Original Article

Effect of Pharmacist Intervention on Medication Adherence and Clinical Outcomes of Type 2 Diabetes Mellitus Outpatients in Primary Healthcare in Indonesia

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Abstract

Objective: In Indonesia, the role of pharmacists in primary healthcare is still very limited or even absent. This study evaluates the effectiveness of programs delivered for type 2 diabetes mellitus (T2DM) patients by pharmacists in primary healthcare through counseling, short message service (SMS) reminders, and medication booklets. **Methods:** A quasi-experimental study with a pretest–posttest design was conducted from April to August 2018 at Merdeka and Dempo primary health-care centers, Palembang, South Sumatra Province, Indonesia. Counseling and medication booklets were distributed three times during the study period, while SMS reminders were sent once a week. Counseling was given for the management of diabetes mellitus (DM), including during the Ramadan fasting period, together with management for acute and chronic complications. The medication adherence level was measured using a medication adherence questionnaire (MAQ) and pill count adherence (PCA). The study sample comprised 80 T2DM patients, who were allocated into either the control group (CG) (n = 40) or intervention group (IG) (n = 40). Clinical outcomes were determined by measuring glycated hemoglobin (HbA1c), blood pressure, and lipid profiles. **Findings:** After the intervention, the IG showed significant improvements in most parameters, except for high-density lipoprotein cholesterol and systolic and diastolic blood pressure. HbA1c levels were reduced, while MAQ scores and PCA scores were improved. Lipid parameters were significantly reduced total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), and triglyceride (TG). Compared with the CG, most parameters were significantly improved in the IG. Pharmacist counseling significantly improved almost all clinical parameters (HbA1c, TC, LDL-c, and TG). Pharmacist counseling was 7.1 times greater in lowering HbA1c compared with no counseling, after adjusted by other variables. The variable that most influenced the lowering of HbA1c was infrequent ("not often") consumption of unhealthy foods (OR 14.9; 95% CI 3.5-63.7). **Conclusion:** The pharmacist primary health-care intervention program implemented in this study significantly improved HbA1c, TC, LDL-c, TG, and medication adherence in outpatients with T2DM.

Keywords: *Diabetes mellitus, medication adherence, pharmacist, primary healthcare*

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Introduction

The World Health Organization predicts that the number of people with diabetes mellitus (DM) in Indonesia will increase from 8.4 million in 2000 to 21.3 million by 2030.[1] The majority of DM cases are type 2 diabetes mellitus (T2DM), which occurs when an unhealthy lifestyle (excess calories, inadequate exercise, and obesity) coexists with a susceptible genotype.[2] T2DM is associated with a cluster of risk factors for cardiovascular disease (CVD). Adults with DM have a

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high prevalence of hypertension (77%–87%), elevated low-density lipoprotein cholesterol (LDL-c; 74%–81%), and obesity (62%–67%). The management of modifiable CVD risk factors, such as hyperglycemia, hypertension, dyslipidemia, obesity, cigarette smoking, and physical inactivity, is critical to minimize the risk of macrovascular DM complications. Studies have demonstrated the cardiovascular benefits from stopping smoking, increasing physical activity, decreasing LDL-c values, and lowering blood pressure.[2]

Poor adherence to DM treatment is common among patients and can lead to severe health complications, including increased mortality. The responsibilities of pharmacists include optimization of medical treatment and adherence to medication.[3] A systematic review showed that pharmacist interventions potentially improve adherence to medication for patients with T2DM in different settings, such as face-to-face meetings, group activities, and telephone follow-ups. Adherence to oral hypoglycemic drugs has been reported to be 36%–93%, with adherence to insulin at 63%.[4] DM was the third-most common disease in 2017 in the Merdeka and Dempo primary health-care centers in Palembang, South Sumatra, Indonesia, with 1664 visits by patients with T2DM to the Merdeka Center. Pharmacists are not present at these two primary health-care centers because their placement in health services is not evenly distributed, with most pharmacists working in hospitals and pharmacies. In this study, we developed a pharmacist intervention program comprising counseling, short message service (SMS) reminders, and a medication booklet.

One role of pharmacists that can be effective in improving medication adherence is by providing counseling. However, in Indonesia, the role of pharmacists in primary healthcare, including in DM management, is limited, or even absent, and has not been evaluated. The rationale of this study was to evaluate the effects of a pharmacist intervention program on the management of glycemic control, lipid profile, blood pressure, and adherence to the medication of outpatients with T2DM at the Merdeka and Dempo primary health-care centers. Counseling was given by a pharmacist three times over the 4 months study period for the management of DM, including during Ramadan fasting, and the management of acute and chronic complications. Glycated hemoglobin (HbA1c), total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-c), LDL-c, triglyceride (TG), blood pressure, and adherence were measured at the beginning and end of the study.

Methods

This was a prospective quasi-experimental nonrandomized control study with a pretest–posttest design. It has been registered and approved by the Ethics Committee, Faculty of Medicine, Indonesia University Dr. Ciptomangunkusumo Hospital (No: 0333/UN2.F1/ETIK/2018). Informed consent was collected from all the participants before participation, and the study was conducted at the Merdeka and Dempo primary health-care centers.

The consecutive sampling method was used, with the sample size calculated based on HbA1c variability in patients with T2DM, with Z $\alpha/2 = 1.64$ and Z $\beta = 0.84$[5] The minimum number of samples required was 32 for each group. To account for dropout, the number of samples was increased by 20%, making 40 samples for each group. Inclusion criteria for the study were patients diagnosed with T2DM, use of pharmacological therapy for at least 2 months before the study, age ≥20 years, fasting during Ramadan, and willingness to participate. Exclusion criteria were pregnant and lactating females, those taking birth control hormonal drugs, patients with severe disease (coronary heart disease, stroke, chronic kidney disorders), mental illness, illiteracy, and recent blood transfusion and receiving of hemodialysis. After recruitment, patients were assigned to either the intervention group (IG) or the control group (CG). Intervention was performed by a pharmacist, and patients in the IG received counseling, a booklet, and SMS reminders. Patients in the CG did not receive intervention. The primary endpoints of the study included HbA1c levels.

Participants were assigned into two groups, IG or CG, and received a questionnaire entitled "Sociodemography and Therapy for Type 2 Diabetes Mellitus Patients," a medication adherence questionnaire (MAQ), and a pill count adherence (PCA) questionnaire. The CG (at the Dempo Primary Healthcare Center) did not receive intervention, whereas the IG (at the Merdeka primary health-care center) received pharmacist counseling, SMS reminders, and a medication booklet. HbA1c, lipid profile, and blood pressure were measured at the beginning and end of the study. Counseling was given three times over the 4 months study period, except during Ramadan.

At the start of the intervention, this focused on the management of T2DM (appropriate self-blood glucose monitoring, the purpose of management, management steps, incentives for adherence) and management of DM during Ramadan fasting (risks of fasting with diabetes, more frequent blood sugar level monitoring,

recommended treatment regimen for patients with T2DM who are fasting). In the second month of the intervention, counseling included the management of acute and chronic complications of DM. Finally, in the 3rd month, counseling covered the management of comorbid complications of the disease. Face-to-face interviews were held once every month and SMS reminders (medication reminders, dosing, and administration) sent out once a week until the end of the study period. The reminders included the dosage of DM drugs that must be taken every day according to the doctor's prescriptions and how to use these (e.g., metformin taken immediately after meals or with food). During the face-to-face interviews, the pharmacist discussed medication adherence, self-monitoring of glycemic control, lifestyle modification (exercise, avoidance of unhealthy foods, and smoking) with each patient and explained the side effects and possible drug interactions. Patients were also reminded about their next scheduled visit. After the interview, individual medical history files were maintained for each patient.

Medication adherence was assessed by PCA as the percentage of patient compliance and was calculated as the number of drugs consumed/number of drugs given × 100%. In cases of overuse (calculation result >100%), the patient compliance percentage was calculated as the difference in the amount of drugs consumed minus the excess amount of drug consumed × 100%. Assessment of compliance was performed using the results of the calculation (<80%, not compliant; 80%–100%, compliant).[6] The MAQ scale is based on the belief that drug omission errors can occur when patients are forgetful, careless, or stop taking medication when feeling better or worse. Because patients generally want to answer "yes" when asked questions, they were worded in such a way that answering yes indicated nonadherent behaviors. The MAQ completed during the interview comprised four questions: (1) Did you forget to take medication in the past week?; (2) Were you careless about taking your medicine during the past week?; (3) Did you stop taking your medicine when you felt better in the past week?; and (4) If you felt worse when you took your medicine, did you stop taking it during the past week? Patients received a score of either one or zero for each question when they answered either "yes" or "no," respectively. For each patient, scores ranged from zero to four, with zero representing high adherence and four non-adherence.[7,8]

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) from IBM Corp., released 2013, specifically IBM SPSS Statistics for Windows, Version 22.0. IBM Corp., Armonk, NY, USA. Values of $P < 0.05$ were considered statistically significant, and data were presented as mean ± standard deviation (SD). Pre-test and post-test differences were compared using the Chi-square test, Pearson's exact test, and dependent *t*-test if the data were normally distributed, and the Wilcoxon sign test if they were not normally distributed. IG and CG differences were compared using an independent *t*-test if the data were normally distributed, or the Mann–Whitney test if they were not normally distributed. Multivariate analysis was conducted to determine the relationship between confounding variables using a binomial logistic regression test.

Results

Eighty participants were recruited, who were divided into two groups: IG ($n = 40$) and CG ($n = 40$). All 80 completed the study [Figure 1]. Their baseline demographic characteristics are shown in Table 1. There were no significant relationships between age, sex, education level, occupation, and body mass index (BMI) in the IG, and there was no significant difference between the IG and the CG ($P > 0.05$). The majority of participants were not geriatric and were aged between 41 and 60 (70%), were mostly female (55%), and had secondary level education (48.75%). Their baseline clinical characteristics are shown in Table 1. There were no significant differences between the IG and the CG ($P > 0.05$), except for reminders to take medicine.

The results of the clinical outcomes of HbA1c, TC, HDL-c, LDL-c, TG, and blood pressure are summarized in Table 2. HbA1c, TC, LDL-c, TG, and medication adherence (MAQ and PCA) improved significantly in the IG. On the contrary, the CG showed a decrease in medication adherence and an increase in clinical outcomes, such as HbA1c, TC, and LDL-c.

Analysis of the post-test results showed that medication adherence, in terms of HbA1c, TC, and LDL-c, was better in the IG than the CG ($P < 0.05$). The MAQ results showed that the levels of adherence had improved by the end of the intervention in the IG ($P < 0.05$). Conversely, there was a decrease in medication adherence ($P < 0.001$) in the CG [Table 2]. Multivariate analysis showed that after correcting for the use of herbal medicines, infrequent ("not often") consumption of unhealthy food, and MAQ compliance, pharmacist counseling showed a 7.1-fold greater chance of changing patients' HbA1c compared to those who were not counseled [Table 3]. The most influential variable for changes in HbA1c was infrequent ("not often") consumption of unhealthy food, which showed a 14.9-fold improvement in HbA1c compared with

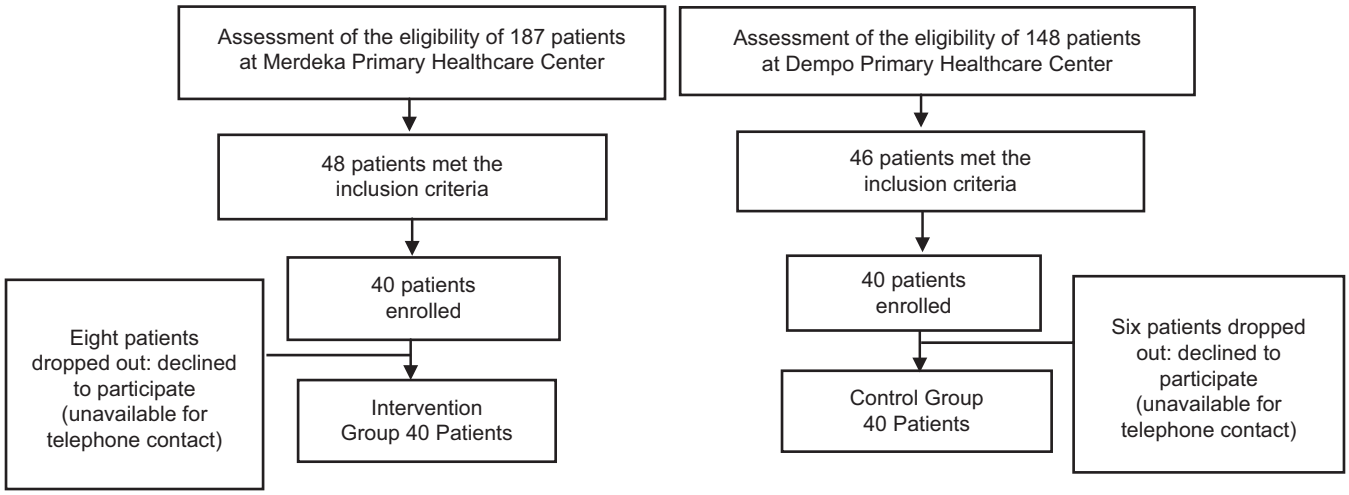

Figure 1: Flowchart of participants selected for the study

frequent ("often") consumption, after correcting for counseling, use of herbal medicines, and MAQ compliance [Table 3].

Table 4 shows that pharmacist counseling is very beneficial because it significantly improves almost all clinical parameters (HbA1c, TC, LDL-c, and TG.

Discussion

Approximately 425 million adults (aged 20–79 years) are currently living with DM, and this number is expected to increase to 629 million by 2045. The proportion of people with T2DM is increasing in most countries, with 79% of adults with diabetes living in low- and middle-income countries, such as Indonesia.[9]

People with diabetes should receive health care from an interdisciplinary team that may include physician, nurses, dietitians, exercise specialists, mental health professionals and pharmacist.[10]

In this study, basic characteristics including age, gender, level of education, working status, weight, height, BMI, DM information from the mass media, and DM information from the health service provider showed no significant difference between the two groups ($P > 0.05$). There were no patients aged 20–40 years in the IG, and this group contained more patients aged 40–60 years than the CG (77.5% vs. 62.5%). This was also associated with a 30% increase in muscle fat levels, which may have led to an increased occurrence of insulin resistance.[11]

The mean BMI of patients was higher in the IG than the CG but was not statistically significant. Obesity is one of the most important risk factors for T2DM, whose basic cause is an imbalance between energy intake and expenditure.[12] Weight loss in patients with T2DM can reduce CVD risk and improve the quality of life.[2] Epidemiological studies have shown that obesity is the most important risk factor for T2DM and may influence the development of insulin resistance and disease progression.[11]

A total of 15 patients (37.5%) in the CG reported that they were reminded to take medication, whereas only 5 (12.5%) in the IG received such reminders. The presence of a family member that prepared the patient's medicine also improved patient compliance because the majority of patients were aged 40–60 years, which may be a factor in forgetting to take medication.

Most of the participants' duration of DM drug use had been for more than two years, using DM therapy and is a combination of two drugs (metformin and glimepiride). According to the doctor in the health-care provider, the patients had experienced complications (hypertension and dislipidemia in the IG was 72.5% and 70% in the CG). HbA1c was 9.78% in the IG before the intervention. High HbA1c values also indicate non-adherence to taking medication and uncontrolled blood glucose, in addition to lifestyle.

There were no differences in lifestyle characteristics between the IG and CG, apart from smoking habits [Table 1]. Patients with T2DM are recommended to participate in low-intensity aerobic physical activity that is rhythmic, repetitive, and uses continuous movements of the muscles (for example, brisk walking, jogging, swimming, or cycling)[13] 3–5 times per week, for a minimum of 150 min/week.[14]

Several studies have shown a 60% reduction in glycogen synthesis due to changes in glucose transport and hexokinase II activity. Discharge of glucose is supported by a lack of phosphorylation of insulin receptor substrate-1 (IRS-1), insulin receptor substrate-2 (IRS-2) or phosphoinositide-3 kinase in response to muscle

Table 1: Baseline demographics, clinical charasteristics and lifestyle of participants

Characteristic	Intervention group (*n*=40)	Control group (*n*=40)	Total (*n*=80)	Inter-group *P*
Age (years)	56.52±6.00	57.17±7.82	56.85±6.93	0.653[a]
20-40	0 (0)	2 (5)	2.5 %	0.185[a]
41-60	31 (77.5)	25 (62.5)	56 (70)	
>60	9 (22.5)	13 (32.5)	27.5 %	
Gender				
Male	19 (47.5)	17 (42.5)	36 (45)	0.653[a]
Female	21 (52.5)	23 (57.5)	44 (55)	
Level of education				
Primary	17 (42.5)	15 (37.5)	32 (40)	0.792[a]
Secondary	18 (45)	21 (52.5)	39 (48.75)	
University degree or above	5 (12.5)	4 (10)	9 (11.25)	
Working status				
Yes	19 (47.5)	21 (52.5)	40 (50)	0.655[a]
No	21 (52.5)	19 (47.5)	40 (50)	
BMI (kg/m^2)	23.34±3.19	22.51±3.10	22.92±3.15	0.246[b]
DM information from mass media				
Yes	25 (62.5)	26 (65)	51 (63.75)	1.000[a]
No	15 (37.5)	14 (35)	29 (36.25)	
DM information from health service provider				
Yes	10 (25)	3 (7.5)	13 (16.25)	0.069[a]
No	30 (75)	37 (92.5)	67 (83.75)	
Duration of DM drug use (months)				
<12	11 (27.5)	3 (7.5)	14 (17.5)	0.059[a]
12-24	6 (15)	9 (22.5)	15 (18.75)	
>24	23 (57.5)	28 (70)	51 (63.75)	
Number of DM drugs				
Single drug	18 (45)	17 (42.5)	35 (43.75)	0.564[a]
Combination of two drugs	22 (55)	23 (57.5)	45 (56.25)	
Metformin (500 mg)	18 (45)	14 (35)	32 (40)	
Glimepiride (1 mg)	0	1 (2.5)	1 (1.25)	
Glibenclamide (5 mg)	0	2 (5)	2 (2.5)	
Metformin (500 mg) + Glimepiride (1 mg)	13 (32.5)	10 (25)	23 (28.75)	
Metformin (500 mg) + Glimepiride (2 mg)	2 (5)	0	2 (2.5)	
Metformin (500 mg) + Glibenclamide (5 mg)	2 (5)	13 (32.5)	15 (18.75)	
Acarbose 50 (mg) + Glimepiride (1 mg)	4 (10)	0	4 (10)	
Metformin (500 mg)+Gliclazide (80 mg)	1 (2.5)	0	1 (1.25)	
Other disease				
Yes	6 (15)	4 (10)	10 (12.5)	0.499[a]
No	34 (85)	36 (90)	70 (87.5)	
Complications				
Yes	29 (72.5)	28 (70)	57 (71.25)	0.805[a]
No	11 (27.5)	12 (30)	23 (28.75)	
Other therapy				
Yes	29 (72.5)	27 (67.5)	56 (70)	0.805[a]
No	11 (27.5)	13 (32.5)	24 (30)	
Allergy of drugs				
Yes	1 (2.5)	0	1 (1.25)	0.314[a]
No	39 (97.5)	40 (100)	79 (98.75)	
Reminder to take medicine				
Yes	5 (12.5)	15 (37.5)	20 (25)	0.020[a]*
No	35 (87.5)	25 (62.5)	60 (75)	
Prepare medicine				
Yes	3 (7.5)	3 (7.5)	6 (7.5)	1.000[a]
No	37 (92.5)	37 (92.5)	74 (92.5)	

Contd...

Table 1: Contd...

Characteristic	Intervention group (*n*=40)	Control group (*n*=40)	Total (*n*=80)	Inter-group *P*
History of DM				
Yes	20 (50)	28 (70)	48 (60)	0.110[a]
No	20 (50)	12 (30)	32 (40)	
History of obesity				
Yes	8 (20)	3 (7.5)	11 (13.75)	0.194[a]
No	32 (80)	37 (92.5)	69 (86.25)	
History of hypertension				
Yes	20 (50)	26 (65)	46 (57.5)	0.258[a]
No	20 (50)	14 (35)	34 (42.5)	
History of dyslipidemia				
Yes	10 (25)	12 (30)	22 (27.5)	0.802[a]
No	30 (75)	28 (70)	58 (72.5)	
Unhealthy food consumption				
Not often	16 (40)	11 (27.5)	27 (33.75)	0.344[a]
Often	24 (60)	29 (72.5)	53 (66.25)	
Smoking				
Yes	1 (2.5)	13 (32.5)	14 (17.5)	0.002[a]
No	34 (85)	25 (62.5)	59 (73.75)	
Smoked	5 (12.5)	2 (5)	7 (8.75)	
Use of herbal medicines				
Yes	16 (40)	8 (20)	24 (30)	0.088[a]
No	24 (60)	32 (80)	56 (70)	
Physical activity				
Active	26 (65)	18 (20)	34 (42.5)	0.116[a]
Inactive	14 (35)	22 (80)	36 (57.5)	

**P*-value by Chi-square test, [a]Chi-square test, [b]Mann-Whitney test. Data were presented as *n* (%) or mean±SD. *P*=Significance, DM=Diabetes mellitus, BMI=Body mass index, SD=Standard deviation

Table 2: Comparison of clinical parameters in both groups

Variable	Intervention group (*n*=40)			Control group (*n*=40)			*P*[c]	*P*[d]
	Pretest	Posttest	*P*[a]	Pretest	Posttest	*P*[b]		
HbA1c (%)	9.78±2.35	9.00±1.78	0.001*	9.78±1.72	9.95±1.70	<0.001	0.600	0.027
TC (mg/dL)	222.42±46.41	196.42±26.31	<0.001*	206.8±43.62	215.65±41.69	<0.001	0.125	0.008
HDL-c (mg/dL)	40.77±15.10	43.2±14.57	0.353	48.375±12.01	46.12±12.17	0.193	0.015	0.282
LDL-c (mg/dL)	144±38.20	119.82±26.43	<0.001*	128.37±36.14	135.42±36.41	0.011	0.114	0.012
TG (mg/dL)	184.82±103.68	161.52±81.88	0.009*	161.65±69.018	171.4±67.932	0.172	0.613	0.186
SBP (mmHg)	129.37±17.98	125.75±6.75	0.160	131.75±14.30	127.67±10.09	0.03*	0.312	0.682
DBP (mmHg)	82.5±8.69	80.5±3.88	0.124	82.8±6.85	80.75±4.74	0.014*	0.963	0.975
MAQ score	1.02±1.14	0.42±0.63	0.003*	1.17±0.93	1.62±0.86	<0.001*	0.242	0.000
PCA	74.52±4.54	91.57±4.90	<0.001*	73.57±7.95	78.97±8.11	<0.001	0.007*	<0.001*

**P*-value by *t*-test. Data were presented as mean±SD. [a]Before versus after intervention for IG, [b]Before versus after intervention for CG, [c]IG versus CG after intervention, [d]IG versus CG after intervention. *P*=significance, SD=Standard deviation, HbA1c=Glycated hemoglobin, HDL-c=High density lipoprotein-cholesterol, LDL-c=Low density lipoprotein-cholesterol, TG=Triglyceride, TC=Total cholesterol, DBP=Diastolic blood pressure, SBP=Systolic blood pressure, MAQ=Medication Adherence Questionnaire, PCA=Pill count adherence

contraction, thus explaining the increase in glucose use in response to physical activity in patients with T2DM. In patients with well-controlled diabetes, physical exercise increases the utilization of blood glucose and free fatty acids in the muscles and lowers blood glucose levels. In addition, long-term, gentle jogging regularly improves the action of insulin.

The IG tended to have a good lifestyle in terms of physical activity, smoking habits, and unhealthy food consumption compared with the CG. There were no baseline significant differences in unhealthy food consumption habits between the two groups. The types of unhealthy food covered in the questionnaire included junk food (e.g., pizza, burgers, and fried chicken), sweet

Table 3: Multiple regression analysis of factors influencing glycated hemoglobin

Model	Variable	Type of OR	OR	95% CI		*P*
				Lower	Upper	
Model 1	Counseling					
	Intervention	Crude	16.333	5.143	51.872	<0.001
Model 2	Counseling					
	Intervention	Adjusted	7.107	1.794	28.154	0.005
	Use of herbal medicines					
	Yes		4.177	0.932	18.717	0.062
	Unhealthy food consumption					
	Not often		14.923	3.498	63.666	<0.001
	MAQ compliance					
	Obedient		1.602	0.327	7.845	0.561

**P*-value by binominal logistic regression test. *P*=Significance of different tests, OR=Odds ratio, CI=Confidence interval, MAQ=Medication adherence questionnaire, HbA1c=glycated hemoglobin

foods, fried foods, coconut milk, salted food (e.g., salted fish and salted eggs), preserved foods (e.g., instant noodles, canned sardines, and corned beef), flavoring (e.g., vitamins, shrimp paste, soy sauce, and sauce), soft drinks (e.g., soda and soft drinks), sugar-free coffee/tea, and sweet drinks (e.g., coffee, tea, syrup, and instant coffee). A reduction in unhealthy food consumption is expected to reduce HbA1c and blood pressure and improve lipid profiles in patients.

Herbal medicines used by the patients included Habbatus Sauda, *Archidendron pauciflorum* stems, bay leaves, bitter herbs, African leaves, red betel vine, *Tinospora crispa* (L) mulberry leaves, lime, turmeric, and mangosteen peel. The patients reported irregular use of these herbal medicines while continuing to take diabetes drugs [Table 1].

In this study, HbA1c, TC, TG, LDL-c, MAQ scores, and PCA were significantly improved after the 4-month pharmacist intervention. In contrast, HbA1c, TC, LDL-c, and MAQ scores were worse in the CG, although systolic blood pressure and PCA were slightly improved.

HbA1c was significantly reduced (7.98%) in the IG [Table 2], despite the intervention only lasting 4 months. This result was similar to those of previous studies, which have shown a significant decrease in HbA1c, ranging from 0.69% to 1.70%, after pharmacist counseling.[3,7,15,16] Another study conducted by Wishah Ruba *et al*.[17] showed a decrease in HbA1c from 8.9% to 7.2% (1.7%) after a 6 month pharmacist intervention in the IG group. However, the HbA1c value did not reach the controlled category after the intervention, while the cCG showed a decrease in HbA1c from 8.2% to 7.9% (a mean decrease of 0.3%). A similar study conducted by Butt *et al*.[15] showed a significant 1.19% decrease in HbA1c after 6 months of counseling by pharmacists another longer intervention study conducted by Mehuys *et al*.[18] for 24 months showed a 0.6% decrease in HbA1c levels. HbA1c values can predict diabetes complications as they reflect glycation sequelae, such as retinopathy and nephropathy, which occur as the result of dangerous end product replication. Since HbA1c measures the average glycemic value over the previous 2–3 months, it is an indicator of overall glucose exposure, which integrates fasting blood glucose and postprandial blood glucose.[19]

TC, LDL-c, and TG levels decreased significantly in the IG, whereas they increased in the CG [Table 2]. Similar studies have also shown a significant 0.24 mmol/L reduction in TC after pharmacist counseling.[7,17,20] However, there was no significant change in HDL-c levels in the IG. Similar findings were also reported in a Brazilian study conducted by Plaster *et al*.,[21] who found that intervention led to a decrease in LDL-c levels from 149 to 111 mg/dL. Dyslipidemia is very common in patients with T2DM and is characterized by high TG concentrations, low HDL-c concentrations, and increased LDL-c concentrations.[2]

A systematic literature review and meta-analysis by van Eikenhorst *et al*.[22] reported that pharmacist interventions improved HbA1c levels by an average of 0.71% ($P < 0.0001$) and had a positive effect on blood pressure (systolic, −5.20 mmHg; diastolic, −3.51 mmHg) and lipids (TC, −0.19 mmol/L; LDL-c, −0.16 mmol/L; and HDL-c, 0.32 mmol/L).

MAQ showed that adherence was significantly increased in the IG but was not evident in the CG [Table 2]. A similar study conducted by Shao *et al*.[7] using the Morisky Medication Adherence Scale (MMAS) questionnaire showed a significant 0.05 point increase in medication compliance scores following intervention. PCA scores also increased in the IG [Table 2]. These results provide clinical evidence that counseling by pharmacists plays a positive role in medication adherence. Pharmacist counseling is 16.3 times more likely to lead to changes in patients'

Table 4: Clinical Outcomes in category

Clinical parameters	Clinical outcomes			OR	95% CI	Inter-group *P*
	Decrease	Undecrease	Total			
HbA1c						
IG	28 (70)	12 (30)	40 (100)	16.33	5.14-51.87	<0.0001*
CG	5 (12.5)	35 (87.5)	40 (100)			
TC						
IG	34 (85)	6 (15)	40 (100)	26.71	8.11-87.89	<0.0001*
CG	7 (17.5)	33 (82.5)	40 (100)			
HDL-c						
IG	18 (45)	22 (55)	40 (100)	0.904	0.37-2.17	1.000
CG	19 (47.5)	21 (52.5)	40 (100)			
LDL-c						
IG	30 (75)	10 (25)	40 (100)	7.90	2.91-21.433	<0.0001*
CG	11 (27.5)	29 (72.5)	40 (100)			
TG						
IG	25 (62.5)	15 (37.5)	40 (100)	3.09	1.24-7.706	0.025*
CG	14 (35.0)	26 (65.0)	40 (100)			
SBP						
IG	15 (37.5)	25 (62.5)	40 (100)	1.58	0.61-4.066	0.474
CG	11 (27.5)	29 (72.5)	40 (100)			
DBP						
IG	12 (30.0)	28 (70.0)	40 (100)	2.02	0.7-5.829	0.293
CG	7 (17.5)	33 (82.5)	40 (100)			

**P* value by Chi-square test. Data were presented as *n* (%). *P*=Significance of different tests, IG=Intervention group, CG=Control group, DBP=Diastolic blood pressure, SBP=Systolic blood pressure, HbA1c=Glycated hemoglobin, HDL-c=High density lipoprotein-cholesterol, LDL-c=Low-density lipoprotein-cholesterol, TC=Total cholesterol, TG=Triglyceride

HbA1c compared to those who do not receive counseling. Furthermore, after correcting for the use of herbal medicines, infrequent ("not often") consumption of unhealthy food, and MAQ compliance, pharmacist counseling showed a 7.1-fold greater chance of changing patients' HbA1c compared to those who were not counseled [Table 3].

Clinical outcomes in categories were based on decrease and increase from clinical parameters showed a greater decrease in HbA1c, TC, LDL-c, TG in IG than CG [Table 4].

Compliance with treatment is 1.6 times more likely to cause changes in patients' HbA1c compared to those who do not adhere to treatment. The most influential variable for changes in HbA1c was infrequent ("not often") consumption of unhealthy food, which showed a 14.9-fold improvement in HbA1c compared with frequent ("often") consumption, after correcting for counseling, use of herbal medicines, and MAQ compliance [Table 3].

The medication adherence level was measured using a MAQ and PCA questionnaire. MAQ is the quickest scale to administer and the simplest for clinicians to score when compared to other methods such as the brief medication questionnaire (BMQ), the Self Efficacy for Appropriate Medication Use Scale, the Hill-Bone Compliance Scale or the Medication Adherence Report Scale. MAQ also has been validated in patients with dyslipidemia, human immunodeficiency virus infection, Parkinson's disease, depression, T2DM, heart failure, and coronary artery disease, and also in patients with low literacy; it is the most widely used scale for research. This adherence scale is a reasonable option to readily and consistently detect patient nonadherence at the point of care.[23]

The study did not use the Eight-Item MMAS 8 because a permit had not been applied for. This scale is based on the MAQ, and was developed by Morisky *et al*. The additional items focus on medication-taking behaviors, especially related to underuse, such as forgetfulness, so barriers to adherence can be identified more clearly.[24]

Because the MAQ test is subjective, being only based on patients' answers, the PCA test was employed. In this test, adherence to the taking of medication can be seen by researchers from the rest of the drug consumed by the patient. If there was the rest of the drugs consumed, it means that the patient was nonadherence. The reason for nonadherence was that patients experienced metformin side effects (diarrhea and gastritis), and the researcher suggested that doctors use acarbose. Another problem is that patients may feel cured and stop taking taking their medication because of poor knowledge and

wrong information about DM and financial problems meaning patients were using health services irregularly. Researcher have provided counseling that T2DM patients should take medication regularly to prevent complications. Continuous education from DM health service providers is needed which DM is a chronic disease and involves pharmacists in the treatment of DM patients.

This study has limitations, the MAQ questionnaire is subjective, which may affect the objectivity of the compliance scores, and all patients in the IG only received intervention for 4 months, which is a relatively short period.

The results of the study show that pharmacist counseling, SMS reminders, and the medication booklet were effective in improving medication adherence and clinical outcomes, such as HbA1c, TC, LDL-c, and TG in T2DM outpatients. Further longer-duration studies, using the MAQ MMAS 8 and multicenter randomized clinical trials, are recommended to confirm our findings.

Authors' contribution

Nani Apriani Besemah was involved in the study design, literature search, sociodemographic and clinical data collection, study interventions, statistical data processing and analysis, manuscript compilation, and manuscript editing. Ratu Ayu Dewi Sartika was involved in the study design, definition of the operational study, statistical analysis, manuscript editing, and manuscript review, while Rani Sauriasari was involved in the concept and design of the study, definition of the operational study, statistical analysis, manuscript editing, and manuscript review.

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Conflicts of interest

There are no conflicts of interest.

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