at a Community Pharmacy in Pakistan: A Randomized Controlled Trial. Inquiry. 2021;58:469580211036283. doi:10.1177/00469580211036283

33. David EA, Soremekun RO, Abah IO, Aderemi-Williams RI. Impact of pharmacist-led care on glycaemic control of patients with uncontrolled type 2 diabetes: A randomised controlled trial in Nigeria. Pharm Pract. 2021;19(3):2402. doi:10.18549/pharmpract.2021.3.2402

34. Sauriasari R, Sakti RM. Impact of a pharmacist-led patient education initiative on glycemic control of patients with type 2 diabetes mellitus: A single-center experience in West Jakarta, Indonesia. Int J Appl Pharm. 2018;10(1):252-6. doi:10.22159/ijap.2018.v10s1.56

35. Wibowo MINA, Setiawan D, Ikhwaniati ND, Sukma FA. Pengaruh Konseling dan Alat Bantu Pengingat Pengobatan terhadap Kepatuhan Minum Obat dan Outcome Klinik Pasien Diabetes Melitus dan Hipertensi. J Ilmu Kefarmasian Indones. 2020;18(2):169-76. doi:10.35814/jifi.v18i2.761

36. Insani WN, Lestari K, Abdulah R, Ghassani SK. Pengaruh Pelayanan Informasi Obat terhadap Keberhasilan Terapi Pasien Diabetes Melitus Tipe 2. J Farm Klin Indones. 2013;2(4):127-35.

37. Wireno EHD, Setiawan AA, Hendrianingtyas M, Pramudo SG. Factors Affecting Glycemic Control in Diabetes Mellitus Patients. Sains Med J Kedokt Kesahat. 2021;12(2):1-9. doi:10.30659/sainsmed.v12i2.7620

38. Kakade AA, Mohanty IR, Rai S. Assessment of factors associated with poor glycemic control among patients with Type II Diabetes mellitus. Integr Obes Diabetes. 2018;4(3):1-6. doi:10.15761/IOD.1000209