A randomized control trial of primary care-based management of type 2 diabetes by a pharmacist in Pakistan

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Abstract

Background: The role of a pharmacist in primary health care settings of Pakistan is still obscure. Thus, we aimed to demonstrate the pharmacist-led improvements in glycemic, blood pressure and lipid controls in type 2 diabetes mellitus (T2DM) patients of Lahore, Pakistan.

Methods: The first open label, randomized control trial conducted at a primary health care facility of Lahore, Pakistan by enrolling 244 uncontrolled type 2 diabetes (hemoglobin A1c, (HbA1c); 10.85 ± 1.74) patients. The pharmacological intervention included identification of drug related problems, drug interactions, change in dose, frequency and therapy switches in collaboration with physician, while non-pharmaceutical intervention consisted of diet, lifestyle and behavior counseling. Outcome measures were glycemic (HbA1c), blood pressure and lipid controls.

Results: In intra-group comparison, compared to control arm (C, n = 52), subjects in the intervention arm (I, n = 83) demonstrated significant differences in process outcome measures; baseline vs final, such as HbA1c (C; 10.3 ± 1.3 vs 9.7 ± 1.3, p < 0.001, I; 10.9 ± 1.7 vs 7.7 ± 0.9, p < 0.0001), systolic blood pressure (SBP) (C; 129.9 ± 13.9 vs 136 ± 7.1, p = 0.0001, I; 145 ± 20.4 vs 123.9 ± 9.9 mmHg, p < 0.0001), diastolic blood pressure (DBP) (C; +4, p = 0.03, I; −7 mmHg, p < 0.0001), cholesterol (C; 235.8 ± 57.7 vs 220.9 ± 53.2, p = 0.15, I; 224 ± 55.2 vs 153 ± 25.9 mg/dL, p < 0.0001), triglycerides (C; 213.2 ± 86.6 vs 172.4 ± 48.7, p = 0.001, I; 273 ± 119.4 vs 143 ± 31.6 mg/dL, p < 0.0001) and estimated glomerular filtration rate (eGFR) (C; 77.5 ± 18.6 vs 76 ± 14.2, p = 0.5, I; 69.4 ± 21.3 vs 93.8 ± 15.2 ml/min/1.73m², p < 0.0001). Likewise, inter-group improvements were more significant in the subjects of intervention group at final follow up in comparison to control for various process outcome measures; HbA1c (p < 0.001), SBP (p < 0.0001), DBP (p = 0.02), cholesterol (p < 0.0001), triglycerides (p < 0.0001), SCr (p < 0.001), eGFR (p < 0.001). Moreover, both male and female subjects exhibited similar responses towards intervention with similar improvements in outcome measures.

Conclusion: These data suggested that pharmacist intervention in collaboration with physician in primary health care settings may result in significant improvements in glycemic, blood pressure and lipid controls in Pakistani population.

Trial registration: The trial was registered retrospectively with International Standard Registered Clinical/sosial sTudy Number (ISRCTN) registry on July 26, 2017 under nutritional, metabolic, endocrine category with assigned registration # ISRCTN22657497 and can be assessed at https://doi.org/10.1186/ISRCTN22657497

Keywords: Lahore, T2DM, Pharmacist, Blood pressure, HbA1c, Pakistan, Pharmaceutical care, Glycemic control, Randomized control

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Background
According to 2017 global estimates by International Diabetes Federation (IDF), there are 451 million people with diabetes between 18 and 99 years of age and these numbers were projected to increase to 693 million by 2045 [22]. The crude prevalence of diabetes mellitus (DM) in Pakistan was 6.9% in 2017 that was expected to increase to 8.5% in adults (20-79 years), thus placing Pakistan 10th on IDF ranking based on number of adults with diabetes [28]. Regardless of the therapeutic headway, the management of diabetes to attain strict glycemic control on a long term basis remains complicated and ponderous, which in case of failure leads to inadvertently poor cardiovascular and microvascular outcomes [36, 51]. Pakistan's healthcare system mainly addresses the acute illnesses while the chronic disease management is not fully taken care of by the health care system [3]. This aloofness could be attributable to several health system and patient related factors, such as limited healthcare human resource to tackle much needed educational demands of diabetic patients, overcrowded hospitals and clinics, lack of pharmaceutical care services under the supervision of a clinical pharmacist, greater emphasis on treating patients rather than disease and therapy related education and counseling, poverty/affordability, lack of education/poor health literacy, patient's easy access to non-evidence based remedies practiced by hakeems (herbalist) and quacks - all leading towards the ineffective management and unwanted progression of diabetes [7, 46, 47].

According to World Health Organization (WHO)-Diabetes Country Profile 2016, Pakistan’s National response to diabetes completely lack comprehensive healthcare policies, guidelines and monitoring services for the disease. There are no operational policies and suggestive action plan in the health care system of Pakistan for an effective management of diabetes to control disease modifying risks, such as physical inactivity, weight gain and obesity [49]. Over and above there is complete absence of evidence based national diabetes standards or guidelines on patient's education and treatment, tenuous referral criteria from primary to tertiary care and absence of diabetes registry and national risk factor surveys [49]. Additionally, in public health settings, there is a provision to obtain oral hypoglycemic agents (OHA), like Metformin and Sulfonylureas but insulin and related amenities are generally not available in primary healthcare facilities, e.g. blood glucose measurement, oral glucose tolerance test (OGTT), HbA1C test, dilated fundus examination, foot vibration perception by tuning fork, foot vascular status by doppler, urine strips for glucose and ketone measurement, and procedures like retinal photocoagulation, renal replacement therapy by dialysis or transplantation [49].

In many developed countries, pharmacist is considered as a pivotal member of a health care workforce and is the most accessible healthcare professional [35]. The role of a pharmacist as member of health care team has been evaluated in various randomized trials in community and clinical settings in managing and sustaining optimal glycemic, blood pressure and lipid controls to avert diabetic complications ([1];M. [5, 19, 20, 27, 33, 34, 38, 42, 44]).

According to 2015 trend report by the International Pharmaceutical Federation (FIP) on global pharmacy workforce intelligence, the median density of pharmacist in Pakistan stands at 0.51, 0.69 and 0.68 per 10,000 population in 2006, 2009 and 2012, respectively [15, 35] almost 12.7 times lower than the mean density of pharmacist in high income countries. Besides, Pakistan lacks doctor-patient-pharmacist loop, defunct pharmaceutical care plan for the management of T2DM with almost no operational policies and strategies to promote appropriate self-management/care practices to prevent disease related complications, disability limitation and encourage apropos rehabilitation, which the diabetic patients must learn to adopt during their visits to the clinics [13]. Currently, there are no published reports from Pakistan on the effectiveness of a standardized and structured model/algorithm for pharmacists to afford and deliver diabetes management services in any level of health care [12]. Therefore, it is high time to start engaging and empowering pharmacist in primary care settings of Pakistan to afford a thoughtful pharmaceutical care plan encompassing multifactorial pharmacological and non-pharmacological approaches that can be tailored according to the needs of individual patients with T2DM for a better glycemic, blood pressure and lipid controls to avert diabetes related complications in Pakistani population. Therefore, the current study is aimed at evaluating the pharmacist's led improvements in glycemic, blood pressure and lipid controls in T2DM patients of Lahore, Pakistan.

Methods
Ethical approval
The study was approved by Ethical Committee of Human Research, Punjab University College of Pharmacy, University of the Punjab, Lahore, reference #: HEC/1000/PUCP/1926. The informed consent was obtained (Additional file 3) from all the subjects. The consent was also obtained from the participants to publish the study results.

Study design
A prospective parallel, single centered, randomized control trial, “Study on A1c Management by Pharmacist in Lahore (SAMPLE) was conducted at a primary care
clinique de Lahore, Pakistan. Les données ont été recueillies sur une période de 9 mois avec trois suivis en tout, chaque suivi après chaque trois mois, conformément aux lignes directrices de l'American Diabetes Association, A. D [8], qui recommandent de mesurer HbA1c après chaque trois mois pour évaluer le contrôle glycémique [11].

**Sample size**

La taille de l'échantillon a été estimée en fonction de la prévalence du diabète au Pakistan [43], c'est-à-dire 6.9%, utilisant la formule de Daniel [25], où la prévalence du diabète au Pakistan est 6.9%, donc \( P = 0.069 \), tandis que \( Z = 1.96 \) (pour un niveau de confiance de 95%) et \( d = 0.05 \).

\[
\begin{equation}
\text{n} = \frac{Z^2 P(1-P)}{d^2}
\end{equation}
\]

La taille de l'échantillon calculée a été trouvée à 99. Cependant, les données de 150 patients, 150 dans chaque bras, ont été recueillies pour compenser les données manquantes ou les abandons.

**Study settings**

L'étude a été menée dans une clinique de soins primaires, Murad clinic Shalamar link road, Lahore, sous la supervision d'un praticien généraliste (fichier supplémentaire 3). La configuration clinique comprenait 3 médecins, 1 apothicaire qualifié, 1 coordinateur, 1 assistant, 1 technicien et 1 pathologiste. Tous les patients, sauf ceux qui souhaitaient se rapprocher de leur coordinateur pour consulter le médecin, ont ensuite contacté le coordinateur pour recevoir leurs médicaments de l'apothicaire et plus tard à un pharmacien. La dernière partie est applicable aux patients du bras d'intervention pour l'éducation et la conseillement.

**Patient recruitment**

Les patients non contrôlés T2DM (HbA1c > 8%) ont été informés de la conduite et des procédures opérationnelles par le pharmacien de recherche. Les sujets ont été recrutés de mars 20, 2016 à août 20, 2016. L'étude s'est terminée le 03 juin, 2017.

**Randomization**

Tous les sujets éligibles ont été assignés à l'identification des numéros de patient. Les sujets avec des nombres pairs ont été séparés dans le bras d'intervention (\( n = 150 \)), tandis que les numéros de sujets impairs dans le bras de contrôle (\( n = 150 \)), ont été suivis par évaluation de base (Fig. 1) par un pharmacien.

**Baseline evaluation**

L'évaluation initiale des participants, globale et spécifique au sexe, a été faite pour les participants qui incluaient des données démographiques, les paramètres d'évaluation physique et les mesures de laboratoire (fichier supplémentaire 1: Table S1). Cela a été suivi par l'évaluation de base clinique des participants dans le bras de contrôle et d'intervention (fichier supplémentaire 1: Table S1).

**Blinding**

Dans l'étude, il n'a pas été utilisé de blinding, ni le pharmacien ni le médecin ne savait auquel des participants intervenait.

**Trial registration**

ISRCTN22657497 (https://doi.org/10.1186/ISRCTN22657497).

**Missing data or dropouts**

Il y avait 40 patients ont abandonné le bras d'intervention (12 patients sont sortis et 28 patients ont été perdus de vue) et 69 dans le bras de contrôle - 24 patients sont sortis et 45 patients ont été perdus de vue. Ainsi, l'analyse finale a été faite sur 52 et 83 patients dans le bras de contrôle et d'intervention, respectivement (Fig. 1). Les patients dans le bras de contrôle ont continué à participer jusqu'au deuxième suivi. Après cela, 69 patients ont été abandonnés (échec du suivi) en raison de leur insatisfaction envers la gestion du diabète, l'échec de réalisation des objectifs de traitement, le passage à d'autres médecins et l'absence d'intérêt pour l'étude.

**Study population**

Parmi les 300 patients non contrôlés T2DM éligibles enregistrés dans l'étude, 56 patients ont refusé de fournir le consentement informé. Le diabète non contrôlé a été confirmé par des niveaux d'HbA1c au-dessus de 8%, conformément aux lignes directrices de ADA [9]. Ainsi, seuls 244 patients étaient considérés pour l'évaluation de base (Fig. 1) comme suit le critère d'inclusion et d'exclusion.

**Inclusion criteria**

Les patients T2DM non contrôlés, âgés de plus de 18 ans, indépendamment du sexe, de l'ethnie et de la classe sociale, doivent visiter le centre pour les six derniers mois, avec ou sans comorbidités et souhaitent participer à l'étude.

**Exclusion criteria**

Les patients de moins de 18 ans, le trouble cognitif, les absences de rendez-vous dans les six derniers mois, les troubles cognitifs et non souhaitant participer ont été exclus.

**Research procedures**

L'évaluation initiale des participants a été réalisée en utilisant le formulaire de collecte de données (fichier supplémentaire 2). L'éducation initiale et le conseil étaient sur les maladies, le traitement, les modifications de style de vie, la surveillance de la glycémie et les problèmes liés aux médicaments. Les patients étaient invités à visiter tous les 4 semaines pour l'évaluation des besoins pharmacologiques et non-pharmacologiques, ainsi que pour le suivi régulier de trois mois. Les patients dans les deux bras étaient informés des visites à venir et de l'évaluation de base clinique des participants dans le bras de contrôle et d'intervention (fichier supplémentaire 1: Table S1).
telephonic calls or short message service (sms). The findings were documented and assessed to formulate Individualized Pharmaceutical Care Plan.

**Pharmaceutical care plan**
A comprehensive pharmaceutical care plan for the patients of intervention arm was designed by the intervening pharmacist (Additional file 1: Figure S1). Briefly, pharmacist work up for drug therapy (PWDT) included CORE (Condition, Outcome, Regime, Evaluation) and PRIME (Problem, Risk, Interaction, Mismatch, Efficacy) components. CORE components included condition/needs, outcome, regimens and continuous evaluation. PRIME components included pharmaceutical based problems (non-adherence, monitoring & screening), risk to patients (Adverse Drug Reactions (ADRs), allergy), interactions, mismatch (drugs and patient's needs) and efficacy parameters (Additional file 1: Figure S1). On every visit after 4 weeks, the intervening pharmacist assessed the patient's individual needs for the modification of Pharmaceutical Care Plan, based on patient's response towards intervention and self-monitoring record of blood glucose and blood pressure measurements. This was done in the form of progress notes followed by discussions with the study physician for treatment modification, if any.

At each follow up visit, every three months, the average pharmacist patient encounter time was between 15 and 30 min.

**Physician collaboration**
After baseline assessment and documentation of patient’s clinical and laboratory parameters, at each follow
up, patients in the intervention arm were received by a pharmacist in a designated room for education and counseling. Patients were bound to bring their laboratory reports and daily blood glucose and blood pressure record, and any necessary documents. Thereafter, progress notes were made regarding patient’s pharmacological (drug related problems and suggestions for therapy changes) and non-pharmacological needs. Non-pharmacological needs were taken care by providing verbal and readable (leaflets, instructions on the back of prescriptions) education and counseling sessions/materials, e.g., insulin administration, medication adherence issues and self-care and monitoring. Progressive revisions in pharmacological needs, drug related problems or intensification of existing therapy, at each follow up taking into account patient’s current medications, clinical and biochemical data were suggested in consultation with study physician on the same day, majorly by progress notes and after a separate discussion in physician’s room or rarely in the presence of a patient, if necessary. Patients were provided instructions on the prescription or on a separate page.

The patients in the control group continued treatment from their physicians and their laboratory reports were collected at each follow up by the physician and nurse as part of a routine checkup.

**Patient-pharmacist interaction**

Patient-pharmacist interaction occurred in a separate room designated for patient education and counseling enrolled in the intervention arm, i.e. right after the patient-physician encounter and pertinent laboratory tests. The average time of sessions was 15–30 min, but time varied depending upon the patient’s needs and issues. During this session pharmacist performed case evaluations, made progress notes and develop intervention plan addressed to the physician. A comprehensive pharmaceutical care plan was designed for each patient by identifying patient’s non-pharmacological and pharmacological needs. A detailed description of pharmacist’s intervention is given below in Pharmacist Intervention section.

**Description of Pharmacist’s intervention**

The intervention arm patients were categorized into three groups namely A, B & C according to follow ups attended, as shown in Additional file 1: Figure S2. The pharmacist intervention was based on Diabetes Self-Management Education criteria (DSME) [30] described below.

**Pharmacist work up for drug therapy (PWDT)**

Pharmacist’s work up of drug therapy (PWDT) included documentation of patient’s demographics and patient medical information, such as medical, social, dietary, family and medication history followed by laboratory results and physical findings. After documentation, pharmacotherapy problems associated with the use of pharmaceuticals were assessed related to patient risk, drug interactions, non-adherence, therapy mismatches and efficacy (drug choice, dose, route and frequency). Pharmacotherapy plans were made based on patient’s medical and non-medical needs to determine most suitable therapeutic regimen, revisions of the existing and appropriateness of the new, and behavioral recommendations on diet, lifestyle modifications, self-monitoring of glucose levels and self-care.

**Pharmacological interventions (DRPs)**

After patient-physician encounter at each follow up, patients in the intervention arm were received by the pharmacist in a designated room for patient education and counseling. Pharmacotherapy follow up activities were focused on issues related to patient’s changing needs with regards to treatment effectiveness and safety. Thus, pharmacotherapy interventions (PI) were processed after careful evaluation of medical prescription considering drug choice switches, dose, overdose, effectiveness, interactions and adverse drug reactions, via progress notes and case evaluation to establish an intervention plan addressed to the physician. Drug related problems (DRPs) like medicine timing, frequency, uncontrolled hyperglycemia and episodes of hypoglycemia were discussed with the physician. Drug interaction like concurrent use of insulin with pioglitazone, which increases the risk of edema, heart failure and hypoglycemia [21], was identified and reconciled by advising insulin and biguanide combination with evidence based discussion and physician’s consent. Following medication reconciliation, patients were advised on the access, storage and use of medicines.

**Oral hypoglycemic agents and insulin administration**

Patients were briefed about the time of administration, i.e; with meal or 15–30 min before meal, dosing schedule, possible side effects and frequently interacting drugs. Patient were counselled on insulin administration focusing on injection technique, use of syringe, insulin pen and correct ways of administration. Subjects were told about the best injection sites, i.e., thighs and abdomen, and remember to keep rotating the injection site.

**Medication adherence and treatment goals**

Patients were thoroughly probed by asking close ended questions, such as did you ever missed to take your dose?, at times, are you careless about taking your drugs? and if you feel better, do you stop taking medicine etc., to determine the reasons behind the skipped doses to later counsel them regarding the importance of
timely doses in controlling the disease symptoms and to prevent disease related complications. Moreover, patients were also asked about appearance of any side effects or allergies.

Besides, patients were also briefed how to assess episodes of hypoglycemia and hyperglycemia and ways to avoid them.

Patients were also briefed about the goals of therapy that is necessary to achieve effective glycemic control, i.e. fasting plasma glucose levels of ≤110 mg/dL, random glucose of ≤180 mg/dL, while HbA1c levels should be < 7%, measured every 3 months. Blood pressure goals for diabetic patients were < 140/90 mmHg, and after dinner, and stretch exercises while sitting only for those who were unable to go out for a walk.

Dietary and lifestyle modifications
Dietary plans were tailored according to patient’s needs considering different factors like weight reduction, hypertension, chronic kidney disease (CKD), chronic liver disease (CLD) and socioeconomic factors, according to ADA Guidelines [10]. Patients were recommended to have 20–30 min of exercise daily, moderately intense and vigorous physical activity, depending upon his/her abilities to encourage weight loss for a healthy Body Mass Index (BMI). Patients were advised brisk walk for 25–35 min in morning and after dinner, and stretch exercises while sitting only for those who were unable to go out for a walk.

Patients were counselled to adopt and adhere to lifestyle and behavioral modifications, such as self-regulation of carbohydrate intake, physical activity and medication doses based on the results of blood glucose monitoring.

Self-monitoring of blood glucose (SMBG)
Generally, patients that require SMBG were educated and trained to acquire basic skills and knowledge to use home blood glucose monitor and to record the results in an organized way. As a routine practice, patients in the intervention arm were advised for self-monitoring of blood glucose, especially when on insulin therapy, in case of modifications in prescription of hypoglycemic agent(s) and modifications in diet and physical activity. Specifically, regular SMBG (2–4 times per day) was recommended for patients using multiple daily injections of insulin, acutely ill and on medications or with illness known to cause hyperglycemia. Increased frequency of SMBG (≥ 2 times a day and as required) was recommended for patients utilizing medications known to cause hypoglycemia (when experiencing symptoms of hypoglycemia), entering a new life experience, such as a new job or change in working hours, unusual routine like stress, not meeting glycemic targets and to learn the effects of various meals on blood glucose levels.

Assessment of diabetic complications and diabetic foot care
Patients in the intervention arm were assessed and advised screening for the followings diabetic complications;

Patients were advised fundus examination to rule out diabetic retinopathy. For diabetic nephropathy, patients were advised urine test for proteinuria and blood test for glomerular filtration rate. For diabetic neuropathy patients were screened for numbness or reduced ability to feel pain, tingling sensation, increased sensitivity to touch and loss of reflexes in consultation with the primary care physicians.

Diabetic foot care included the routine examination of feet for cuts, bruises, cracks, blisters and soars. Major counseling points were aimed at maintaining hygienic conditions, which included change of socks every day, wear comfortable shoes and clip your nail straight across. Patients were told to avoid following actions, cutting their own corns and calluses, avoid using Over The Counter (OTC)/non-prescription medicine for treating corns or warts, use of lotions between the toes, walking barefoot and applying heat to the feet.

Counselling for personal care and hygiene
Following points were covered under this section;

Advice on skin care included routine examination for the appearance of any unusual discoloration, wart, carbuncle, bruises, cuts etc. On every visit, patient’s feet were examined by visual inspection and with monofilament. Patients were also advised to daily wash/clean the feet, moisturizing and self-examination of feet using mirror or with the help of a family member. Patients were counseled for eye examination in case of changes in their vision, e.g., appearance of spots in vision. Patients were also advised for oral hygiene and tooth brushing/cleaning after every meal and referrals to dentist for occurrence of dental caries.

Outcome measures
The outcome measures examined to assess the impact of pharmacist intervention in the management of T2DM are described below as;

Primary outcome measures
HbA1c and plasma glucose levels, measured by taking plasma venous samples and sending them to Trust laboratory and Citilab and Research center, Jinnah Hospital, Lahore.
Blood pressure and lipid profiles, measured via sphygmomanometer and by sending samples to Citilab and Research center, Jinnah Hospital, Lahore.

All the laboratory measurements were performed by laboratory technician while the samples were collected by a trained nurse.

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Data analysis
Data was analyzed using Statistical Package for Social Sciences (IBM SPSS 20). Descriptive statistics was used to compare frequency distribution patterns of categorical variables. Baseline characteristics between control and intervention arm were compared using Pearson chi-square. All continuous and discrete variables were reported as mean and standard deviations from their respective means. The outcome measures, blood glucose levels, HbA1c, blood pressure and lipid profiles were measured at the same time with similar procedures for patients in both the arms. The averages of outcome variables were computed for baseline and for each follow up in the two arms. Intra-group variations in the means of continuous and discrete variables were compared between baseline and final follow up. Likewise, inter group differences in means of outcome variables were compared between final follow up of control versus final follow up of intervention arm. The means of all the laboratory parameters were compared between control and intervention arm, baseline vs final, and final of control vs final of intervention, on Microsoft Excel, version 2010, using paired student’s t-test. To examine the effect of pharmacist’s intervention on outcome measures, over 9 months period, from baseline to each follow up, repeated-measures analysis of variance (ANOVA) was used. An alpha value equal to 0.05 or less will be considered statistically significant.

Results
Overall participants baseline demographics and clinical characteristics
The demographic data and clinical characteristics are summarized in Additional file 1: Table S1. Data suggested that average age of the participants was 50 ± 9.2 years with T2DM duration of 6.8 ± 5.4 years and mostly married. The clinical characteristics included uncontrolled diabetes (HbA1c: 10.8% ± 1.7), average BMI of 30.7Kg/m² ± 5.7, average systolic (SBP) and diastolic blood pressure (DBP) of 138.9 ± 19.3 and 89.7 ± 11.364 mmHg, respectively. Other included, lipid profiles [Cholesterol; 226.7 ± 53.6 mg/dL, triglycerides (TG, 231.8 ± 105.3 mg/dL), high density lipoprotein-C (HDL-C, 48.3 ± 15.6 mg/dL), low density lipoprotein-C (LDL-C, 132 ± 50.9 mg/dL) and VLDL-C, 46.4 ± 21.1 mg/dL] and elevated serum creatinine levels:1 ± 0.3 mg/dL. (Additional file 1: Table S1).

Gender wise differences existed in average baseline values for BMI (M: 29.3 ± 4.4, F: 31.3 ± 6.2, p = 0.004), cholesterol (M: 238.3 ± 61.3, F: 220.7 ± 48.4, p = 0.026), LDL-C (M: 143.39 ± 58.4, F: 126.2 ± 45.9, p = 0.013) and serum creatinine (M: 1.1 ± 0.4, F: 1.02 ± 0.3, p = 0.36) (Additional file 1: Table S1).

Participants baseline characteristics; control vs intervention
Patients baseline clinical characteristics of both arms are summarized in Table 1. At baseline, control (C) vs intervention (I), significant differences were observed regarding

| Table 1 Baseline clinical characteristics of participants; control & intervention |
|-------------------------------|-------------------------------|-------------------------------|
| Parameters                     | Control Arm, n = 121          | Intervention Arm, n = 123     | p-values          |
| Age (Yrs)                      | 50.4 ± 7.7                    | 50.3 ± 10.5                   | 0.89              |
| Age at diagnosis of DM(Yrs)    | 42.8 ± 7.9                    | 44.2 ± 9.8                    | 0.24              |
| Duration of DM (Yrs)           | 7.6 ± 5.4                     | 6.1 ± 5.3                     | 0.029*            |
| Haemoglobin (mg/dL)            | 13.2 ± 4.1                    | 13.9 ± 1.1                    | 0.69              |
| Weight (Kg)                    | 78.3 ± 14.4                   | 77.5 ± 17.6                   | 0.72              |
| Waist (cm)                     | 110 ± 16.5                    | 109 ± 16.5                    | 0.86              |
| BMI (Kg/m²)                    | 30.6 ± 4.9                    | 30.8 ± 6.4                    | 0.79              |
| Systolic BP (mmHg)             | 133 ± 15.4                    | 145 ± 20.9                    | 0.0001**          |
| Diastolic BP (mmHg)            | 85 ± 10.4                     | 94 ± 10.7                     | 0.0001**          |
| eABG (mg/dL)                   | 261 ± 49.8                    | 268 ± 50.2                    | 0.25              |
| HbA1c                          | 10.7 ± 1.7                    | 11.0 ± 1.7                    | 0.25              |
| Cholesterol (mg/dL)            | 231 ± 55.7                    | 223 ± 51.3                    | 0.26              |
| Triglycerides(mg/dL)           | 191 ± 79.7                    | 272 ± 112.1                   | 0.0001**          |
| HDL-C (mg/dL)                  | 48 ± 12.5                     | 49 ± 18.2                     | 0.45              |
| LDL-C (mg/dL)                  | 145 ± 48.5                    | 119 ± 50.3                    | 0.0001**          |
| VLDL-C (mg/dL)                 | 38 ± 15.9                     | 54 ± 22.4                     | 0.0001**          |

| Serum Creatinine (mg/dL)       | 1.0 ± 0.3                     | 1.1 ± 0.4                     | 0.007*            |

Treatments

| Treatments                     | Control Arm, n= 121 | Intervention Arm, n= 123 | p-values |
|-------------------------------|--------------------|--------------------------|----------|
| None                          | 2 (1.7%)           | 1 (0.8%)                 | 0.51     |
| OHA                           | 66 (54.5%)         | 72 (58.5%)               |          |
| OHA + Insulin                 | 43 (35.5%)         | 45 (36.6%)               |          |
| Insulin                       | 10 (8.3%)          | 5 (4.1%)                 |          |

Abbreviation: SD Standard Deviation, DM Diabetes Mellitus, BMI Body Mass Index, eABG Estimated Average Blood Glucose, HbA1c Glycosylated Haemoglobin, HDL-C High Density Lipoprotein-Cholesterol, LDL-C Low Density Lipoprotein-Cholesterol, VLDL-C Very Low Density Lipoprotein-Cholesterol, OHA Oral Hypoglycaemic Agents, I Intervention, C Control, M Male, F Female
duration of T2DM (C; 7.6 ± 5.4, I; 6.1 ± 5.3, \( p = 0.029 \)), \( SBP \) (C; 135 ± 15.4, I; 145 ± 20.9, \( p = 0.0001 \)), \( DBP \) (C; 85 ± 10.4, I; 94 ± 10.7, \( p = 0.0001 \)), \( triglycerides \) (C; 191 ± 79.8, I; 272 ± 112.1, \( p = 0.0001 \)), LDL-C (C; 145 ± 48.5, I; 119 ± 50.5, \( p = 0.0001 \)) and \( serum creatinine \) (C; 1.0 ± 0.3, I; 1.1 ± 0.4, \( p = 0.007 \)) (Table 1). No differences were noticed at baseline with regards to age, treatment choices, \( HbA1c \), cholesterol, weight, HDL-C and hemoglobin (Table 1).

**Intra and inter-group comparisons of process outcome measures**

In intra-group comparisons, from baseline (I), starting from 1st follow up till final follow up. Notables ones included, \( HbA1c \) (I; 11 ± 1.7, \( p = 0.0001 \)), \( systolic blood pressure \) (SBP) (B; 145 ± 20.9, \( p = 0.0001 \)), \( cholesterol \) (B; 223 ± 51.3, \( p = 0.0001 \)), \( Diastolic blood pressure \) (DBP) (B; 85 ± 7.9, \( p = 0.0001 \)) and \( estimated glomerular filtration rate \) (eGFR) \( (B; 70 ± 2, \( p = 0.0001 \)) and Triglyceride \( (B; 272 ± 112.1, \( p = 0.0001 \)) \) exhibited a significant increase (Table 2). While in the control group only \( HbA1c \) (B; 10.7 ± 1.7, \( p = 0.0001 \)), \( DBP \) (B; 85 ± 10.4, \( p = 0.0001 \)) and \( Diastolic blood pressure \) (DBP) (B; 85 ± 7.9, \( p = 0.0001 \)) exhibited significant differences among baseline and the follow-ups (Table 2). However, the differences were similar in both the arms, baseline to final follow ups, for \( LDL-C \) and \( VLDL-C \) levels (Table 2).

Inter-group changes over time in the process outcome measures were compared between control final (Cf) and intervention final (If) follow ups as shown in the last column of Table 2. Data suggested that almost all the outcome measures exhibited significant differences at final follow ups between control and intervention arms, except for weight, waist, BMI and HDL-C (Table 2).

Notable outcome measures demonstrating significant differences at final follow ups included \( HbA1c \) (Cf; 9.7 ± 1.3, If; 7.7 ± 0.9, \( p = 0.0001 \)), \( SBP \) (Cf; 137 ± 7.1, If; 124 ± 9.9, \( p = 0.0001 \)), \( DBP \) (Cf; 89 ± 4.2, If; 87 ± 5.4, \( p = 0.0001 \)), \( cholesterol \) (Cf; 221 ± 53.2, If; 153 ± 25.9, \( p = 0.0001 \)), \( TG \) (Cf; 172 ± 48.7, If; 143 ± 31.6, \( p = 0.0001 \)), \( SCR \) (Cf; 1 ± 0.1, If; 0.8 ± 0.1, \( p = 0.0001 \)) and eGFR (Cf; 76 ± 14.2, If; 94 ± 15.2, \( p = 0.0001 \)) (Table 2).

**Gender wise comparison of process outcome Measures**

Gender wise comparison of process outcome measures at final follow up for both control and intervention arms are summarized in Table 3. Data suggested that significant differences were observed in majority of the process outcome measures between final follow ups, control versus intervention arm, for male and female patients, such as \( HbA1c \) (M; 9.7 ± 1.3 vs 7.6 ± 0.9, \( p = 0.0001 \)), \( SBP \) (M; 137.1 ± 6.4 vs 125.8 ± 8.3, \( p = 0.0001 \)) and \( cholesterol \) (M; 229.1 ± 78 vs 152.6 ± 27, \( p = 0.0001 \)) and \( Scr \) (M; 0.9 ± 0.1 vs 0.8 ± 0.2, \( p = 0.0001 \)). While, \( VLDL-C \) and \( triglycerides \) showed significant differences in female patients only, control versus intervention (Table 3).

**Impact on glycemic goals and other targets of diabetes care**

As shown in Tables 4, 16.9% & 39.8% patients in the intervention arm achieved <7% and <8% \( HbA1c \) controls, respectively, compared to none (0%) and 5.8% in the control arm. Conversely, 69.2% in control arm sustained ≥9% \( HbA1c \) levels in comparison to 8.4% patients in the intervention arm (Table 4). At final follow up, 7.7% patients in the control and 54.2% in the intervention arm achieved \( SBP \) goals of <130 mmHg. While, 55.8% patients in the control and 9.6% in the intervention arm achieved \( SBP \) goal of ≥140 mmHg, respectively (Table 4). As for \( DBP \), compared to 82.7% subjects in control arm, 57.8% subjects in the intervention arm achieved ≥90 mmHg (Table 4). In terms of cumulative reduction in \( HbA1c \) levels, combining 1st, 2nd & 3rd follow ups, the percentage of patients in control and intervention arms started to decline from 1 to 1.9% \( HbA1c \) reduction quartile onward, yet not a single patient in control arm met \( HbA1c \) reduction quartiles of 5–5.9% and onward, (Additional file 1: Table S2), however, a few in the intervention arm met \( HbA1c \) reduction quartiles of 6–6.9% (Additional file 1: Table S2).

**Discussion**

The health care system of Pakistan lacks structured programs to manage non-pharmacological aspects of chronic diseases, such as therapy and disease related education and counseling, majorly due to lack of human resource and suboptimal health professionals to population ratio [41]. Despite clinical pharmacy education in Pakistan almost a decade ago, pharmacists in hospitals and primary care settings are providing conventional services [4, 14]. In the present study, pharmacist’s intervention regarding therapy, diet, lifestyle changes, self-care and management resulted in significant improvements in several process outcome measures, such as glycemic, blood pressure and lipid controls along with serum creatinine levels in comparison to control arm.
### Table 2: Inter and intra-group changes in process outcome measures in control and intervention arms

| Process Outcomes | Control Arm |          |          |          |          | Intervention Arm |          |          |          |          |
|------------------|-------------|----------|----------|----------|----------|-------------------|----------|----------|----------|----------|
|                  | Baseline, n = 121 | Follow up Every 3 Months | p-values | Baseline, n = 123 | Follow up Every 3 Months | p-values |
|                  | 1st, n = 121 | 2nd, n = 121 | 3rd, n = 52 | 1st, n = 123 | 2nd, n = 105 | 3rd, n = 83 |
| Weight [Kg]      | 78.2 ± 14.4 | 78.4 ± 15.1 | 78.8 ± 14.9 | 76.3 ± 14.8 | 77.5 ± 17.6 | 75.9 ± 16.9 | 74.6 ± 16.2 | 73.7 ± 16.6 | 0.258 | 0.35 |
| Waist [cm]       | 110 ± 16.6  | 109 ± 16.1  | 110 ± 16.2  | 106 ± 14.3  | 0.967 | 0.030 |
| BMI [Kg/m²]      | 30.6 ± 4.9  | 30.6 ± 5.1  | 30.8 ± 5.1  | 30.7 ± 5.6  | 0.986 | 0.030 |
| HbA1c (%)        | 10.7 ± 1.7  | 10.6 ± 2.1  | 10.2 ± 1.9  | 9.7 ± 1.3   | 0.001** | 0.030 |
| eABG [mg/dL]     | 261 ± 49.8  | 257 ± 58.9  | 246 ± 54.7  | 232 ± 38.0  | 0.915 | 0.030 |
| SBP [mm/Hg]      | 133 ± 15.4  | 132 ± 13.4  | 134 ± 13.2  | 137 ± 7.1   | 0.082 | 0.030 |
| DBP [mm/Hg]      | 85 ± 10.4   | 85 ± 7.9    | 86 ± 9.8    | 89 ± 4.2    | 0.03* | 0.030 |
| Cholesterol [mg/dL] | 231 ± 55.7  | 229 ± 49.6  | 223 ± 43.7  | 221 ± 53.2  | 0.3  | 0.030 |
| TG [mg/dL]       | 191 ± 79.8  | 186 ± 67.7  | 175 ± 53.1  | 172 ± 48.7  | 0.1  | 0.030 |
| HDL-C [mg/dL]    | 48 ± 12.5   | 46 ± 10.9   | 47 ± 12.3   | 49 ± 13.9   | 0.437 | 0.030 |
| LDL-C [mg/dL]    | 145 ± 48.5  | 143 ± 43.1  | 141 ± 39.4  | 82 ± 77.9   | < 0.0001** | 0.030 |
| VLDL-C [mg/dL]   | 38 ± 15.9   | 37 ± 13.5   | 35 ± 10.6   | 20 ± 18.5   | < 0.0001** | 0.030 |
| SCr [mg/dL]      | 1.0 ± 0.3   | 1.0 ± 0.2   | 1.0 ± 0.1   | 0.8         | 0.9 ± 0.2 | 0.9 ± 0.2 | 0.8 ± 0.1 | < 0.0001** | 0.030 |
| eGFR [ml/min/1.73m²] | 77 ± 18.1  | 77 ± 15.8  | 76 ± 16.2  | 76 ± 14.2  | 0.5  | 0.030 |

**Abbreviations:** HbA1c Glycated hemoglobin 1c, eABG Estimated average glucose, SBP Systolic blood pressure, DBP Diastolic blood pressure, HDL-C High Density Lipoprotein-Cholesterol, LDL-C Low Density Lipoprotein-Cholesterol, VLDL-C Very Low Density Lipoprotein-Cholesterol, SCr Serum Creatinine, eGFR Estimated Glomerular Filtration Rate, FC Final control arm vs FI final intervention arm

### Table 3: Gender wise comparison of process outcome measures at final follow up; control vs intervention

| Parameters | Control Arm | Intervention Arm | Comparison of Male Participants | Comparison of Female Participants |
|------------|-------------|------------------|---------------------------------|----------------------------------|
|            | Mean ± SD   | Mean ± SD        | (p-values)                      | (p-values)                       |
|            | Final follow up, n = 52 | Final follow up, n = 83 |                      |                                  |
| HbA1c (%)  | 9.7 ± 1.4   | 9.7 ± 1.3        | 7.9 ± 0.7                      | 7.6 ± 0.9                        | 0.0001** | 0.0001** |
| eABG [mg/dL]| 233.2 ± 39.9 | 231.4 ± 37.7    | 179.2 ± 21.6                   | 171.4 ± 27.1                     | 0.0001** | 0.0001** |
| SBP [mm/Hg]| 137.1 ± 6.4 | 136.7 ± 7.6      | 125.8 ± 8.3                    | 123.1 ± 10.5                     | 0.0001** | 0.0001** |
| DBP [mm/Hg]| 88.8 ± 3.8  | 88.7 ± 4.4       | 85.9 ± 4.7                     | 87.1 ± 5.7                       | 0.077 | 0.148 |
| Cholesterol [mg/dL] | 229.1 ± 78 | 217 ± 36.5       | 152.6 ± 27                     | 153.8 ± 25.6                     | 0.0001** | 0.0001** |
| TG [mg/dL] | 170.2 ± 47.3 | 173.4 ± 50      | 141.2 ± 24.1                   | 143.1 ± 34.7                     | 0.283 | 0.0001** |
| HDL-C [mg/dL]| 48.3 ± 12.3 | 49.9 ± 14.8      | 47.8 ± 7.7                     | 49.4 ± 8                         | 0.210 | 0.170 |
| LDL-C [mg/dL]| 75.6 ± 93.5 | 85.8 ± 67.3      | 76.5 ± 25.2                    | 75.7 ± 20.2                      | 0.0001** | 0.0001** |
| VLDL-C [mg/dL]| 17 ± 18.5  | 22.3 ± 18.4      | 28.3 ± 4.8                     | 28.6 ± 6.9                       | 0.284 | 0.0002** |
| SCr [mg/dL] | 0.9 ± 0.1   | 0.9 ± 0.1        | 0.8 ± 0.2                      | 0.8 ± 0.1                        | 0.0001** | 0.0001** |

**Abbreviation:** SD Standard deviation, eABG Estimated average blood glucose, SBP Systolic blood pressure, DBP Diastolic blood pressure, TG Triglycerides, HbA1c Glycated Haemoglobin, HDL-C High Density Lipid-Cholesterol, LDL-C Low Density Lipid-Cholesterol, VLDL-C Very Low Density Lipid-Cholesterol, Sr Cr Serum Creatinine, eGFR Estimated Glomerular Filtration Rate, FC Final control arm vs FI final intervention arm

*p-values; **p < 0.001–0.0001
It has been reported that majority of adults with T2DM have at least one co-existing chronic condition [26], while almost 40% adult diabetic patients have 3 or even more, especially in patients having history of uncontrolled diabetes [50]. Thus, the management of diabetes in patients with co-existing diseases require multifaceted approach by a team of health care professionals [12, 40]. Numerous literature evidences, randomized control trials (RCTs) in community and hospital settings, suggested that the addition of pharmacist to health care team for the management of chronic diseases, such as diabetes, not only resulted in strict glycemic control but also improved other targets of diabetes care, such as blood pressure and lipid profiles [34, 45].

Data from the present study suggested that majority of the clinical parameters at baseline were similar, except for blood pressure, lipid profiles and serum creatinine. Nevertheless, except for LDL-C, mean values for blood pressure, VLDL-C, triglycerides and SCr were significantly higher in patients of intervention arm. However, these differences might not have a negative impact on trial primary outcomes regarding comparison between control and intervention arm, probably because of insignificant differences in HbA1c values between both the arms and higher mean baseline values of outcome measures in the intervention arm in comparison to control. Thus higher mean baseline values in intervention arm can only underestimate the pharmacist improvements in the outcome measures in comparison to control. Similarly, no significant differences were observed in baseline values in most of the outcome variables, especially HbA1c and blood pressure, between male and female patients, thus, the intervention footprint on these population cannot be attributed to gender base differences rather can be ascribed to pharmacist's intervention in collaboration and cooperation of physician and patient, respectively.

In the present study, we observed a reduction in HbA1c of 3.3%, i-e., from 11 to 7.7% by introducing apt dietary and lifestyle modifications and allied self-management approaches by a pharmacist that presumably affected other targets of diabetes care. Conversely, in the control arm, there was only 1% reduction in HbA1c, from 10.7 to 9.7%, as a result contriving negligible effects on other targets of diabetes care, possibly due to still higher than ADA target goal of HbA1c levels. Numerous previous studies have suggested that pharmacist provision of pharmaceutical care in the management of diabetes could result in HbA1c reduction from 0.5–3.4% compared to almost no or minor changes in HbA1c levels in control subjects [6, 23, 24, 32, 37]. Our observation of 3.3% reduction in HbA1c - higher than already reported reductions, could be attributable to factors associated with Pakistan's health care services and patient factors, i-e. lack of any form of disease or therapy related education & counseling for patients helpful in empowering them with the skills to self-manage their disease, poor health literacy and affordability among patients [46, 47] and lastly health seeking behavior of patients in Pakistan, i-e., most of the patients aspire less

### Table 4 Percentage of patients achieving glycemic and blood pressure goals

| Outcome Measures | Control Arm Follow Up | Intervention Arm Follow Up |
|------------------|-----------------------|---------------------------|
|                  | 1st, n = 121 (%)      | 2nd, n = 121 (%)         | 3rd, n = 52 (%)          | 1st, n = 123 (%)      | 2nd, n = 105 (%)       | 3rd, n = 83 (%) |
| **Glycaemic Goals** |                      |                           |                          |                      |                           |              |
| % of patients achieving goal HbA1c < 7% | 0 (1.7) | 2 (1.7) | 0 (0)                     | 4 (3.3) | 5 (4.1) | 9 (8.6) | 14 (16.9) |
| % of patients achieving goal HbA1c < 8% | 2 (1.7) | 8 (6.6) | 3 (5.8)                   | 0 (0)  | 14 (11.4) | 28 (26.7) | 33 (39.8) |
| % of patients achieving goal HbA1c < 9% | 15 (12.4) | 24 (19.8) | 25 (20.7) | 13 (25) | 18 (14.6) | 27 (22) | 39 (37.1) | 29 (34.9) |
| % of patients at HbA1c ≥ 9% | 106 (87.6) | 93 (76.9) | 86 (71.1) | 36 (69.2) | 105 (85.4) | 77 (62.6) | 29 (27.6) | 7 (8.4) |
| **Blood Pressure Goals** |                      |                           |                          |                      |                           |              |
| % of patients with SBP < 130 mmHg | 42 (34.7) | 41 (33.9) | 27 (22.3) | 4 (7.7) | 22 (17.9) | 31 (25.2) | 39 (37.1) | 45 (54.2) |
| % of patients with SBP ≥ 130 mmHg | 79 (65.3) | 79 (66.1) | 94 (77.7) | 48 (92.3) | 102 (82.1) | 92 (74.8) | 65 (62.9) | 38 (45.8) |
| % of patients with DBP < 80 mmHg | 49 (40.5) | 40 (33.1) | 45 (37.2) | 29 (55.8) | 84 (68.3) | 51 (41.5) | 19 (18.1) | 8 (9.6) |
| % of patients with DBP ≥ 80 mmHg | 12 (9.9) | 11 (9.1) | 9 (7.4) | 0 (0) | 3 (2.4) | 2 (1.6) | 2 (1.9) | 1 (1.2) |
| % of patients with DBP ≥ 90 mmHg | 56 (46.3) | 72 (59.5) | 76 (62.8) | 43 (82.7) | 97 (78.9) | 89 (72.4) | 69 (65.7) | 48 (57.8) |

**Abbreviations:** HbA1c Glycosylated Haemoglobin, SBP Systolic blood pressure, DBP Diastolic blood pressure

*Note: Inclusion criteria of study was >8% HbA1c i.e. patients with uncontrolled diabetes mellitus*
waiting time, spending more time with health care professional, free medicines, free laboratory tests, free health related education and counseling etc. [31]. Several randomized control trials (RCTs) demonstrated that pharmacist intervention resulted in greater number of patients achieving ADA target goal of <7% HbA1c influenced by study duration and number of follow ups – for example, pharmacist intervention resulted in <7% HbA1c levels in 23.4% patients in intervention arm compared to 15.2% in control arm at 6 months assessment [34]. Another study reported glycemic control in 45.4% subjects in the intervention arm and 30.3% in control arm at 12 months assessment [39]. Likewise, we observed that at final follow up greater number of patients (39.8%) in the intervention arm achieved <8% HbA1c target compared to only 5.8% in the control arm, yet more surprisingly, not a single patient in the control arm achieved <7% HbA1c target compared to 16.9% in the intervention arm. These findings clearly demonstrated that when pharmacist interventions appropriately addressed drug related problems (DRPs) [18] followed by pertinent lifestyle modifications [2, 17] and diabetes self-management education [16, 27], patient’s in the intervention arm exhibited greater reductions in HbA1c levels compared to control subjects.

Regarding impact on other targets of diabetes care, compared to control arm, starting from first follow up, i-e., after 3 months, the outcome measures were significantly improved at final follow up in the intervention arm in comparison to baseline, such as BMI, a switch from obese category (30.7 ± 6.4) to overweight category (28.9 ± 5.9), 21 mmHg reduction in SBP, 70 mg/dL reduction in cholesterol, 129 mg/dL reduction in triglycerides, 0.3 mg/dL reduction in serum creatinine and an increase of 24 ml/min/1.73m2 in eGFR. Similar to our findings, number of previously reported RCTs have suggested that pharmacist managed diabetes care could improve glycemic control and other outcome of diabetes care such body weight, blood pressure, LDL-C and cholesterol levels [29, 48]. According to a literature report, a blood pressure increase of 10 mmHg could increase the risk of cardiovascular events by 20% [1]. We found that compared to final follow up of the control arm, in the intervention arm, there was almost similar reductions in SBP in both males (12 mmHg) and females (13 mmHg) corroborating previous report that pharmacist intervention resulted in significant improvements in SBP and DBP [39]. Thus, it is reasonable to deduce that pharmacist intervention may contribute in averting the risk of cardiovascular events. Thus, in Pakistan, with almost negligible role of pharmacists in the management of chronic diseases (I. [4, 14]), this study signifies the pivotal role of a pharmacist in the management of diabetes in collaboration with primary care physician in a primary care settings.

The present study could have several practical implications in Pakistan’s health system, as it provides a first structured pharmaceutical care model in primary health care settings for the implementation of pharmaceutical care plan (PCP) in the management and care of T2DM patients by a pharmacist. Thus, a qualified pharmacist with prior knowledge of diabetes related pharmacological and non-pharmacological issues or a more formal training could suitably implement this model. Moreover, the current practice model utilizes and applies all the recommendations put forth by international associations and organizations for the management of diabetes using information system, evidence based management and multifaceted patient centered approaches in collaboration with a primary care physician. Moreover, this model initiates and encourages the development of good relationships between pharmacist, physician and patient, a factor that might have contributed in improved outcomes in patients of intervention arm.

Thus, followings are the recommendations to implement this practice model; the model can be implemented in all three tiers of health care system, i-e. primary, tertiary (hospitals) and even community care settings because of several reasons; this model allows frequent communication among physician, patient and diabetes management team, the model very well targets patients with poor glycemic control having multiple barriers to care, face to face interaction between pharmacist and the patient allows the patients to build a trusting relationship with mid-level provider, i-e. the pharmacist, which may improve self-care and adherence to medication and behavioral modifications, and finally, clinical pharmacist may have led to better management of complex therapy regimens. Similar practicing models can be developed and implemented for hypertension and dyslipidemia management.

Study limitations

The study has a few limitations; though the enrolled subjects were from diverse backgrounds and localities of Lahore, it’s a single center study due to scarcity of funds and human resource. The study was of limited duration, therefore, long term impact of pharmacist’s intervention on disease outcomes could not be ascertained. Some of the baseline values of clinical variables, such as SBP, DBP, VLDL-C, triglycerides and serum creatinine were higher in intervention arm, which may indicate a possible underestimation of the impact of pharmacist’s intervention on these outcomes.
Conclusion

In conclusion, results from the first RCT on pharmacist’s role in primary care settings in the management of T2DM in Lahore, Pakistan, employing individualized pharmaceutical care plan (PCP), demonstrated significant improvements in process outcome measures, such as blood glycemic levels, blood pressure, dyslipidemia, BMI and kidney functions.

Additional files

Additional file 1: Figure S1. General Pharmaceutical Care Plan. Figure S2. Categorization of participants in intervention arm based on follow-ups. Table S1. Patients Overall and Gender wise distribution of Baseline Demographics and Clinical Characteristics. Table S2. Percentage of Patients in HbA1c Reduction Quartiles. (DOCX 1053 kb)

Additional file 2: Data collection form. (DOCX 76 kb)

Additional file 3: Patient’s consent form. (DOCX 291 kb)

Abbreviations

B: Baseline; BMI: Body mass index; C: Cholesterol; Cr: Final control; DBP: Diastolic blood pressure; DMSE: Diabetes self-management education criteria; eABG: Estimated average blood glucose; eGFR: Estimate glomerular filtration rate; F: Female; F: Final follow up; HbA1c: Hemoglobin A1c; glyced hemoglobin; HDL-C: High density lipoprotein - cholesterol; I: Intervention; I: Final intervention; LDL-C: Low density lipoprotein - cholesterol; M: Male; OHA: Oral hypoglycemic agents; PWDT: Pharmacist work up of drug therapy; RCTs: Randomized control trial; SBP: Systolic blood pressure; SCR: Serum creatinine; S/NBG: Self-monitoring of blood glucose levels; T2DM: Type 2 diabetes mellitus; TG: Triglyceride; VLDL-C: Very low density lipoprotein – cholesterol

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Authors’ contributions

ZJ collected and analyzed data and did intervention, UI collected the data and involved in study design, IK referred the patients and help in designing the study, HS designed the study, analyzed data and wrote the manuscript, RJK collected the data and prepared the first draft, MI; analyzed data and edited the manuscript, ZS analyzed data and wrote the manuscript, FS helped in data collection and edited the article, ZD edited the manuscript and assisted in data collection, FB; helped in data collection and edited the manuscript, NA analyzed data and edited manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

Data will be available upon request to corresponding author at hamid.pharmacy@pu.edu.pk

Ethics approval and consent to participate

The study was approved by Ethical Committee of Human Research, Punjab University College of Pharmacy, University of the Punjab, Lahore, reference #: HEC/1000/PUCP/1926. The informed written consent was obtained (Additional file 3) by all the subjects.

The study followed the professional ethics codes of the Helsinki Declaration of 1964 and its subsequent revisions.

Consent for publication

The consent was also obtained from the participants to publish the study results.

Competing interests

The authors declare that they have no competing interests.

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