

A Review of Pharmacist-led Interventions on Diabetes Outcomes: An Observational Analysis to Explore Diabetes Care Opportunities for Pharmacists

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ABSTRACT

A strict and adherence treatment is required by the patient with diabetes mellitus and it demands a proper self-medication by the patient. Pharmacists are involved in providing self-management support to the patients. This review evaluates the interventions of pharmacist for patients to improve self-management with diabetes mellitus and also to improve the clinical outcomes of diabetes mellitus. A comprehensive literature search was performed by using different keywords “pharmacist-led intervention,” “diabetes,” “effect of pharmacist on outcome of diabetes,” and “self-management of diabetes” with the help of various electronic databases such as PubMed, Science Direct, Embase, Web of Science, and the Cochrane Library from the beginning of the database through September 2018. The primary outcome was glycated hemoglobin (HbA1c), whereas the secondary outcomes were blood glucose level, blood pressure (BP) measure, body mass index, lipids, adherence to medication, and quality of life. Twenty-five studies comprising 2997 diabetic patients were included in the analysis. Pharmacist-led intervention was involved in all included studies in the form of education on diabetes and its complications, medication adherence, lifestyle, and education about self-management skills. Pharmacist-led interventions are able to reduce HbA1c levels with a mean of 0.75%. Most studies do not expose the material and methods used in pharmacist-led intervention. The variation in the reduction of HbA1c, fasting blood sugar, BP, and lipid profile was due to the lack of this standardization. The included studies indicated that pharmacist-led interventions in diabetes mellitus can significantly improve the outcomes of diabetes mellitus and its complication later on. Hence, these long-term improvements in outcomes added more value of pharmacists in health-care system of the world.

KEYWORDS: *Blood pressure, body mass index, diabetes mellitus, diabetic complications, glycated hemoglobin, lipid profile, pharmacist intervention*

INTRODUCTION

Diabetes mellitus is a complicated metabolic disorder. The management of diabetic mellitus is very difficult and it became a persisted task all over the world. The prevalence of type 2 diabetes is continuously increasing throughout the globe.^[1] The risk of diabetes incidence/progression in adults is more in developing countries such as in Malaysia.^[2] The National Health and Morbidity Survey (NHMS) Malaysia 2011

reported diabetes prevalence more than 20.8% in the age of 30 years and above.^[3] The development of diabetic microvascular and macrovascular complications is usually due to poor control of diabetes mellitus. Proper glycemic control plays a vital role in decreasing the

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chances to develop complications in patients.^[4-6] In order to achieve the targeted glycemic control, the patient awareness and compliance toward the treatment is really important.^[7]

Patient-oriented management interventions led by physicians, pharmacist, nurses, dieticians, and diabetes educators have been proven to improve the outcomes among patients with diabetes.^[8-10] The awareness and compliance toward the treatment of diabetes can be increased by giving proper counseling to the patient with the help of health-care providers: physicians, nurses, and pharmacists.^[11-14] Looking into the past, numerous reviews have proven that the contribution of pharmacists in achieving better control of diabetes is significant.^[14-16] These reviews focused on many types of pharmacist interventions including self-care-related interventions, adherence, and compliance or on counseling but always resulted in a significant effect on the outcomes of diabetes mellitus.

In Malaysia, a pharmacist is keenly involved in patient counseling.^[10] The Malaysian picture concerning about the management of diabetes mellitus and the future projections to decrease its prevalence, Health ministry identified the improved management of diabetes as a key strategic priority. Within the Malaysia, there is currently a policy to use clinical pharmacists more efficiently in all tertiary hospitals in the form of DMTAC (Diabetes Medication Therapy Adherence Clinic) department. It was established in 2014 to improve the clinical outcomes of diabetes in the presence of clinical pharmacist.^[10]

Recently published studies reveal that pharmacist intervention can improve the outcome of the disease in the form of glycated hemoglobin (HbA1c), fasting blood sugar (FBS), body mass index (BMI), cardiovascular (CV) incidences, blood pressure (BP) measure, and lipid profile.^[8,9,12] To date, however, no systematic reviews have focused on the effectiveness of DMTAC department and pharmacist-led intervention in Malaysia on the outcome of the disease in the form of HbA1c, FBS, BMI, CV incidences, BP measure, and lipid profile. The main aim of this narrative and systematic review is to evaluate the effectiveness of pharmacist-led interventions on clinical outcomes of diabetes mellitus and prevention of diabetes-related complications in patients.

MATERIALS AND METHODS

Study design

The guidance for this review study was taken from Cochrane Handbook and it is in line with the preferred reporting items for systematic reviews and meta-analyses statement. Keywords used to find database studies were as follows: “diabetes,” “pharmacist-led intervention,”

“intervention,” and “randomized controlled trial.” Databases used included the PubMed, Web of Science, ScienceDirect, ProQuest, Scopus, and Ovid MEDLINE. Searches were restricted to English language and type 1 and type 2 diabetes mellitus articles only which were published from January 2012 to September 2018. The facts and results from the search are presented as a narrative review.

Inclusion criteria

The inclusion criteria of the study were as follows:

1. If the study population was diagnosed with diabetes mellitus other than gestational diabetes mellitus (GDM).
2. If the involvement of pharmacist, or a member of the pharmacy team, is there to do intervention.
3. If the data on one or more outcome measures were reported, for example, HbA1c in both the control and intervention groups.
4. If the study design was a randomized controlled trial.
5. The full original research was published in English.
6. If the study was original study and published in a peer-reviewed journal.

Exclusion criteria

The exclusion criteria of the study were as follows:

1. Studies contain patients with GDM.
2. Non-pharmacist interventions.
3. If the study design was not a randomized controlled trial.
4. The full original research that was not published in English.

Data extraction

The data that were extracted from the studies include demographic features, study participants, follow-up dates and times, and number and duration of follow-up pre- and post-interventions. The description of the intervention includes counseling on diabetes education, quality of life, medication details, lifestyle, patient compliance toward the treatment, and clinical outcomes (HbA1c, fasting and random blood glucose levels, BP, BMI, and lipid profile).

The biasness risk in original research studies was measured with the Cochrane risk-of-bias tool (RoB 2.0). This assessment was verified again by researchers and co-researchers by measuring the risk of bias in original research studies. Any divergences were deliberated till consensus was reached.

Data synthesis and analysis

Pharmacist interventions were evaluated in all the included studies. Outcomes in the form of HbA1c,

random and fasting glucose levels, BP, BMI, and lipid profiles were evaluated in all included studies. The results for these outcomes were combined and presented in a meta-analysis.

Meta-analyses were accomplished with the help of Review Manager 5.3 via a random effects model as clinical heterogeneity was there in included studies. Subgroup analyses were also conducted for the outcomes such as HbA1c, follow-up time, and baseline HbA1c 7% to explain any heterogeneity (I^2) and to explore key intervention components in all the studies. Sensitivity analyses were conducted to check the strength of the results for included studies with a group randomization design and studies with a high risk of biasness which can affect the outcome, that is, HbA1c.

Results for all the outcomes in the form of HbA1c, FBS, BMI, CV incidences, BP measure, and lipid profile were described accordingly.

RESULTS

From the E-database searches, a total of 5828 studies were identified. Of these, 3889 were categorized as unique studies. After the initial screening by title and abstract, 3820 references were omitted as they were not found in line with the inclusion criteria. The full texts of 59 papers were evaluated, and finally 25 papers were included in the review process. See Figure 1 for extended data extraction information.

The main characteristics and study population along with outcomes of the included studies are presented in Table 1.

All the included studies were randomized controlled trials. Out of included 25 studies, six studies were published in 2016, four in 2011, four in 2012, three in 2013, three in 2010, two in 2017, and one in 2009, 2016, and 2018 each. Five studies were conducted in Malaysia followed by five studies in the USA. Two studies were conducted in Jordan and two in Iran, followed by one in Pakistan, Cyprus, the United Kingdom, Belgium, Hong Kong, Portugal, Nigeria, Brazil, and China each. All studies focus on type 2 diabetes mellitus. The study duration for most of the studies was 1 year, followed by 6 months, 5 months, and 9 months. The minimum follow-up was two visits, whereas the maximum follow-up was eight visits.

DISCUSSION

In all the included studies, the interventions were provided by trained pharmacist alone or by the department of pharmacy. Most of the included studies targeted individual diabetic patients. On the other

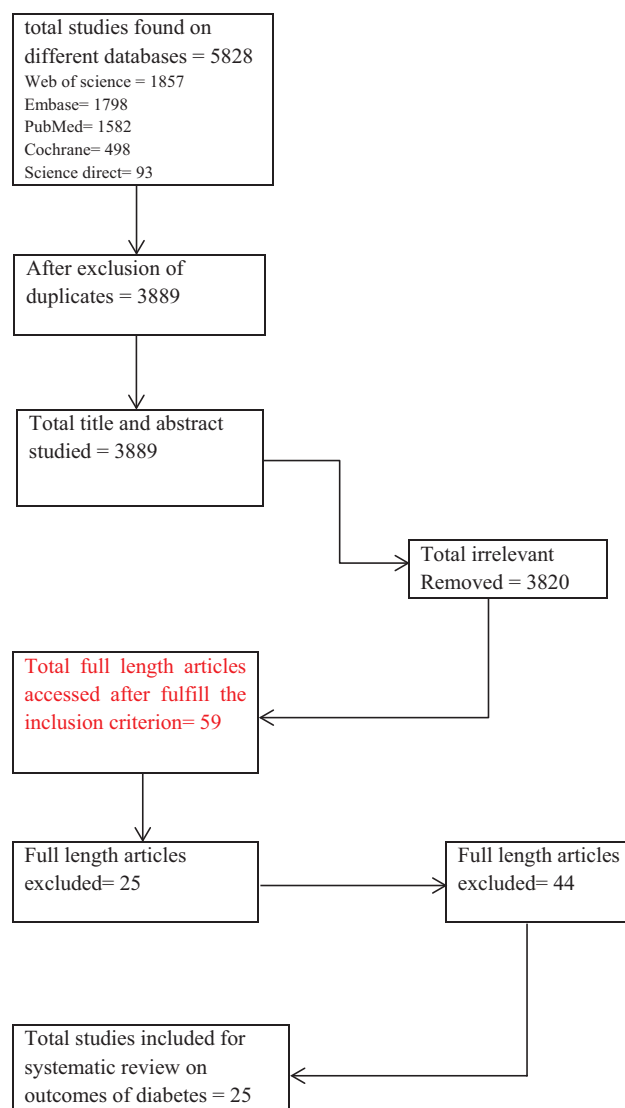


Figure 1: Flow chart study selection

hand, one of the included studies did not specify about the intervention, either it was offered by individual pharmacist or by the department of pharmacy.^[26] Some of the included studies reported personalized kind of interventions that were based on specific needs of diabetic patients.^[23,25,26,30-32,34]

The type, intensity, and frequency of interventions were different in all the included studies. The number of visits for face-to-face interactions was also different in all the included studies. The variation was from once in a week to once in a year.

Some of the included studies do have face-to-face contact with the pharmacists or pharmacy departments^[9-12] and some have combination of face-to-face contacts along with telephone contact with the pharmacists or department of pharmacy.^[25,27]

Table 1: The main characteristics and outcomes of included studies

Serial no.	Author, country, and year of publication	Study design	Participants (N) IG and CG	Study duration	Follow-ups with pharmacist	Main outcome measures	Outcomes
1.	Lau <i>et al.</i> , Malaysia, 2018 ^[8]	Pilot retrospective cohort study	58 IG = 29 CG = 29	1-year records	Four visits	HbA1c	A significant mean HbA1c reduction ($P < 0.001$) from the baseline to 12 months after enrollment was observed in the pharmacist program but not in the usual medical care group.
2.	Lim <i>et al.</i> , Malaysia, 2016 ^[9]	Prospective randomized open-labeled study.	76 IG = 39 CG = 37	1 year	Eight visits	HbA1c, FBG (mmol/L), BMI (kg/m ²), and systolic and diastolic BP (mm Hg) ($P = 0.01$).	HbA1c decreased up to 0.9% in the intervention group, whereas in the control group it only decreased up to 0.08%. Between the two groups significance association was seen ($P = 0.01$). No significance association was observed between the two groups for BMI calculation. Significance association was observed between the two groups for systolic BP ($P = 0.026$), whereas no significance association was observed between the two groups for diastolic BP ($P = 0.320$).
3.	Butt <i>et al.</i> , Malaysia, 2016 ^[12]	Randomized controlled study	73 IG = 37 CG = 36	6 months	Three visits	HbA1c, FBS, BMI, TC, HDL-C, LDL-C, triglycerides, QoL, and MMMAS scores	HbA1c level decreased significantly from 9.66% to 8.47% ($P = 0.001$) in the intervention group. However, no significant change was observed in the control group.
4.	You <i>et al.</i> , Malaysia, 2015 ^[10]	Multicenter retrospective	56 Pre- and post-intervention	1 year	Four visits	HbA1c, MMMAS scores	BMI was significantly reduced in the intervention group (29.34–28.92 kg/m ² ; $P = 0.03$); however, lipid profiles were unchanged in both groups. The mean HbA1c was significantly decreased from 10.7% (1.51) pre-intervention to 9.7% (1.75) post-intervention.
5.	Lim and Lim, Malaysia, 2010 ^[7]	Retrospective study	43 Pre- and post-intervention	1-year records	Eight visits	HbA1c, FBG, TC, HDL-C, LDL-C, triglycerides, MMMAS scores	There was a significant change (6.5–7.4) pre- and post-intervention in MMMAS scores. A mean fall in HbA1c level was 1.73% ($P < 0.001$), mean fall in FBG was 2.65 mmol/L ($P = 0.01$), and mean fall in LDL cholesterol was 0.38 mmol/L ($P = 0.007$). There were no significant differences noticed in TG and HDL-C.

Table 1: Continued

Serial no.	Author, country, and year of publication	Study design	Participants (N) IG and CG	Study duration	Follow-ups with pharmacist	Main outcome measures	Outcomes
6.	Samtia et al., Pakistan, 2013 ^[8]	Randomized controlled study	348 IG = 178 CG = 170	5 months	Eight visits	HbA1c, BMI, smoking cessation, adherence to medications	HbA1c decreased up to 1.01 % ($P < 0.001$) in the intervention group. The intervention significantly reduced BMI and waist circumference by a difference of 1.87 ($P = 0.014$) and 1.27 ($P = 0.002$) between the control and intervention groups. A significant increase in disease-related knowledge was seen in the intervention group.
7.	Adibe et al., Nigeria, 2013 ^[11]	Randomized, controlled study	192 IG = 99 CG = 93	1 year	Three visits	CVD risks, HbA1c, LDL, medication understanding	Significant reductions were observed in HbA1c (7.77 ± 1.12 to 7.23 ± 1.09 ; $P = 0.0009$); fasting glucose level reduces from (mg/dL) (168.7 ± 11.49 to 129.34 ± 9.97 ; $P < 0.0001$). Similar kind of changes were observed in LDL-C, HDL-C, triglycerides, and total cholesterol, respectively.
8.	Chan et al., Hong Kong, 2012 ^[9]	Randomized controlled study	105 IG = 51 CG = 54	9 months	Three visits	CHD risks, stroke risks, HbA1c, HDL-C, LDL-C, triglyceride, and BP	Patients in the intervention group had a statistically reduction risk of CHD ($P = 0.013$) as compared to those in the control group.
9.	Jameson and Batty, USA, 2010 ^[20]	Randomized controlled trial	103 IG = 52 CG = 51	12 months	Four visits	HbA1c	For stroke, similar reduction risk was noted in the intervention group. Furthermore, HbA1c levels were also significantly decreased ($P = 0.001$) in the intervention group. No significant difference was observed for BP in both groups. HbA1c decreased up to 1.50% for the intervention group and 0.40% for the control group ($P = 0.06$).
10.	Ali et al., UK, 2012 ^[21]	Randomized controlled study	46 IG = 23 CG = 23	12 months	Six visits	HbA1c, BMI, BP, blood glucose, and lipid profile	HbA1c decreased from 8.2% to 6.6% ($P < 0.001$) in the intervention group, whereas it decreased from 8.1% to 7.5% in the control group ($P = 0.03$). In the intervention group, a significant increase was observed in BP ($P = 0.01$), lipid profile, BMI ($P < 0.001$), and quality of life ($P = 0.001$).

Table 1: Continued

Serial no.	Author, country, and year of publication	Study design	Participants (N) IG and CG	Study duration	Follow-ups with pharmacist	Main outcome measures	Outcomes
11.	Mourão <i>et al.</i> , Brazil, 2013 ^[22]	Open randomized controlled trial	100 IG = 50 CG = 50	6 months	Two visits	HbA1c, fasting plasma glucose, total cholesterol, LDL cholesterol, triglycerides, and systolic blood pressure	In comparison to the control group, the intervention group showed a significant reduction of HbA1c (-0.6 vs. 0.7%, $P = 0.001$), fasting plasma glucose, total cholesterol, LDL cholesterol, triglycerides and systolic blood pressure, and a significant increase in HDL cholesterol.
12.	Kraemer <i>et al.</i> , USA, 2012 ^[23]	Randomized trial	67 IG = 50 CG = 50	12 months	Two visits	HbA1c	A reduction of 0.50% from baseline in HbA1c was observed in the intervention group which was statically significant ($P = 0.0008$).
13.	Mehyus <i>et al.</i> , Belgium, 2011 ^[24]	Randomized controlled study	288 IG = 34 CG = 33	6 months	Two visits	Fasting plasma glucose and HbA1c	A significant reduction was observed in HbA1c (between-group difference: 0.5%, $P = 0.009$) in the intervention group.
14.	Jarab <i>et al.</i> , Jordan, 2012 ^[25]	Randomized controlled trial	156 IG = 77 CG = 79	6 months	Eight (weekly) telephone follow-ups	HbA1c, HDL-C, LDL-C, triglyceride, and BP	HbA1c decreased up to 0.8% ($P < 0.019$) in the intervention group, whereas it increased up to 0.1% in the control group ($P = 0.838$). LDL-C decreased up to 0.6 mmol/L ($P = 0.031$) in the intervention group. HDL-C decreased up to 0.15 mmol/L ($P = 0.728$) in the intervention group. Systolic BP decreased up to 5.8 mm Hg ($P = 0.026$) and diastolic BP decreased up to 7.1 mm Hg ($P = 0.040$). Mean fasting blood glucose and HbA1c of the patients in the intervention group decreased significantly compared to control group ($P < 0.001$).
15.	Farsaei <i>et al.</i> , Iran, 2011 ^[26]	Randomized controlled trial	172 IG = 86 CG = 86	9 months	Two visits	FBS and HbA1c	

Table 1: Continued

Serial no.	Author, country, and year of publication	Study design	Participants (N) IG and CG	Study duration	Follow-ups with pharmacist	Main outcome measures	Outcomes
16.	Cohen <i>et al.</i> , USA, 2011 ^[27]	Randomized controlled trial	99 IG = 50 CG = 49	6 months	Five monthly visits	HbA1c, LDL-C, and BP	HbA1c decreased up to 0.74 in the intervention group ($P = 0.028$) whereas in the control group it decreased up to 0.61 ($P = 0.21$). Lower baseline levels of LDL cholesterol, 96.1 ± 25.4 mg/dL ($P = .024$) and significantly decreased in BP ($P = 0.011$). The control of disease in the form of fasting blood glucose was higher in the intervention group as compared with the control group (50.2 mg/dL), with a significant difference ($P < 0.05$); a decrease in HbA1c level was also observed in the intervention group.
17.	Nascimento <i>et al.</i> , Portugal, 2016 ^[3]	Parallel randomized controlled trial	87	12 months	Two visits	FBS and HbA1c and self-reported medication adherence	In the intervention group HbA1c decreased from 7.38 ± 1.71 to 6.69 ± 0.77 , whereas in the control group it increased from 7.37 ± 1.44 to 7.46 ± 1.11 , respectively.
18.	Shao <i>et al.</i> , China, 2017 ^[28]	Parallel randomized controlled trial	240 IG = 44 CG = 43	6 months	Two visits	HbA1c, FBS, and BP	FBS also decreased significantly from 7.34 ± 2.25 to 6.26 ± 1.00 ($P = 0.001$). Systolic and diastolic BP also decreased significantly ($P = 0.014$). HbA1c decreased up to 0.9% ($P = 0.04$). Systolic BP also decreased up to 7.1 mm Hg ($P = 0.10$).
19.	Taveira <i>et al.</i> , USA, 2011 ^[29]	Parallel randomized controlled trial	88 IG = 44 CG = 44	6 months	Four weekly visits	HbA1c, BP, and lipid profile	Improvement in lipid profile was also seen in the intervention group. More number of participants in intervention group achieved an HbA1c of less than 7% and a systolic blood pressure less than 130 mm Hg.
20.	Taveira <i>et al.</i> , USA, 2010 ^[30]	Parallel randomized controlled trial	109 IG = 58 CG = 51	4 months	Four weekly sessions	HbA1c, BP, and lipid profile	On the other hand, no significant change was found in lipid control in both groups. HbA1c and FBS of intervention group decreased significantly as compared to the control group ($P < 0.05$).
21.	Wishah <i>et al.</i> , Jordan, 2015 ^[31]	Randomized controlled trial	106 IG = 53 CG = 53	6 months	Three visits	HbA1c, FBS, BMI, and lipid profile	No significant change was observed in lipid profile of the both groups.

Table 1: Continued

Serial no.	Author, country, and year of publication	Study design	Participants (N) IG and CG	Study duration	Follow-ups with pharmacist	Main outcome measures	Outcomes
22.	Korcegez <i>et al.</i> , Cyprus, 2017 ^[32]	Randomized controlled study	152 IG = 75 CG = 77	12 months	Three visits	HbA1c, BP, BMI, waist circumference, medication adherence, and lipid profile	At the end of the study, patients in the intervention group showed more reduction in HbA1c level than those in the control group (-0.74% vs. -0.04%; $P < 0.001$).
23.	Jahangard-Rafsanjani <i>et al.</i> , Iran, 2015 ^[33]	Randomized controlled trial	85 Pre- and post-intervention	5 months	Five visits	HbA1c, BP, BMI, and medication adherence	Reduction in FBS level was also detected in both groups but the difference between the groups was statistically non-significant ($P = 0.410$). No significant difference was observed in HbA1c after the intervention. However, the amount of HbA1c reduction was higher in the intervention group ($1.0\% \pm 1.5\%$ vs. $0.5\% \pm 1.5\%$).
24.	Cani <i>et al.</i> , Brazil, 2015 ^[34]	Parallel randomized controlled trial	70 IG = 34 CG = 36	6 months	Six visits	HbA1c, FBS, and quality of life	BP, BMI, and medication adherence were improved significantly after intervention. HbA1c and FBS improved significantly ($P < 0.001$) in the intervention group but it remained unchanged in the control group.
25.	Doucette <i>et al.</i> , USA, 2009 ^[35]	Parallel randomized controlled trial	78 IG = 36 CG = 42	12 months	Four visits	HbA1c, LDL-C, and BP	Quality of life of the patients improved in the intervention group ($P < 0.001$) and it became worsen in the control group. No significant difference was observed in HbA1c, LDL-C, and BP in both of the groups. Although interventions were given by pharmacist, these interventions did not show statistically significant improvements in clinical outcomes during the study period.

IG = intervention group, CG = control group, HDL-C = High-density lipoprotein cholesterol, LDL-C = Low-density lipoprotein cholesterol, TC = Total cholesterol, QoL = Quality of life, FBG = Fasting blood glucose

Fifteen included studies used patient education about diabetes as interventions; the diabetes education was either in the form of general information about disease or about short-term and long-term diabetic complications. Patient education on medication was as given by pharmacists in 13 included studies and this education was to increase the adherence of patients, decrease dosage of drug-related problems, storage, and proper use of the medicines.

In the 19 included studies, education was given on lifestyle modification, exercise requirements, foot cares, management of proper diet and smoking termination were the important part of the intervention by the pharmacists.

Various kinds of clinical outcome measurements were reported in all the included studies [Table 1]. The clinical outcomes of the disease were in the form of HbA1c, FBS, BMI, BP measurements, Modified Morisky Medication Adherence Scale (MMMAS) scores, patient-reported medication adherence, lipid profile, and quality of life. The analysis shows generally a significant improvement in HbA1c, with the mean reduction of 0.75%. The effects on other outcomes were also significant.

Various guidelines for diabetes recommend that a target HbA1c of a diabetic patient should be 7% or less, but Malaysian guideline recommends that the targeted HbA1c for diabetic patients should be equal or less than 6.3% (Clinical Practice Guideline for Management of T2DM, Malaysia 2015). In order to decrease the chances of diabetic complication in those patients who have HbA1c more than 7%, it is recommended to reduce the HbA1c up to 1% or more. Similar results were reported by United Kingdom prospective diabetes study trial. Thus, a tight control of FBS and random blood sugar (RBS) is needed to decrease diabetes complications.^[36] Thus, pharmacist intervention is needed to reduce the FBS and RBS of patients as shown in the included studies of analysis.^[9,12,19,21-23,25,27-29,32,34]

Adherence of patients toward medication was measured in seven studies.^[10,12,13,17,18,32,33] MMMAS was used in three studies.^[10,12,17] All studies show that the improvement was seen in the control of the disease between intervention groups as compared with the control group.

Twelve included studies^[9,11,19,21,22,25,27-30] measure the effect of intervention on the BP of the patients. Of these studies, only two reported no effect of pharmacist intervention on the control of BP of the patients.^[19,35] The American Association of Clinical Endocrinologists and American College of Endocrinology CPGs on diabetes recommends that the target BP of diabetics

should be less than 140/80–90 mm Hg to decrease the chances of complications.^[34] According to Malaysia guideline, the BP should be less than 150/85 mm Hg in diabetic patients to decrease the risk of microvascular and macrovascular complications.^[25] On the other hand, Australian guideline recommends this target 130/80 mm Hg or lower and if patients are having proteinuria with diabetes then it should be less than 125/75 mm Hg. Diabetes guidelines from Australia, USA, and Malaysia recommend to decrease the daily sodium intakes, increase potassium intakes, and moderate intakes of alcohol in patients with diabetes mellitus.^[11,35] These guidelines recommend prescribing of an Angiotensin Converting Enzyme Inhibitor or Angiotensin Receptor Blocker unless contraindicated, as the preferred antihypertensive in patients with diabetes mellitus in comorbidity of hypertension.^[37,38]

Only two included studies^[12] measure and compare the quality of life of diabetic patients in both the control and intervention groups. From these two studies, one study used validated EQ-5D(3L) questionnaire,^[12] whereas the other study used the validated Brazilian version of Diabetes Quality of Life Measure.^[34] Because of using different versions of the questionnaire to measure the quality of life of diabetic patients and also differences in reporting strategies, it was not possible to pool the results. Both studies were reported to be significantly improving the quality of life of patients from the used questionnaires.

Thirteen included studies measure the lipid profile of the patients.^[11,12,17,19,21,22,25,27,29-32,35] Most of the studies reported the improvement in lipid profile in intervention group, whereas only four^[12,17,30,31] studies showed no effect of the intervention in the intervention group. Guidelines of various countries such as Australia, UK, USA, and Malaysia strongly recommend the use of a lipid-profile control medication such as a statin if it is not contraindicated to decrease the risk of cardiovascular disease (CVD) development.^[36] Although the chances of development of diabetes with statin use are reported,^[38,39] many meta-analyses on randomized trials reported the advantages of statins to decrease the CV risks.^[16,37,40]

Four of the included studies measure the CV risk factors in diabetic patients.^[11,18,19,32] These studies reported a significant reduction in CV risk factors in diabetic patients after pharmacist intervention. European, American, and Malaysian guidelines recommend the initiation of aspirin therapy (75–162 mg/day) for primary preventative approach to decrease the CVD risks.^[7,41-43] In Australia, Framingham risk equation was developed for calculating the absolute CVD risk.^[44] The US guidelines recommend the use of the Framingham risk score to

calculate the risk of CVDs. Framingham risk score can calculate the percentage of CVD risk in 10 years with the help of demographic data of the patients', that is, family history of CVD, gender, total cholesterol level, and high-density lipoprotein cholesterol level of the patients.^[44]

STRENGTHS AND LIMITATIONS

This review contains numerous strengths. All of the included studies reported the measurement of HbA1c values pre- and post-intervention by pharmacist, owing to that it was easy to measure and compare the effect of the pharmacist interventions in a meta-analysis. Similarly, the results for FBS, RBS, BP measurement, BMI, and lipid profiles can easily be pooled in meta-analyses. Although most of the included studies used different strategies to observe the effect of pharmacist intervention, a few studies directly measured the self-management. The results of these included studies show a direct positive relation between the pharmacist intervention and control of the disease. It is because the most of the interventions already addressed all common drug-related problems of diabetic patients.^[45,46]

This study includes certain limitations as well. The types and method of used interventions and study results were very incomplete in some of the studies.^[18,23,24,26,27,29-31,33-35] It can result into the biasness in the study. However, the risk of biasness will not change the results of meta-analysis in HbA1c values. All the used interventions can be combined together to make a complex and perfect intervention, because all used interventions in included studies contained multiple useful components. This review shows all those multiple interventions resulted in a positive impact on the outcomes of diabetes mellitus. More refined analyses, such as meta-regression analyses, could have given more understanding about the main components.^[47] However, due to the limited number of studies and also the type of available data from the included studies, it was not possible. Although we have provided different components of pharmacist interventions from different included studies, the ideal composition of pharmacist-led intervention is not available yet.

CONCLUSION

The review reveals the pharmacist's contribution in improving the self-management support and awareness in patients with diabetes. This narrative review has highlighted the various factors involved to achieve the target therapy outcomes. Overall, pharmacist interventions have a positive effect on the outcomes of diabetes mellitus. Furthermore, pharmacist intervention in diabetic patients can be resulted in the better control of disease and its complications, and it can help to improve the quality of life of the patients.

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Conflicts of interest

There are no conflicts of interest.

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