CLINICAL PHARMACY MANAGEMENT OF PATIENTS WITH TYPE 2 DIABETES IN AN OUTPATIENT DEPARTMENT AT A TERTIARY CARE HOSPITAL- A RANDOMIZED COMPARATIVE STUDY

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Abstract
Diabetes is the most common disorder resulting in many long term complications such as retinopathy, neuropathy and nephropathy. These long term complications are prevented by maintaining the target glycemic level (HbA1c <7%) which is often not achieved by the diabetic patients despite the availability of many treatment modalities. Several studies depicted the positive influence of clinical pharmacist-led programs on achieving and maintaining glycemic control and other biomedical marker outcomes in diabetes patients. To assess the impact of clinical pharmacist-led program on achieving glycemic control in diabetic patients is the primary objective and the improvement in other outcomes like blood pressure, BMI and self-reported medication adherence are the secondary objectives. Clinical pharmacist-led pharmaceutical intervention program improved the glycemic control in diabetic patients whereas the traditional treatment control group did show any improvement. The secondary biomarkers blood pressure and medication adherence also has improved in the intervention group.

Keywords: Diabetes, Pharmacist, Glycemic control, Medication adherence.

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INTRODUCTION:

Diabetes is one of the most common non communicable disease that occurs either due to inadequate production of insulin from pancreas or ineffective use of insulin (insulin resistance). Hyperglycaemia, or increased blood sugar, is a common effect of diabetes that inevitably affects many of the body's systems, especially the nerves and blood vessels (microangiopathy and macroangiopathy).[1]

India is facing an epidemic of diabetes and well known as the diabetes capital of the world.[2] India is experiencing rapid socioeconomic progress and urbanization and carries the highest burden of diabetes with escalating prevalence in both urban and rural populations.[3]

During the last 3 decades, the prevalence of diabetes has increased to 12-18% in urban India and 3-6% in rural India with significant regional variations.[2,4-6] These regional variations are due to different levels of urbanization and lifestyle factors such as different dietary patterns and varying obesity levels.[5,6]These prevalence rates in India are 50-80% higher compared to China (10%).In India, 14% of people are having prediabetes which is a forewarning indicator of future diabetes.[2,3]

Management and control of type 2 diabetes is complex and need scontinuing medical care and patient self-management, education and support to avert acute complications and to lessen the risk of long-term complications.[7]Glycemic control is the main indicator inthe reduction of long-term microvascular and macrovascular complications. But the target glycemiclevels (hemoglobin A1c < 7%) are notmaintained in patients with type 2 diabetes, in spite of easily available and effective treatments.

Clinical pharmacists could be playing an important role in tailoring pharmaceutical care programs (including lifestyle modifications) and pharmacological drug therapy.[8]They devise the therapeutic plans according to the patients' participation and involvement to get the optimal therapeutic outcomes with an emphasis to the treatment adherence.[9,10]

Several trials reported that clinical pharmacist-led management programs resulted in good improvement in glycemic control and other clinical outcomes in diabetes patients. In this study, we are exploring the clinical pharmacist-led intervention to attain glycemic target and self-management behaviour in diabetes patients.

OBJECTIVE

To evaluate the impactof a clinical pharmacist-led pharmaceutical care program onglycemic control (HbA1c<7%)inoutpatients with type 2 diabetes.

MATERIALS AND METHODS

Study Design: prospective randomized comparative controlled study with two groups.

Study population and study setting: more than 18 years old diabetic patients who are attending Medicine outpatient department at a tertiary care hospital.

Study duration: Ten months duration from(May 2020-Feb 2021)
Each patient followed up for 6 months from the enrolment into the study.

Inclusion criteria

1. Patients diagnosed to have diabetes at least one-year back
2. Patient should be on at least one anti diabetic drug
3. HbA1c>7.5%

Exclusion criteria

1. Patients with convulsive disorder
2. Patients diagnosed with diabetic retinopathy, nephropathy and neuropathy.

Sample size

The primary outcome was a reduction in HbA1c (intervention vs control) at the end of the 6-month study period. As per Kinmonth AL et al study, sample size calculated using the variability (standard deviation =2.22%) and the difference of more than 1% reduction in HbA1c with power of 90% and $\alpha = 0.05$, the sample size was 104 in each group. Considering the lost follow up 10%, the required sample for each group was 115.[11]

Methods:

The patients with type 2 diabetes who are attending the outpatient department of the tertiary care hospital were enrolled over a period of 4 months after obtaining their consent to participate in the study. Enrolled patients were randomly allocated to intervention group and the control group. The intervention group patients received a one-on-one objective directed education and counselling session from clinical pharmacist about the prescribed medications for diabetes, recommended

lifestyle changes and 8 weekly telephonic follow up calls to discuss about their treatment plans and clarify their queries. The primary outcome was glycemic control and all other markers like blood pressure, BMI, self-reported medication adherence (4 question Morisky scale) were the secondary outcome measures. Outcome measurement was done at baseline and at the end of 6-month study period. The outcome difference between both the groups at baseline, at 6 months and the changes occurred in the study duration also compared to report the results.

Methodology

Diabetic patients attending outpatient department, who met the inclusion and exclusion criteria were informed about the study after their baseline assessment of HbA1c, Blood pressure and body mass index (BMI). Patients who are willing and gave their consent were included in the study. The option to opt out of the study was kept open and complete confidentiality was Then the patients were randomly assigned to intervention and control group using sealed envelope system. Baseline data like demographic details, detailed disease history, medications and Morisky scale questionnaire also collected from the patients.

Following the randomization, the clinical pharmacist made certain that the intervention group received the evidence-based antidiabetic therapy after discussion with physician when needed.

After the physician meeting, the clinical pharmacist took the patient to a separate room and provided health education and discussion about type 2 diabetes, risks for and types of complications, drug therapy and its proper dosage, possible side effects and in last the importance of medication adherence. The clinical pharmacist also educated the patients about lifestyle management as follows: (a) healthy diet – assessment of dietary habits and provided the healthy dietary schedule and advised to stop unhealthy dietary habits;(b) regular physical activity according to their daily schedule; and (c) monitoring of their blood glucose levels. Baseline assessments (HbA1c and blood pressure) were specified for each patient. A booklet was specially made about diabetes medications and lifestyle changes and given to the patient. Follow up 8 weekly telephone calls were made by the clinical pharmacist to discuss and review the prescribed treatment, to enforce the importance of adherence to treatment and to answer patient questions. The average length of each telephonic discussion was 15 minutes.

Patients in the control group received the usual care provided by the physician and nursing staff, which included patient assessment at 3- or 6-month review at which blood glucose and blood pressure were measured and nutrition counselling. They did not receive clinical pharmacist-led health education, intervention and follow-up telephonic calls.

Follow up assessment was done after 6 months of the initial assessment including HbA1c, blood pressure, BMI and medication adherence.

Study Instruments

Self-Reported Morisky Medication Adherence Scale (MMAS-4 item) was used.[12] This scale estimated the likelihood of prescribed medication adherence of the patients. The survey questions were as follows:

1. Do you ever forget to take your antidiabetic medicine?
2. Do you ever have problems remembering to take your antidiabetic medication?
3. When you feel better, do you sometimes stop taking your medicine?
4. Sometimes if you feel worse when you take your medicine, do you stop taking it?

To score the survey, score of '1' is given to 'yes' response and '0' to 'no' response (range 0 to 4). According to the Morisky classification, adherence is divided into 3 groups:

- High – 0 score
- Medium – 1 to 2 score
- Low – 3 to 4 score

For analysis in the present study we divided the group into 2 groups. patients with '0' score considered as adherent patients, '1-3' score considered as non-adherent.

DATA ANALYSIS

Data collected at baseline and at the 6-month assessments were entered in MS Excel and analysed by SPSS 17. Categorical variables were expressed in percentages with 95% confidence interval and analysed using Pearson chi-square test. Continuous variables were expressed as mean ± standard deviation and examined using t test or Mann-Whitney test. P value< 0.05 was considered statistically significant.

RESULTS

A total of 230 diabetic patients (115-intervention group, 115-control group) attending outpatient department during the initial 4 months of study

period were enrolled in the study. During the study period, 9 patients from intervention group and 11 patients from control group were dropped out from the study. Hence a total of 210 patients (106 intervention group, 104 control group) were followed up for the complete study period.

Baseline patients' characteristics

Baseline characteristics like age, sex, duration of diabetes, education, marital status and monthly income of both the groups were analysed and found out that there is no statistically significant difference between both the groups.

Biomedical outcome

At the baseline, the HbA1c values were indistinguishable between the intervention group and control group patients. At 6 months' assessment, intervention group patients showed 0.9% mean reduction in HbA1c, whereas the control group patients reported 0.1% mean increase in HbA1c. The percentage of patients attaining the ADA recommended HbA1c value of less than 7% was significantly (p=0.015) higher in intervention group (29.2%) compared with the control group (15.4%) at 6th month assessment.

The mean reduction in systolic (p=0.016) and diastolic BP (p=0.042) was significantly higher in the intervention group than the control group. The target BP was achieved by more number of intervention group patients (70.7) than the control group (56.7) and the difference was statistically significant (p=0.034).

In spite of the intervention group patients' mean BMI reduction and control group patients' increase in mean BMI, this difference was not statistically significant.

During the analysis, the number of prescribed medications were similar in both the groups. The outcomes like patients on insulin therapy and hypertensive medications did not show much difference between both the study groups. At the six-month follow up assessment, the intervention group (26.4%) showed significantly (p=0.001) lower number of medication non-adherent patients when compared to control group (52.9%).

A total of 210 diabetic patients (intervention-106, control-104) completed the 6-month study period. While comparing the baseline values, intervention group had 0.9% reduction in mean HbA1c whereas 0.1% increase in mean HbA1c was detected in the control group (p<0.05). The secondary outcomes like systolic, diastolic blood pressure, self-reported medication adherence showed significant improvement in the clinical pharmacist-led intervention group except BMI.

Table 1: Baseline characteristics of intervention and control groups

Characteristics	**Intervention group N= 115**	**Control group N=115**	**P value**
Age (mean ± standard deviation)	51.4 ± 10.7	53.6 ± 9.8	0.105
Sex			
Male n (%)	72 (62.6)	68 (59.1)	0.588
Female n (%)	43 (37.4)	47 (40.9)	
Duration of diabetes years (mean ± standard deviation)	7.6 ± 5.3	8.1 ± 5.9	0.499
Education n (%)			
University	51 (44.3)	44 (38.3)	0.348
Up to high school	64 (55.7)	71 (61.7)	
Marital status n (%)			
Married	98 (85.2)	101(87.8)	0.562
Single, divorced or separated	17 (14.8)	14 (12.2)	
Monthly income, n (%)			
<10000 Rs	79 (68.7)	74 (64.3)	0.484
>10000 Rs	36 (31.3)	41 (35.7)	

P value <0.05 considered as significant

Table 2: Key output values at baseline and at 6 months for intervention and control group

Outcome	**Intervention group**		**Control group**		**P value[c] (baseline)**	**P value[d] (change)**
	Baseline[a]	**Change[b]**	**Baseline[a]**	**Change[b]**		
% HbA1c	8.3 (6.5 to 10.1)	-0.9 (-1.6 to -0.1)	8.5 (6.7 to 10.4)	+ 0.1 (-0.3 to 0.7)	0.816	0.021
Systolic BP (mm Hg)	134 (124-143)	-5.4(-7.9 to -3.1)	132 (125 to 142)	+0.9 (0.2 to 2.1)	0.423	0.016
Diastolic BP (mm Hg)	86 (76 to 94)	-6.7 (-9.1 to -4.6)	85 (81 to 89)	+1.6 (-1.2 to 3.9)	0.869	0.042
BMI (kg per m^2)	31.9 (21.2 to 38.7)	-0.4 (-1.7 to 1.9)	32.6 (27.4 to 38.3)	+0.3 (-0.5 to 1.7)	0.721	0.128

[a]Baseline values are presented as median (IQR).
[b]Changes over 6 months are shown as the mean difference (95% confidence interval).
[c]P values from Mann-Whitney U test for the between-group comparisons of baseline values.
[d]P values from t test for independent samples for the between-group comparisons of baseline to follow-up change amounts.

Table 3: Baseline and Follow-Up Assessments of Study outcomes for clinical pharmacist-led Intervention group and control group

Outcome	Baseline		P value	6 months follow up		P value[a]
	Intervention N=115	Control N=115		Intervention N= 106	Control N= 104	
Number of medications[b]	7 (6-8)	7 (6-9)	0.582	6 (5-7)	7 (6-8)	0.324
Number of antidiabetic medications[b]	2 (1-3)	2 (1-3)	0.653	2 (1-4)	2 (1-3)	0.329
Patients on insulin therapy n (%)	67 (58.3)	65 (56.5)	0.789	79 (74.5)	75 (72.1)	0.692
Patients taking antihypertensive therapy n (%)	85 (73.9)	87 (75.6)	0.761	91 (85.8)	89 (85.8)	0.955
Patients who achieved target HbA1c <7% n (%)	0	0	1.0	31 (29.2)	16 (15.4)	0.015
Patients who achieved target BP 130/80 mm Hg n (%)	45 (39.1)	49 (42.6)	0.591	75 (70.7)	59 (56.7)	0.034
Patients who self-reported medication non-adherence n (%)	73 (63.5)	69 (60)	0.587	28 (26.4)	55 (52.9)	0.001

[a]P values from Pearson chi-square test for categorical variables and Mann-Whitney U test for continuous variables. Values expressed as median (interquartile range).

Figure 1: Gender wise distribution of intervention and control group

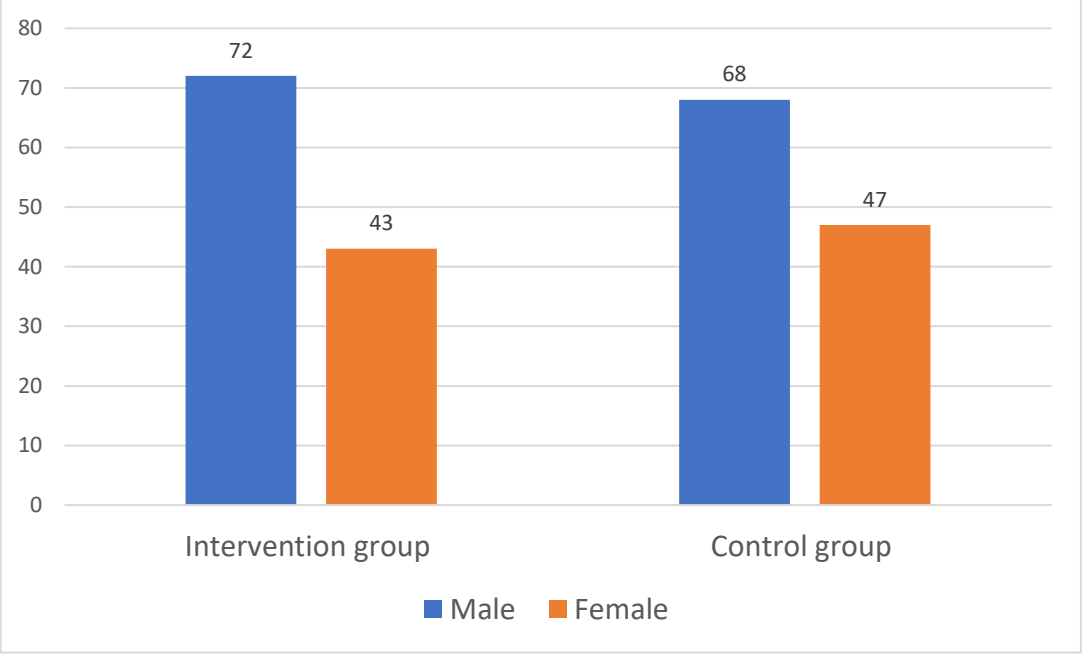
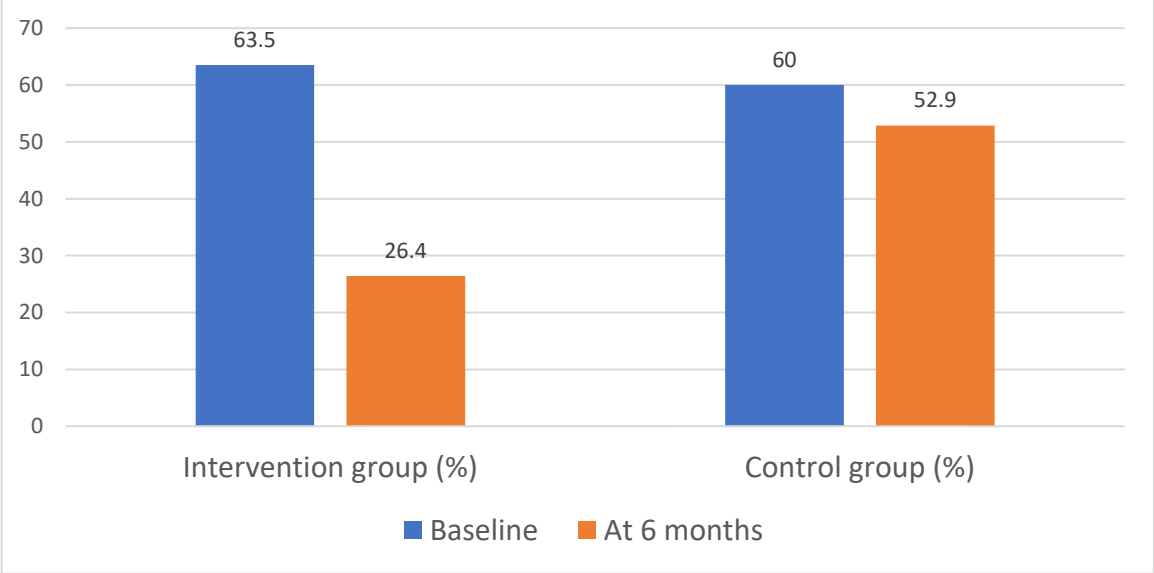


Figure 2: Self-reported non-adherence to medications (Morisky scale) at baseline and at 6 months of both groups



DISCUSSION

The role of clinical pharmacists is slowly expanding and the reason were lack of pharmaceutical care training and the attitude of physicians.[13]A clinical pharmacist intervention consists of appropriate pharmacotherapy, individualized health education, medication adherence support and regular telephonic follow-up calls which showed significant improvement in HbA1c level.

The present study showed significant (p=0.021) reduction in mean HbA1c level in the intervention group (-0.9%) compared to the control group (0.1%) which depicted an increase in mean HbA1c level. Several studies from different geographical region study showed the similar significant reduction in mean HbA1c level in the intervention group.[14-16] In contrast to the present study finding, Wu et al study found that there was no significant difference in study arms in HbA1c levels.[17]

The key finding of the present study was significantly (p=0.015) more number of patients in the intervention group (29.2%) than the control group (15.4%) attained the target glycemic level (HbA1c <7%). Al Mazroui et al study also found that significantly (p=0.021) more number of intervention group patients attained the target glycemic level than control group.[18]The reason for the glycemic control in the present study may be attributed to appropriate pharmacotherapy, individually tailored health education, counselling to improve the medication adherence and regular follow up through telephonic call.

Similar to the previous studies, the present study also reported significant reduction in systolic and diastolic blood pressure.[19]Significantly higher proportion of intervention group patients attained the target blood pressure in the present study. Since both the groups received the same pharmacotherapy for hypertension, the reduction in blood pressure may be attributed to comprehensive education, lifestyle modifications and medication adherence.

Earlier study has shown that adherence to medication in type 2 diabetes is low and this is one of the main barrier to the optimal diabetic care and main reason for unnecessary hospital admissions.[20] Present study was consistent with the earlier studies and showed that the patients receiving clinical pharmacy care are more adherent to medications.[16,18]

CONCLUSION

In conclusion, addition of clinical pharmacy care which include appropriate pharmacotherapy, individualized health education and counselling for medication adherence along with traditional treatment may improve the biomarkers like HbA1c, blood pressure and self-reported medication adherence.

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