A Community Pharmacy-Based Intervention in the Matrix of Type 2 Diabetes Mellitus Outcomes (CPBI-T2DM): A Cluster Randomized Controlled Trial

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ABSTRACT

INTRODUCTION: Egypt has the ninth highest diabetes mellitus (DM) prevalence in the world. There is a growing interest in community involvement in DM management.

AIM OF THE STUDY: The aim of the study was to evaluate the tailored diabetes care model (DCM) implementation in Alexandria governorate by community pharmacy-based intervention (CPBI) from a clinical, humanistic, and economic aspect.

METHODS: This is a 6-month period cross-over cluster randomized control trial conducted in Alexandria. Ten clusters owing 10 community pharmacies (CPs) recruited 100 health insurance-deprived T2DM patients with >7% HbA1c in 6-months. The study was divided into 2 phases (3 months for each period) with a 1-month washout period in between. After CPs training on DCM, the interventional group received pictorial training for 45 minutes in first visit, and 15 minutes in weekly visits, whereas the control group patients received the usual care (UC). At baseline and end of each phase (3 months), patients had clinical and physical activity assessments, filled all forms of study questionnaire (knowledge, self-management, satisfaction, and adherence) and did all laboratory investigations (Fasting Blood Glucose [FBG]), HbA1c, protein-creatinine clearance (PCR), creatine clearance (GFR), and lipid profile.

RESULTS: There was no significant difference in the basal systolic and diastolic blood pressure between patients in the CBPI and UC groups, but the CBPI had significantly decreased the mean SBP and DBP by ($P = .008, .040$, respectively). Also, significant waist circumference and BMI reductions (-5.82 cm and -1.86 kg/m^2, $P = .001$) were observed in the CBPI. The CBPI patients achieved a greater reduction in FBG and HbA1C than the UC patients (102 mg/dL and 1.9%, respectively $P < .001$). Also, significant reductions in total cholesterol, LDL, and triglyceride (-6.4, -15.4, and -6.3 mg/dL respectively, $P = .001$) were achieved in the CBPI group. No significant differences were found in HDL, GFR, and PCR. Moreover, significant improvements of behavior, score of knowledge, self-management, satisfaction, and adherence were observed in CBPI patients. After multivariate analysis, HbA1C readings were significantly influenced by baseline HbA1C and eating habits. The cost saving for CPBI was -1581 LE per 1% HbA1c reduction.

CONCLUSION: This is the first study in Egypt that illustrated the positive impact of pictorial DCM delivered by CPBI collaborative care on clinical, humanistic, laboratory, and economic outcomes to local T2DM patients.

KEYWORDS: Diabetes mellitus, community pharmacy, patient education, diabetes education, cost effectiveness

Introduction

The Middle East and North Africa (MENA) has an estimate of 35.3 million diabetic patients; 9 million of whom live in Egypt.[1] Care of Diabetes Mellitus (DM) patients aspires to prevent or delay the development of its complications and improve patients' quality of life. Chronic care model (CCM) is a method of restructuring health care services through interactions between health systems and communities aiming to enable patients to control diabetes.[2] This model emphasizes person-centered close follow up and adherence to treatment plan including medication, lifestyle measures, and blood glucose monitoring.[3] However, such strategy has a challenge due to shortage of resources and economic exhaustion.

Discrete communities in Egypt have high prevalence of illiteracy and low socioeconomic states. Low educational attainment in these communities may also affect diet quality, physical inactivity, and unhealthy behaviors resulting to increased diabetes cases.[4] Due to their accessibility and flexibility, community pharmacies are well suited to support and reach out to this vulnerable group about optimal diabetic care, in developing countries as Egypt.
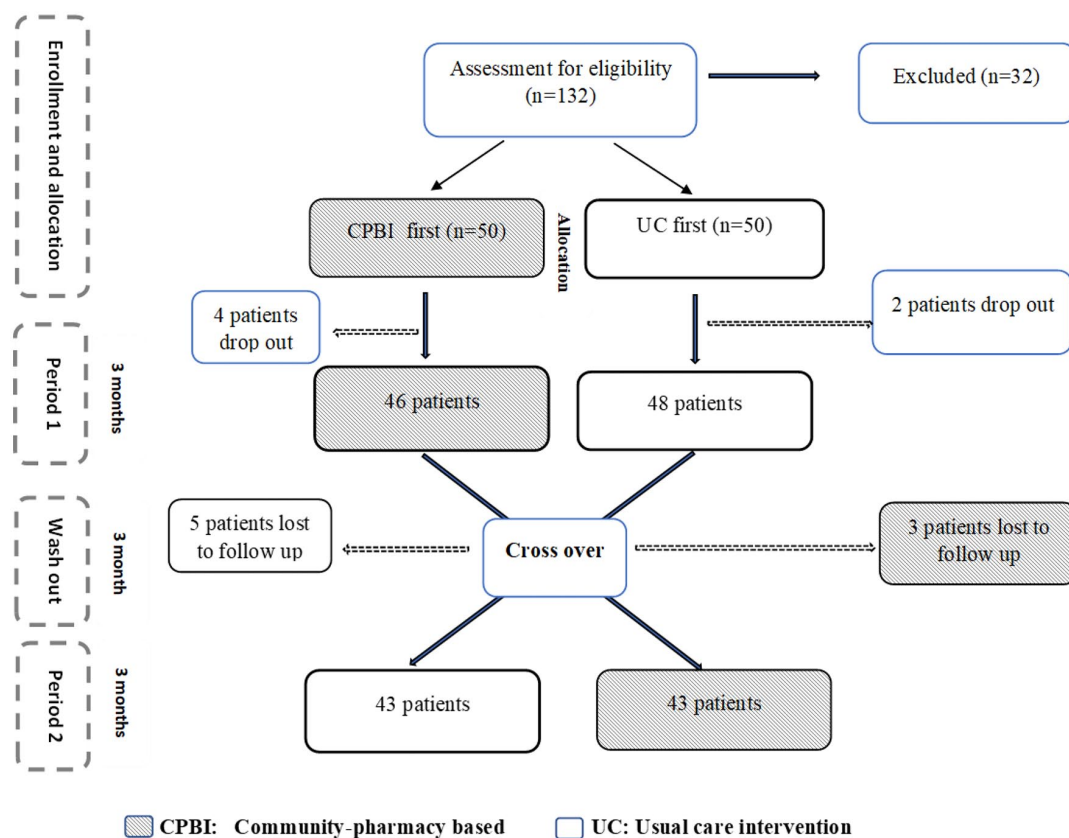
Figure 1. Flow chart of the study periods and participants.

The effectiveness of pharmaceutical care interventions should be appraised in research by measuring diabetic patients' knowledge, self-efficacy, quality of life, and cost.

Aim of the Study

The aim of the study was to evaluate the community pharmacy-based chronic care of diabetic patients on diabetes control in Alexandria governorate. Also, to assess a simple diabetes care model (DCM) related to Egyptian culture from clinical, humanistic, and economic perception.

Subjects and Methods

Study design

A cluster randomized control trial (RCT) with simple 2×2 crossover was adopted for 6-months. Eligible patients and pharmacists were identified at the 10 community pharmacies located in Amryia governorate, Alexandria. The study was divided into 2 phases (3 months for each period) with a 1-month washout period in between followed by cross over of groups (see Figure 1).

Participants

To achieve 90% power with a target significance level at 5%, we calculated that 68 patients should be enrolled. Sample size was increased to 100 patients to compensate for attrition. Using

simple random sampling 2 groups were allocated, 1 group was randomly allocated to the community pharmacy-based intervention (CPBI) implementing the DCM (the CPBI group also received UC in addition to the intervention); while the other was allocated to UC only. Ten clusters (Shiakhas) which included 10 pharmacies were selected; with each aiming to enroll 10 patients.

The targeted patients were >18 years old, with uncontrolled Type 2 Diabetes Mellitus (T2DM) (HbA1c: ≥7%), resident within the pharmacy catchment area, regularly visiting the pharmacy performing the study and without health insurance (thus permitting the study to offer them laboratory analysis). Patients with mental and physical disabilities (including dementia, stroke, advanced retinopathy/blindness, deafness, and/or muteness) were excluded. Also, pregnant/lactating females, decompensated liver, renal, and heart failure were excluded to exclude gestational diabetes, or uncontrolled diabetes due to co-morbidities, respectively.

Usual care is dispensing drugs with accurate reading of the signature as stated by the physician.

Intervention

After face-to-face training of the pharmacists, they provided face-to-face patient education in the interventional group, whereas the pharmacists providing usual care were not invited

to the patient education session and the control group patients received UC.

The patient-oriented diabetic care model (DCM) was constructed according to American diabetes Association guidelines.[4] The intervention included: (a) an educational component comprising of pictorial posters of DM and its complications, (b) a non-pharmacological component in the form of lifestyle changes comprising; nutritional therapy, smoking cessation strategies, physical exercise: walking at least 3 times weekly for 30 minutes, (c) a pharmacological component in the form of a review of medication indications, doses, and frequency, and (d) regular weekly visits of CPBI patients to their assigned pharmacies (45 minutes in the initial visit and 15 minutes in subsequent visits) for consolidation of the education, goal review insisting on drug adherence.

At baseline and end of each phase (3 months), the patients were subjected to history taking, clinical assessments (including blood pressure [BP], Body Mass Index [BMI], waist circumference [WC], and physical activity assessments [including weekly duration and intensity (light [less than 150 minutes], moderate [150-300 minutes], heavy [more than 300 minutes or resistance training at least 30 minutes, more than 2 times a week], and no physical activity)]), questionnaire completion, and all laboratory investigations. However, both groups of patients visited the relevant pharmacy monthly for medication supplies, assessment of vital signs, and fasting blood glucose (FBG).

Measurement tools

- The structured interview questionnaires assessed the level of patient knowledge of diabetes management,[5] patient adherence to treatment using Morisky Medication Adherence Form,[6] and patient self-efficacy using 6-items self-efficacy scale for managing chronic diseases.[7] Also, patient satisfaction was assessed using 18-item short term patient satisfaction questionnaire (PSQ-18).[8]
- The laboratory investigations were carried out at 2 private health clinics located within the catchment area of the pharmacies, where the assessors were blinded, and included glycated hemoglobin (HbA1c%), lipid profile (cholesterol, LDL, triglycerides (TG), and HDL-cholesterol), and Protein creatinine ratio (PCR).

Ethical consideration

Ethics approval was obtained from the Ethics Committee of the High Institute of Public Health. Written informed consent was obtained from all study participants.

The study is registered in pactr.samrc.ac.za (Registration no.: PACTR201909534333056).

Statistical analysis

Demographic and baseline clinical data was summarized as frequency or mean ± SD. Repeated-measures ANOVA, and *t*-test were applied to compare the laboratory profiles of both groups, for normally distributed data; otherwise, Kruskal Wallis, and Mann-Whitney tests were used. The questionnaires were compared using Chi squared test and paired analysis (McNamara test, Marginal homogeneity test).

There was no significant carry over effect revealed by summation of HbA1C at the end of the period 1 and 2 ($P = .390$). A P value of $<.050$ was considered to be statistically significant. All data analysis was performed accordingly using IBM SPSS Statistics 25 (SPSS, statistical package for social science Chicago, IL).

Economic analysis

An incremental cost-effectiveness analysis (ICER) was performed, with costs and effectiveness of CPBI compared with that of usual pharmacy care. The health sector's perspective was used. All direct costs of providing CPBI, including training costs, and medications' cost were included. Also, the absenteeism directed to DM or it is complications (absenteeism [from work] attributed to DM or it is complications [absenteeism days] within the last 3 months multiplied by 100 Egyptian Pound [EGP]) was calculated. Also, cost of diabetes-related healthcare resources: included the doctors and emergency department and hospital admissions based on the receipt of the hospital was estimated. We excluded costs of the time pharmacists spent in the training and implementation of the study. Because pharmacists participated voluntary on their free time. In addition, the implementation was during their working hours, so it did not take additional time.

Incremental Cost-Effectiveness Ratio (ICER) = (C1–C2)/(E1–E2).[9] C1 = cost of CPBI; C2 = cost of the UC; E1 = mean change in HbA1c for CPBI; E2 = mean change in HbA1c for the UC.

Results

Socio-demographic features and medical history of the studied patients

More than half (57%) of the enrolled patients were female. The patients were aged between 40 and 60 and had poor socio-demographic features with almost 40% being illiterate. The most frequent comorbidity was hypertension (see Table 1).

Blood pressure and anthropometric measures

At baseline, there was no significant difference in the basal SBP and DBP between the CBPI group versus the UC group. After the intervention, the CBPI had significantly decreased the mean of SBP by (–7 mmHg vs +0.96 mmHg, $P = .008$) and mean of DBP by (–3.3 mmHg vs +2.1 mmHg, $P = .040$). However, there was no significant effect of UC on SBP nor DBP. Also, significant reductions in the waist circumference (–5.82 cm vs +2.13 cm, $P < .001$) and BMI (–1.86 kg/m² vs +0.69 kg/m², $P = .001$) were observed in the CBPI group versus the UC group (see Figures 2 and 3).

Table 1. Sociodemographic features and medical history of studied patients.

PERCENT	UC-CPBI	CPBI-UC	P
Age			
−40	18	16	.093
40-60	62	78	
>60	20	6	
Sex			
Male	40.00	46.00	.545
Female	60.00	54.00	
Occupation			
Not working	48	48	.571
Working	52	48	
Retired	0	4	
Education			
Illiterate	44	36	.51
Read and write	46	56	
Basic	10	6	
University	0	1	
Marital status			
Single	0	4	.517
Married	82	84	
Divorced	6	4	
Widow	12	8	
Crowding index			
−2	64	66	.264
−4	18	26	
−6	18	8	
Smoking			
Never	68	70	1
Current	26	24	
Ex-smoker	6	6	
Physical activity			
Light	18.0	18.0	.94
Moderate	4.0	6.0	
No	68.0	76.0	
Co-morbidities			
Hypertension	20.0	12.0	.54
IHD	6.0	2.0	
Gout	2.0	2.0	
Age at onset of T2DM (y)	38.5 ± 10.3	36.0 ± 9.3	.12
Duration of T2DM (y)	7.0 ± 6.2	9.2 ± 8.1	.07

Abbreviations: CPBI, community pharmacy-based intervention; OHGD, oral hypoglycemic drugs; UC, usual care.

Laboratory tests result of the studied patients

FBG showed marked decrease among the patient in CPBI-UC group (121.5 mg/dL) during the intervention (period 1). Also, the patients within UC-CBPI group had marked decrease in FBG (82 mg/dL) during the intervention (period 2). The CBPI patients achieved a greater reduction in FBG values than the UC patients (−0.44% vs +0.12%, $P < .001$) at the end of the study (see Figure 4).

Despite no significant difference in the basal HbA1c, the CBPI groups achieved a double reduction in HbA1c than the UC patients (−1.88% vs +1.89%; $P < .001$) at the end of the intervention period (see Figure 5).

A significant reduction in total cholesterol (−6.4 mg/dL vs +9.8 mg/dL, $P = .001$) and LDL (−15.4 mg/dL vs +10 mg/dL, $P = .001$) was achieved in the CBPI group versus the UC group. Moreover, TG was significantly decreased in the CBPI group versus the UC group (−6.3 mg/dL vs +3.8 mg/dL, $P = .001$). No significant differences were found in HDL levels between the groups ($P = .530$). No significant differences were found in GFR or PCR levels between the groups ($P = .300$, and $P = .400$, respectively) (see Table 2).

Knowledge acquisition, behavioral, self-management, patient satisfaction, and adherence to medications

Despite an insignificant difference in the baseline score, there was a significant increase in the knowledge of the study participants after the intervention compared to baseline knowledge by 30% ($P < .020$). False knowledge significantly decreased after the intervention from 59.6% to 12.4% ($P < .001$). The highest correct answer before and after intervention for question (High blood sugar may happen because you eat too much); 63.9% and 94.4%, respectively (see Table 3).

Comparatively to the UC, exposure to CPBI significantly increased physical activity from mild or no physical activity to moderate activity (23.6% for UC vs 45% for CPBI); whole grain weekly intake (n = 41.6% UC vs 60% CPBI) as well as vegetables/fruits weekly (n: 43% UC vs 55% CPBI). There was no significant reduction in smoking habits with CPBI ($P > .050$). Exposure to CPBI significantly raised the mean score self-management in comparison to exposure to the UC (4.7 ± 1.1 vs 6.2 ± 1, respectively, $P < .001$) (see Table 3).

For the CPBI group, regardless of accessibility and convenience, there was a statistically significant increase in patient satisfaction score in all domains and in the composite score following the intervention ($P < .001$) (see Table 3).

Despite insignificant difference in the baseline score, there was a significant shifting to moderate and high adherence to medications in both groups after CPBI than exposure to UC (MS: 40.4% vs 64% and 18% vs 25.8%, respectively, $P < .001$) (see Figure 6).
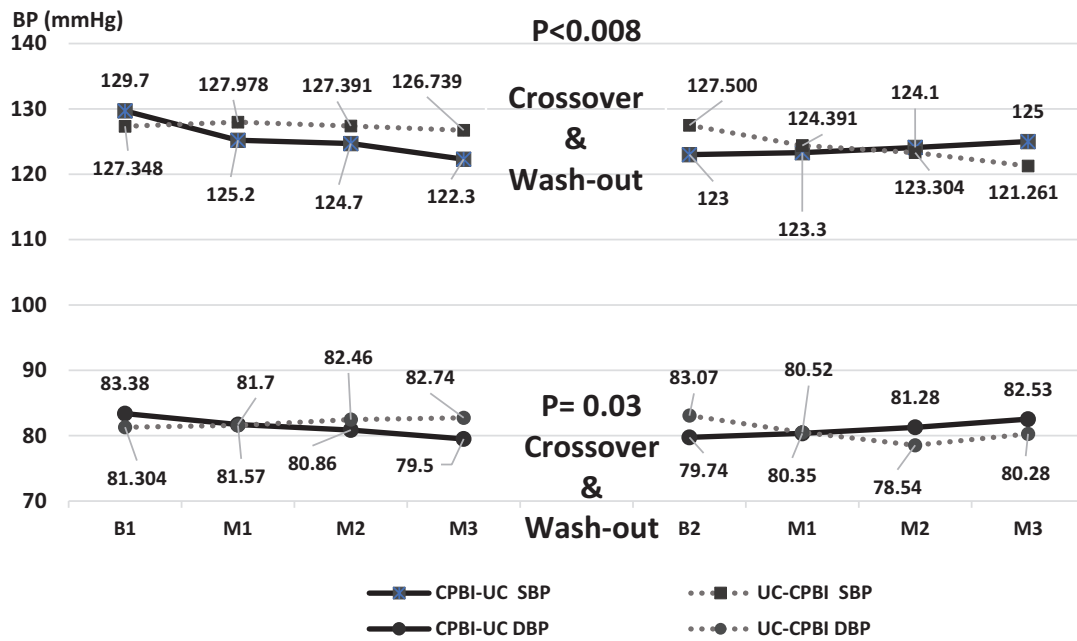
Figure 2. Month wise SBP and DBP of studied patients on exposure to UC and CPBI.
Abbreviations: B1, baseline period 1; B2, baseline period 2; CPBI, community pharmacy-based intervention; DBP, diastolic blood pressure; M1, first month; M2, second months; M3, third months; SBP, systolic blood pressure; UC, usual care.
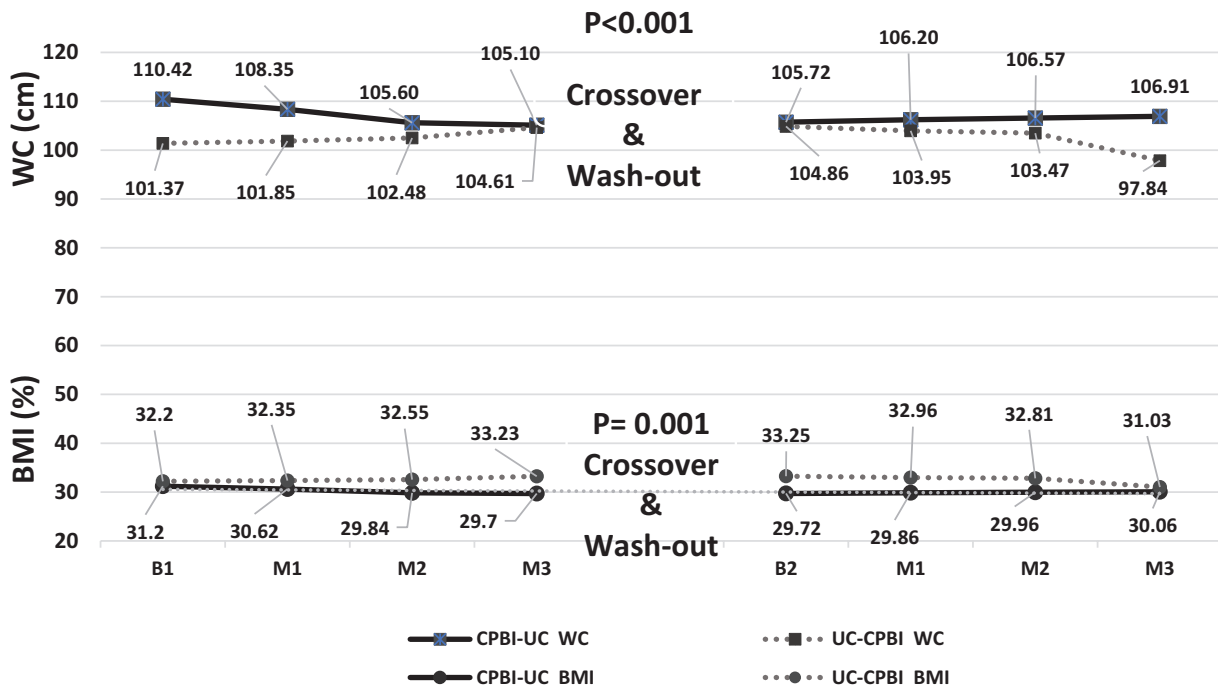

Figure 3. Month wise WC & BMI of studied patients on exposure to UC and CPBI.
Abbreviations: B1, baseline period 1; B2, baseline period 2; BMI, body mass index (kg/m²); CPBI, community pharmacy-based intervention; M1, first month; M2, second months; M3, third months; UC, usual care; WC, waist circumference (cm).

Multivariate regression analysis of factors affecting DM control and lipid profile

The univariate analyses entailed the age, sex, marital status, education, family history, comorbidities, regular checkup, age at onset of DM, duration of DM, smoking, physical activity, dietary habits, BMI/ WC, SBP/ DBP, LDL, HDL, TG, GFR, PCR, as well as patient satisfaction, knowledge of DM, adherence to drugs and self-management scores. The most significant factors affecting HbA1C were baseline HbA1C and eating habits. Likewise, eating habits were the main driving force affecting LDL-cholesterol. Regarding triglycerides level, baseline HbA1C, WC, and patient knowledge were the main modifiable factors (see Table 4).
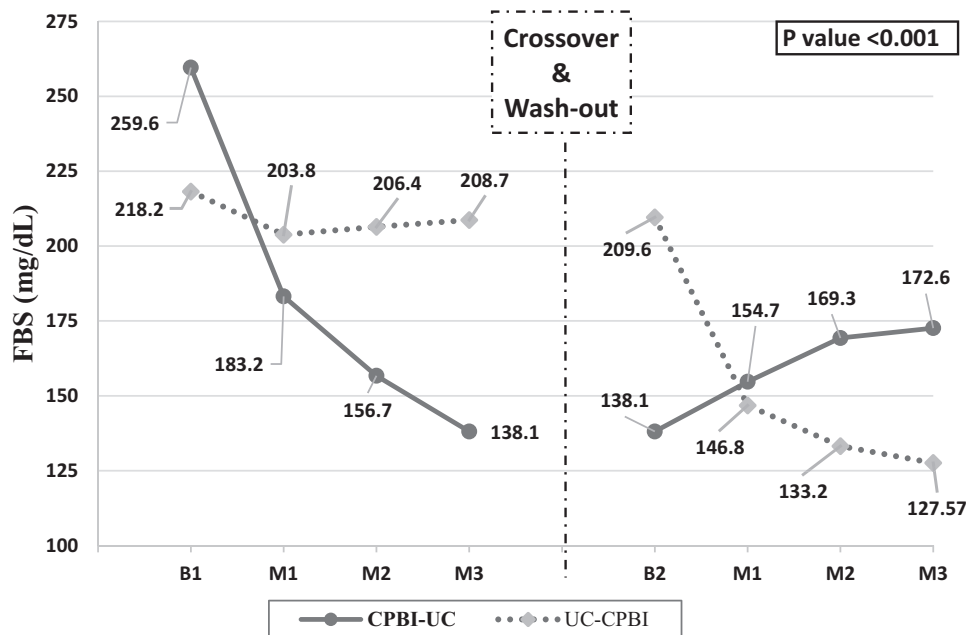
Figure 4. Month wise FBS of studied patients on exposure to UC and CPBI.
Abbreviations: B1, baseline period 1; B2, baseline period 2; CPBI, community pharmacy-based intervention; FBS, fasting blood sugar; M1, first month; M2, second months; M3, third months; UC, usual care.
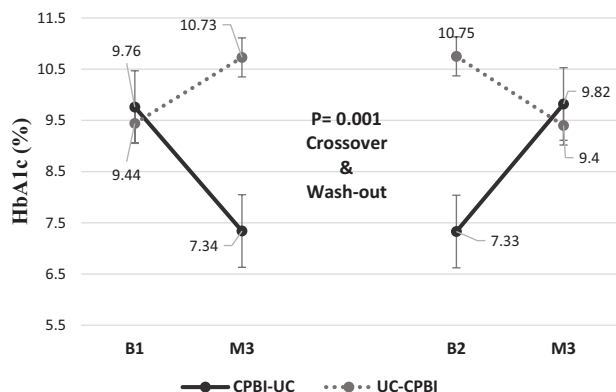

Figure 5. Month wise HbA1c of studied patients on exposure to UC and CPBI.
Abbreviations: B1, baseline period 1; B2, baseline period 2; CPBI, community pharmacy-based intervention; M1, first month; M2, second months; M3, third months; UC, usual care.

Economic outcome post exposure to UC and CPBI

Unlike UC, exposure to CPBI significantly dropped average cost of medicines/patient, frequency of dosage, and insulin doses ($P < .010$, $P < .010$, and $P < .030$, respectively) monthly. Lower frequency of GP and specialist consultations, hospitalization cost, and absenteeism days with CPBI than UC were documented but they failed to reach a significant level, $P > .050$.

A significantly reduction in HbA1C of CPBI led to a lower total cost with the CPBI (20 023.35 EGP) than the UC (25 983.65 EGP). The incremental costs and HbA1c reduction for CPBI compared to UC were 5961 EGP and 3.77%, respectively. Thus, the ICER was –1581 EGP per 1% HbA1c reduction for patient maintained on CPBI for 3 months (see Figure 7).

Discussion

To the best of our knowledge, this study is the first to address the role of community pharmacy in the management of diabetic patients in Egypt using an CCM model on patient self-management, satisfaction, adherence to treatment, and disease knowledge.

A significant reduction in mean FBG and HbA1c levels (–102 mmHg, –1.88%, $P < .001$) in the CPBI group was observed. According to the UKPDS, each 1% reduction in A1c levels reduces the risk of death related to diabetes by 21%, the risk of myocardial infarction by 14%, and the risk of microvascular complications by 37%.[10] A recent literature review found that interventions performed by pharmacists showed a significant reduction of 0.18%-2.1% in HbA1c levels, after an average interval of 3-12 months.[11] Also, a recent meta-analysis showed that integrated DM education-pharmaceutical care intervention had a significant role in lowering the HbA1C and FBG (–0.86%, –34.95 mg/dL, respectively).[12] The improvement of HbA1C was influenced by baseline HbA1C and eating habits. Likewise, the educational pharmacist-led care program improved glycemic control (mean HbA1C-0.5%) through lifestyle changes and controlling patients' eating habits.[13,14] In contrast to this result, the Fremantle Diabetes Study reported a smaller reduction in HbA1C and FBG (<0.5%, <15 mg/dL, respectively).[15] A study was conducted in Iran, 85 patients were recruited, the level of HbA1C was insignificantly decreased after the intervention.[16] Also, the effect of adding pharmacists to primary care teams in T2DM patients, didn't achieve any statistical significance.[17] The lack of HbA1C effect was attributed to either contamination between cases and control or mildly uncontrolled basal level of HbA1C.

Table 2. Lipid profile, GFR, and PCR post exposure to UC and CPBI.

MEAN ± SD	UC-CPBI GROUP				CPBI-UC GROUP				P*
	B1	M3U	B2	M3I	B1	M3I	B2	M3U	
TGs (mg/dL)	139 ± 23.3	143 ± 22.6	143 ± 22.4	135 ± 20.3	164 ± 46.1	139 ± 27.8	139 ± 27.7	143 ± 31.2	<.001
HDL (mg/dL)	47 ± 9.5	47 ± 9.1	47.5 ± 9.3	46 ± 8.0	47 ± 10.6	47 ± 10.2	47 ± 10.2	46 ± 8.3	.538
LDL (mg/dL)	138 ± 28.9	138 ± 28.9	138 ± 28.7	130 ± 13.0	145 ± 28.1	122 ± 16.7	123 ± 15.9	143 ± 7.0	<.001
Cholesterol (mg/dL)	206 ± 63.9	203 ± 64.2	203 ± 63.3	174 ± 40	212 ± 43.9	183 ± 46.8	183 ± 45.9	205 ± 34.9	<.001
PCR	0.6 ± 0.6	0.5 ± 0.6	0.5 ± 0.6	1.1 ± 3.8	0.6 ± 0.8	0.4 ± 0.4	0.4 ± 0.4	0.3 ± 0.4	.404
GFR (mL/min/1.7)	89 ± 16.5	88 ± 15.8	87 ± 14.9	89 ± 14.6	89 ± 18.5	92 ± 17.6	91 ± 17.5	115 ± 15.6	.303

Abbreviations: B1, baseline period 1; B2, baseline period 2; CPBI, community-pharmacy based intervention; GFR: glomerular filtrations rate; HDL, high density lipoproteins; LDL, low density lipoproteins; M3I, third months after community-pharmacy based intervention; M3U, third months after usual care; PCR: protein creatinine ratio; UC, usual care at period 1.
*Repeated measure ANOVA.

Non-pharmacological measures have an essential role in diabetes control and HbA1C reduction.

In this research the level of LDL showed a significant decline after CPBI under the effect of changing eating habits. Just like our results, Lee et al[18] and Huete et al[19] demonstrated that LDL cholesterol level was statistically decreased by the effect of CPBI educational program targeted food intake. Nonetheless, a systematic review studied the effect of pharmacy-based intervention on the control of dyslipidemia, revealed that, the intervention decreased the level of LDL among the intervention group but this reduction was not statistically significant.[20] In line with this, a recent study revealed that LDL-c levels did not change under the effect of CPBI.[13] This controversy could be explained by low basal values already close to international recommended values leaving no room for further improvement.

TG was significantly decreased in the CBPI group versus the UC group and baseline HbA1C, WC, and patient knowledge were the main modifiable factors. Similarly, Paulós et al[21] discussed a 16-week CPBI to manage hyperlipidemia, and the level of triglycerides significantly decreased in the intervention compared to the control group. On the other hand, findings from a RCT of a 100 diabetic patients aiming to assess the effectiveness of CPBI in the management of lipid profile, the intervention showed no significant change on the TG level.[22] The difference in their results to ours could be due to the telephone call-based intervention, not face to face which could be less effective in some models.

In this study, HDL did not show any significant difference after the intervention. Similarly, a meta-analysis that evaluated the role of pharmacists in modifying cardiovascular risk factors found that CBPI interventions have no significant effect on HDL level.[23] The failure to increase HDL level may be due to short period of the study.

In our study, the intervention significantly decreased SBP (*P* = .010) and DBP (*P* = .040) compared with the UC group. Other studies have shown heterogeneous results for any effect of pharmaceutical care programs on blood pressure control. Consistent with our results, a systematic review showed significant reductions statistically and clinically significant improvement in BP in the intervention group at follow-up.[24] A CPBI for a year revealed a significant reduction in SBP and DBP (–5, –3 mmHg; *P* < .040, respectively).[25] On the contrary, other interventions were not associated with changes in blood pressure which attributed to different characteristics of patients and most of them almost well-controlled hypertension.[19,26]

The CBPI group had a significant reduction in the WC and BMI (*P* = .001). Published results regarding the effectiveness of pharmaceutical care for reducing BMI and WC demonstrate considerable discrepancies. In a 12 month study, CPBI achieved significant reductions in BMI (–1.24 kg/m² vs +0.4 kg/m², *P* < .001) and WC (–1.94 cm vs +0.64 cm, *P* < .001) in the intervention group.[27] In a 3-month study, a significant reduction (–0.4 kg/m²) was achieved in BMI values.[28] However, Correr et al,[29] demonstrated a smaller reduction in BMI (–0.2 kg/m²) over 12 months from a higher baseline value in the Brazilian health system.

Unlike the UC, CPBI saliently improved the patient's self-management score and behavior (physical activity, increased the intake of whole grain and vegetables, while processed meat, trans fats, and sugary drinks were decreased). However, it failed to exert any significant change on smoking; most probably due to preponderance of non-smokers (66.3%), and females (57%) among the participants as in our country, females are less likely to smoke. Similar to our results, Northern Cyprus study showed significant improvements were observed in self-care activities such as diet without significant improvement in the smoking behavior domains.[27] A non-blinded RCT conducted on 34

Table 3. Patient knowledge, self-management, and satisfaction of T2DM post exposure to UC and CPBI.

QUESTIONNAIRE SCORE (MEAN ± SD)	UC		P*	CPBI		P*
	PRE-EXPOSURE	POST-EXPOSURE		PRE-EXPOSURE	POST-EXPOSURE	
Knowledge sore (%)						
Poor	33.0	31	.7	24.0	0.0	.001
Moderate	58.0	60		57.0	6.7	
Good	9.0	9		19.0	93.3	
Self-management						
All	4.6 ± 1	4.7 ± 1.1	.2	4.2 ± 0.9	6.2 ± 1.0	.001
CPBI/UC	4.7 ± 1.2	4.8 ± 0.99	.6	4.6 ± 1.2	6.3 ± 1.3	.001
UC/CPBI	6.1 ± 0.8	6.2 ± 0.7	.09	5.8 ± 0.8	6.7 ± 1.3	.001
Patient satisfaction						
General satisfaction	2.98 ± 0.29	2.99 ± 1.17	.7	2.7 ± 0.21	3.45 ± 0.24	.001
Technical quality	3.13 ± 0.42	3.19 ± 1.38	.5	2.95 ± 0.44	3.31 ± 0.42	.001
Interpersonal manner	2.99 ± 0.25	3.04 ± 1.14	.08	2.5 ± 0.14	3.66 ± 0.24	.001
Communication	3.07 ± 0.33	3.1 ± 1.26	.2	2.78 ± 0.16	3.44 ± 0.21	.001
Financial aspects	2.79 ± 0.21	2.82 ± 1.17	.06	2.26 ± 0.15	3.42 ± 0.13	.001
Time spent with doctors	2.76 ± 0.27	2.81 ± 1.32	.09	2.28 ± 0.25	3.44 ± 0.18	.001
Accessibility and convenience	2.95 ± 0.43	2.95 ± 0.39	.9	3.3 ± 0.31	3.34 ± 0.33	.881
Composite satisfaction score	2.95 ± 0.32	2.98 ± 1.96	.07	2.67 ± 0.24	3.43 ± 0.25	.005

Abbreviations: CPBI, community-pharmacy based intervention; UC, usual care.
*t-test.
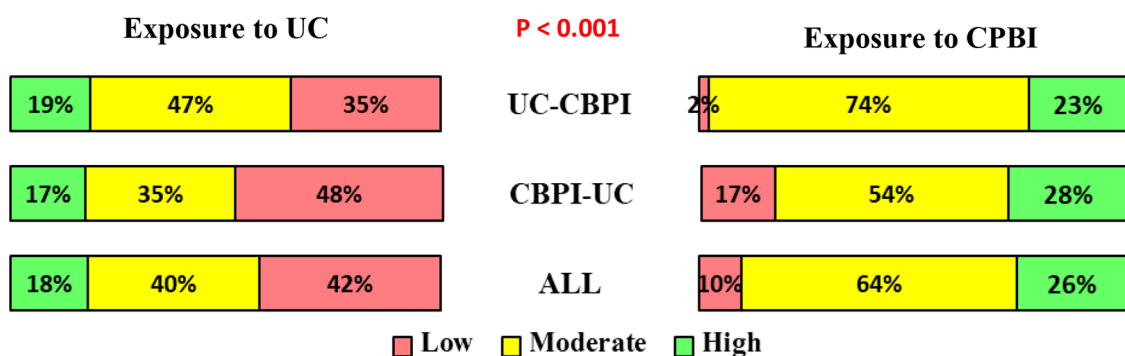
Figure 6. Morisky score of adherence to medications upon exposure to UC and CPBI.
Abbreviations: CPBI, community pharmacy-based intervention; UC, usual care.

patients who received daily educational messages (via SMS) about DM management through mobile phones. The intervention group experienced significant increment in the self-management score, however the drop in the HbA1C level unexpectedly couldn't reach a significant level.[30] The significant improvements in self-care activities in our study might be attributable to the intense pictorial education, and close follow up.

Unlike the UC, there was an upgrading of patient satisfaction in conjunction with exposure to the CPBI compared to the baseline level. The availability of costless and comprehensive individualized healthcare and medical consultation at any time of a patient-centered approach makes it reasonable. The interventions of pharmacists have been proven to improve glycemic control, and increase patients' satisfaction.[31] In contrast,

Table 4. Multivariate models of factors affecting exposure output and outcomes.

MODEL	KEY FACTOR	β	T	P
HbA1C	Patient satisfaction	−.16	2.57	.01
	Baseline HbA1c	.71	10.66	.001
	Habit of eating vegetables	−.21	−3.23	.001
	Habit of eating trans-fats	.44	5.73	.001
	T2DM duration	−.13	−1.9	.01
LDL-Cholesterol	Eating tans-fats	.343	3.221	.002
	Patient knowledge score	−.247	−2.341	.022
	Eating processed meat	.268	2.494	.015
Triglycerides	Baseline HbA1C	.327	3.041	.003
	WC	.303	2.829	.006
	Patient knowledge score	−.27	−2.49	.015
	Age	.231	2.18	.033

Abbreviations: CPBI, community-pharmacy based intervention; LDL, low density lipoproteins; WC, waist circumference.
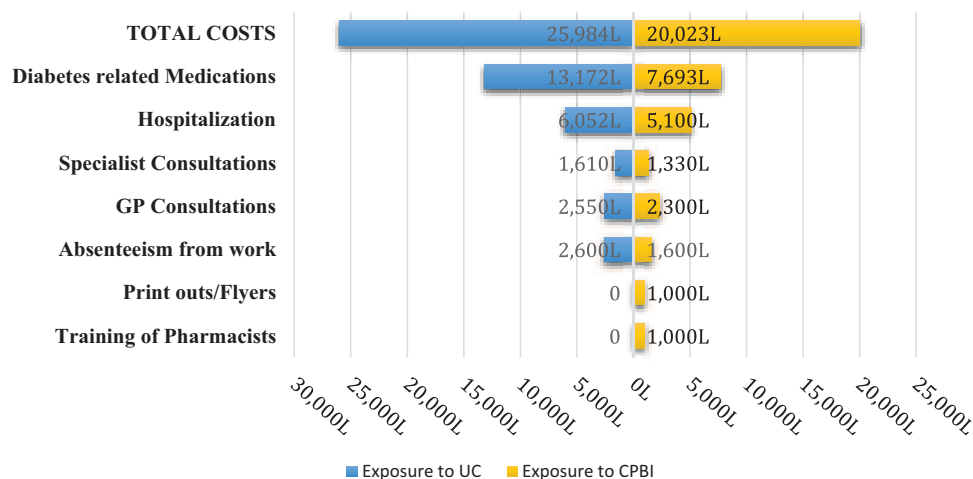

Figure 7. A tornado diagram of different costs on exposure to UC and CPBI for 3 months.

Schroeder couldn't assure the role of community pharmacy in improving patient satisfaction. However; increased satisfaction was insignificant because of higher basal score and both groups of patients received care by the same pharmacy team.[32]

Compared to the baseline values, there was a significant increase in moderate and high drug adherence to 90% of patients. Many studies have approved the role of community pharmacy in improvement of patient's adherence, which was explained by the knowledge gained from the trained pharmacist.[33] On the other hand, patient adherence was not statistically increased after CPBI in a study conducted in Washington University.[34] This was explained as 40% of the enrolled participants did not attend diabetes care plan, and 50% of people taking a drug are considered unsuitable, mainly due to the expenses of treatment.

The economic evaluation of CPBI revealed that the gross cost incurred per patient for 3 months was 23% less in CBPI than UC. Similarly, 1 study demonstrated a 15% decrease in total direct costs for patients with diabetes who received pharmacist multidisciplinary care in an outpatient setting over a 6 month period.[35] Our cost savings were comparable to a 6-months study in the United States, which found savings equivalent to 450 EGP per patient.[36] The cost savings observed in our study were attributed to the lower medication costs, closer therapeutic monitoring, and decrease work absenteeism. On contrary, others showed no significant difference in total healthcare costs after CPBI among patients with type 2 diabetes.[37] A Canadian study showed no significant difference at 3 or 12 months healthcare cost between the CPBI and UC.[38] The variations of the results could be explained by contamination bias between groups, irrespective

different GDP in high income country, lack of adequate perspective, and uncertainty treatment adherence were observed.

This study has some limitations. A relatively small number of participants, as this study will be a base for future studies to confirm the capacity of such interventions in T2DM practice. Also, the long-term economic impact cannot be ascertained, due to the short study duration. However, the anticipated economic impact of this care approach in the long-term may be greater than our analysis suggests, as sustained improvements in HbA1C would lower the risk of future diabetes-related complications and, as a result, further reduce the costs associated with diabetes. This study's success can be attributed to 3 critical elements. First, the adopted study design and type of study (cross over-RCT) makes the results of this study reliable for providing invaluable diabetic patient-centered pictorial CCM to healthcare-deprived T2DM patients. Second, the risk of contamination between the UC and CPBI was ensured as the 2 sets of study were enough away from each other. Third; on contrary to most of other studies who enrolled well trained clinical pharmacists, we involved community pharmacists who did not received any previous training. This may increase a generalizability of the results of the study.

Conclusion

This is the first RCT in Egypt revealing that CPBI can deliver a simplified, convenient, effective, and cost-effective guided care to local T2DM patients using a pictorial patient centered DCM. This improves patient's behavior, knowledge, self-efficacy, and adherence which in turn control their glycemic and cardiometabolic parameters. As a future plan, this study could be tailored to other chronic diseases: hypertension, hyperlipidemia. Some parts of the CPBI could also be performed by phone calls or online for the time being due to the COVID-19 situation, especially in quarantine time.

Author Contributions

HM has participated in the development of the study plan, implementation of the study plan, and contributed to the interpretation of cases, and critically reviewed the manuscript. MA has participated in the development & implementation of the study plan, development of the study questionnaire, training of pharmacists, contributed to the interpretation of cases, and critically reviewed the manuscript. NH has participated in the development & implementation of the study plan, development of the study questionnaire, training of pharmacists, and critically reviewed the manuscript. RG has participated in the development of the study questionnaire, training of pharmacists, implementation of the study plan, and contributed to the interpretation of cases. RE has participated in the development of the study questionnaire, and training of pharmacists.

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