MARMARA
PHARMACEUTICAL JOURNAL

Research Article

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Medication adherence and clinical outcomes in type 2 diabetes mellitus patients with depression: A prospective interventional study

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Received: 23 October 2017 / Revised: 22 December 2017 / Accepted: 23 December 2017

ABSTRACT: The aim of the study was toassess the level of depression in type 2 diabetes mellitus patients using Patient Health Questionnaire (PHQ-9), to evaluate the range of medication adherence and to identify the reasons for non-adherence to medication in type 2 diabetes mellitus patients with depression. Study tools such as Morisky Medication Adherence Scale (MMAS), Patient Health Questionnaire 9 (PHQ- 9) and Daily Diabetes Record Sheet were used. Chi-square test was used to test the association for categorical variables and the Student's t-test was used for group comparisons. Patients with high adherence to medication were found to have good glycemic control than low medication adherence patients. The level of depression of more than half of the patients (51.9%) lies in between PHQ score of 10 and 14 in this study. Reasons for non-adherence were accidental and intentional. The most prevalent among accidental reasons was patient forgetting to take medicines (25.0%), and the most prevalent among intentional reasons was achievement of treatment goals (17.59%). The result outcome of the study states that the level of depression has a significant effect on poor metabolic control, poor diet and non-adherence to the medication regimen.

KEY WORDS: Diabetes mellitus; depression; medication adherence; gycemic control.

1. INTRODUCTION

Diabetes is a major contributor to the global burden of disease and growing number of studies show a bidirectional association between depression and diabetes [1]. Patients with diabetes are more likely to experience depression than the general population. Depression is adversely associated with diabetes, from incidence to mortality [2, 3] and it is a risk factor for diabetes, and diabetes increases risk for the onset of depression. The prevalence of depression can be higher in patients with multiple diabetes related complication. Such an association would suggest the possibility that depression treatment might have favorable effects on diabetic outcomes. Clinical and subclinical expressions of depression are present in > 25% of patients with type 1 or type 2 diabetes mellitus (DM) [4,5] and have adverse effects on normal daily activities functioning and quality of life [6]. A review of studies found that depression was associated with a 60% increase of type 2 diabetes while type 2 diabetes was only associated with a moderate (15%) increase in risk of depression. There is evidence that when depression occurs in individuals with diabetes, it is associated with poor metabolic control, poor diet and adherence to the medication regimen, and decreased quality of life [7-9]. The PHQ-9 is widely used to identify the people with depression among those with diabetes or heart disease [10]. In the present study we investigated the level of depression using PHQ-9and the range of patient adherence to medication using the 8 item self support morisky medication adherence questionnaire and identified the reasons for non-adherence to the medications in type 2 diabetes mellitus patients.

How to cite this article: Sankar V, Justin A, Payman H, Swathy P, Sai Charan Kumar N, Senthil Kumar R. Medication adherence and clinical outcomes in type 2 diabetes mellitus patients with depression: a prospective interventional study. Marmara Pharm J. 2018; 22 (4): 599-606.

https://doi.org/10.12991/jrp.2018.102
ISSN: 1309-0801

2. RESULTS AND DISCUSSION

Totally 130 patients were approached for screening. Among them, 64 were not eligible based on exclusion criteria of this study. Among the 66 eligible patients, 12 (18.1%) patients refused to participate. Sociodemographic characteristics of the respondents are detailed in (Table 1). Among 54 patients, 27 (50%) were male patients and 27 (50%) were females patients. The mean age (SD) of the participants was found to be 55.30 (9.03). The distribution of population regarding education showed that majority of the patients has completed secondary level of education. Out of 54 patients participated in the study, 12 patients (22.2%) were smokers and 12 (22.2 %) were alcoholics. The most common comorbidity with Diabetes mellitus was hypertension seen in around half of the participants (43.3%) and then 16.7% were having coronary heart disease as their major co-morbidities, followed by 11.3% with hyperlipidemia, 8.3% for thyroid disease, and 5.0% for each asthma, Diabetes complications in which retinopathy and nephropathy were more common.

Table 1. Sociodemographics of the respondents.

Variable	No. of Patients	Percentage
Age		
30-35	1	1.85
36-40	1	1.85
41-45	5	9.26
46-50	8	14.81
51-55	11	20.37
56-60	14	25.93
61-65	8	14.81
66-70	4	7.41
71-75	2	3.70
Gender		
Male	27	50
Female	27	50
Educational level		
Basic (up to 8th grade)	19	35
Medium (Higher Secondary)	27	50
High (Degree/Graduate)	8	15
Social Habits		
Smokers	12	22.2
Alcoholics	12	22.2

The results of glycemic control are represented in (Table 2) showed that patients who have a high adherence to medication had shown higher glycemic control in compared with patient with low medication adherence. A significant reduction in the level of HbA1c was found in high-adherence group when compared to low-adherence group. It also shows that there is a statistical significance ($p<0.000$) between the groups in the percentage of patients achieving glycemic control as recommended by American Diabetes Association (HbA1c ≤ 7%). Medication adherence was classified as low, mediumand high based on the validated Morisky Medication Adherence Scale (MMAS-8).While comparing medication adherence at the baseline and after follow-up using paired t-test, a statistically significant difference was found (Table 3). Level of depression was classified as less than 10, between 10 and 14, and greater than 14 based on the Patient Health Questionnaire (PHQ-9). When the level of depression was compared at the baseline and after

follow-up using Paired t- test, a statistically significant difference was found (Table 4). It was found out that there is an association between gender and level of depression from the chi-square test. The result showed that women are more depressed than men as 44.4 % of the women suffered from high level of depression in compared with men (18.5 %) (Fig. 1). Earlier studies have suggested the higher prevalence of depression in women with type II DM than men with type II DM. The higher prevalence of depression in women may be attributed by the factors like adverse experiences, socio cultural roles, women may be attributed by the factors like adverse experiences, socio cultural roles, psychological attributes, biological factors including hormones and poor social support [11, 12].

Table 2. Glycemic control at baseline and follow-up in recruited patients.

	Poor Adherence Group (n=10) Mean ± S.D.		Significance Level
HbA1c			
Baseline	9.27± 1.82	± 1.10	(p<0.001)[a]
Follow-up	7.97 ± 1.39	±1.43	(p<0.001)[a]
N (%) of patients with HbA1c ≤ 7% (Glycemic control)			
Baseline	0 (0)	0 (0)	(p<0.001)[a]
Follow-up	12 (27.2)	1 (10)	(p<0.001)[a]

[a.] : Paired t-test

Table 3. Distribution of patients based on medication adherence in recruited patients (n=54).

Adherence Level	Low Number (%)	Medium Number (%)	High Number (%)	p-value
Baseline	11 (20.4)	21 (38.9)	22 (40.7)	(p<0.001)[a]
Follow-up	2 (3.7)	9 (16.7)	43 (79.6)	(p<0.001)[a]

[a] : Paired t-test

Table 4. Distribution of patients based on level of depression (n= 54).

Level of depression	Less than 10 Number (%)	Between 10 & 14 Number (%)	Greater than 14 Number (%)	p-value
Baseline	0 (0)	28 (51.9)	26 (48.1)	(p<0.001)[a]
Follow-up	24 (44.4)	13 (24.1)	17 (31.5)	(p<0.001)[a]

[a.] : Paired t-test

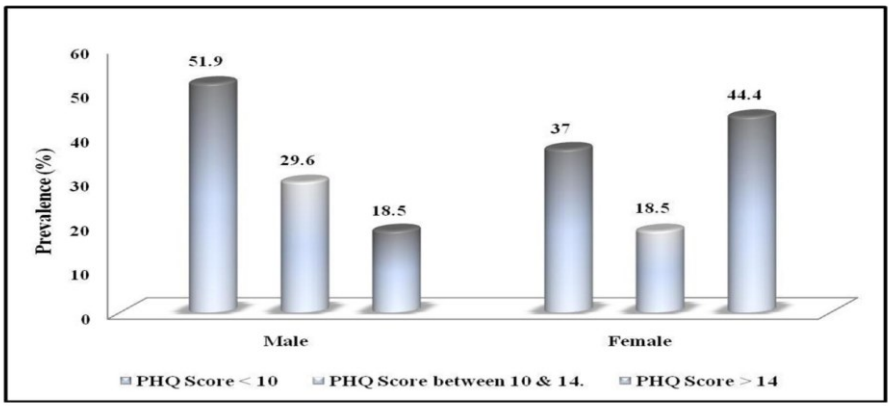

Figure 1. Percentage of level of depression in males and females.

Table 5. Correlation of HbA1c level and level of depression.

	Level of Depression (Mean)	HbA1c (Mean)	p-value
Participants (n=54)	12.12 ± 0.52	8.13 ± 0.36	(p<0.008)[a]

[a] : Correlation.

A significant relationship was found out between HbA1c and level of depression (Table 5) as well as between medication adherence and level of depression (Table 6) among recruited patients. We found out that patients with depressive symptoms had higher HbA1c and were less likely to achieve target HbA1c than those without depressive symptoms. The percentage of patients after the follow up significantly achieved HbA1C (≤7%) level when compared to the baseline values. A number of studies have evaluated the effect of depression on glycemic control Results from these studies suggest that improvements in glycemic control helps to overcome the closely related depressive symptoms.

Table 6. Correlation of medication adherence and level of depression.

	Level of depression (Mean)	Medication adherence (Mean)	p-value
Participants (n=54)	12.13 ±0.51	0.48 ±0.03	(p<0.001) [a]

[a] : Correlation.

Other study reports [13] also state that the number of depressive episodes correlated positively with HbA1c levels. Association with medication adherence indicated that patients with depressive symptoms are more likely to be non-adherent to their prescribed medication than those without depressive symptoms. A significant relation was seen between medication adherence and level of depression which were similar to the reported study results [14]. Compared with patients who are not depressed, patients with co morbid diabetes and depression are more likely to be non-adherent to medication regimens. In our study, after a 2 month follow-up the percentage of the patients with high adherence increased from 40.7% to 79.6%(p<0.001). A drop in the percentage of the patients with low adherence and medium adherence was seen with a difference of 16.7% and 22.2% respectively(p<0.001). More than half of the patients (51.9%) lies in between PHQ score of 10 and 14. During follow up period, a difference of about 44.4% was seen in low level of depression, whereas 27.8% and 16.6% difference was seen in medium and high level of depression respectively. A statistically significant difference was found. Patients screened had multiple reasons for non-adherence to medication. Reasons were accidental and intentional. Among these, the most prevalent among accidental reasons was forgot to take medicines (25.0%), and the most prevalent among intentional reasons was achievement of treatment goals (17.59%) (Fig. 2).

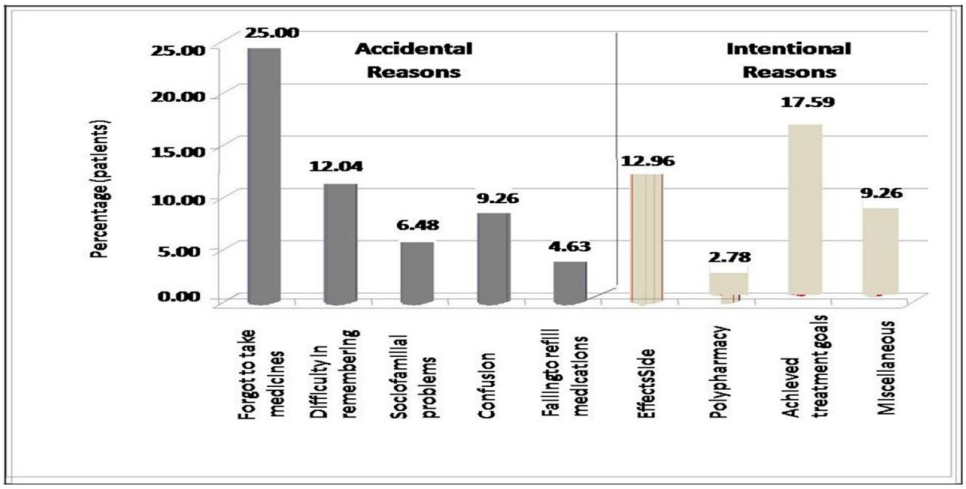

Figure 2. Reasons for non-adherence.

3. CONCLUSION

The results of the study confirmed level of depression has a significant effect on poor metabolic control, poor diet and adherence to the medication regimen, and decreased quality of life. The study also highlighted the factors associated with depression like female gender and level of HbA1c. Major reason for non-adherence was found to be forgetting to take the medicines. Pharmacists, especially those working in community and primary care, should identify the patient at the risk of experiencing a depression and those already on regular antidepressants. It is also important that pharmacists should make the patients to understand the importance of continuing the medication for at least six months after symptoms resolve, as this reduces rates of relapse. Moreover, giving proper counseling to DM patients to maintain the glycemic control could be effective tool to decrease the depression occurrence which can improve the quality of life of patients.

4. MATERIALS AND METHODS

4.1. Study site and population

Prospective, open – labeled, interventional study was conducted in a multi-specialty 900 bedded tertiary care teaching hospital of PSG Medical Sciences and Research Institute (PSGIMS&R), Coimbatore, located in the south region of Tamil Nadu, India for over a period of 6 months. This study was approved by the Institutional Human Ethics Committee (IHEC, PSGIMSR) of the Hospital with the proposal number of 13/343. The study was followed for a period of 2 months. The study was monitored by the clinical pharmacist and a physician at the baseline and at the end of 2 months treatment with respect to HbA1c level and level of depression, medication adherence and level of depression. This study included inpatients (during discharge) and outpatients with Type II DM visiting department of endocrinology. A total of 125 patients (expecting 20% drop out) were included, with 50 patients in each arm i.e. 100 patients (variable).

4.2. Inclusion criteria

Patients with diagnosis of type 2 DM,Patients who are willing to give consent for study participation, Patient with PHQ-9 ≥10

4.3. Exclusion criteria

Inability to give informed consent. Patients with inability to read and write Tamil or English. Patients who reside in a care facility that provides medications on schedule. Patients who had psychiatric problems before diagnosis of diabetes. Patients with family history of depression. Patients aged below 25 years or above 75 years. Patients with type 1 and gestational diabetes mellitus. Severe physical illness like cancer, multiple sclerosis, dementia.

4.4. Morisky medication adherence scale (MMAS)

Medication non-adherence range was assessed which was developed by Donald E. Morisky and it is a valid instrument used in large-scale studies in primary care using close-ended questions with yes or no type responses. Adherence levels were classified into low adherence (more than 2), medium adherence (1 or 2) and high adherence (Zero) based on MMAS **(**Table 7**).**

Table 7. Eight-item Morisky Medication Adherence Scale.

Question	Response Options
1. Do you sometimes forget to take your medicine?	Yes/No
2. Over the past two weeks, were there any days when you did not take your medicine?	Yes/No
3. Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?	Yes/No
4. When you travel or leave home, do you sometimes forget to bring along your medications?	Yes/No
5. Did you take your medicine yesterday?	Yes/No
6. When you feel like your blood pressure is under control, do you sometimes stop taking your medicine?	Yes/No
7. Do you ever feel hassled about sticking to your treatment plan?	Yes/No
8. How often do you have difficulty remembering to take all your medicine?	Never Almost Never Sometimes Quite Often Always

4.5. Patient health questionnaire (PHQ)

PHQ-9 was used to measure the extent and level of the depressive disorder (Table 8) .The PHQ-9 consists of 9 items on a scale rated from 0 (not at all) to 3 (nearly every day). The instrument is scored by adding the item ratings. Total scores of the PHQ-9 can range from 0 to 27; higher scores indicate worse depressive symptoms. Patients who score 10 are considered to have clinically significant depressive symptoms (positive for mild to severe depression). Those patients with PHQ-9 ≥10 were taken into study.

4.6. Daily diabetes record sheet

Glycemic control was assessed by recording recent Fasting Blood Sugar (FBS), Post Prandial Blood Sugar (PPBS) and their HbA1c which was reported to be a reliable indicator of blood glucose level for the last 3 months prior to testing. Patient's data including demographic, past medical and medication history, present medications, biochemical test results, presence of other co-morbidities or complications due to DM were collected using a developed data collection form.

4.7. Statistical analysis

All data analyses were performed with statistical package for social science (SPSS version 20.0, Chicago, IL, USA); a significance level of 0.05 was considered as statistical significance. Data were expressed as mean ± SD, median (inter quartile range) or number (%), as appropriate. Chi-square test was used to test the association for categorical variables. The Student's t-test was done for group comparisons.

Ethical approval

All procedures performed were in accordance with the ethical standards of the institution. Formal consent is obtained from the patients.

Table 8. Patient Health Questionnaire (PHQ-9).

	Not at all	Several days	More than half the days	Nearly every day
1. Over the *last 2 weeks*, how often have you been bothered by any of the following problems?				
a. Little interest or pleasure in doing things	☐	☐	☐	☐
b. Feeling down, depressed, or hopeless	☐	☐	☐	☐
c. Trouble falling/staying asleep, sleeping too much	☐	☐	☐	☐
d. Feeling tired or having little energy	☐	☐	☐	☐
e. Poor appetite or overeating	☐	☐	☐	☐
f. Feeling bad about yourself or that you are a failure or have let yourself or your family down	☐	☐	☐	☐
g. Trouble concentrating on things, such as reading the newspaper or watching television.	☐	☐	☐	☐
h. Moving or speaking so slowly that other people could have noticed. Or the opposite; being so fidgety or restless that you have been moving around a lot more than usual.	☐	☐	☐	☐
i. Thoughts that you would be better off dead or of hurting yourself in some way.	☐	☐	☐	☐
2. If you checked off any problem on this questionnaire so far, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?	Not difficult at all ☐	Somewhat difficult ☐	Very difficult ☐	Extremely difficult ☐

Acknowledgements: We would like to thank PSG College of Pharmacy, Department of Endocrinology, PSG Hospitals, Clinical sites and the patients for their participation. We also thank Dr Sivaram Hariharan, for his extensive English proof reading and editing services.

Author contributions: Author contributions: Concept –V.S., A.J.; Design –V.S., A.J., PHM.; Supervision –V.S., A.J.; Resource – PHM., NSCK., SP.; Materials – PHM., NSCK., SP.; Data Collection and/or Processing - PHM., NSCK., SP., A.J., V.S.; Analysis and/or Interpretation - A.J., V.S.; Literature Search – PHM., NSCK., SP.; Writing – PHM., NSCK., SP.,A.J.; Critical Reviews – PHM., NSCK., SP., A.J., V.S.

Conflict of interest statement: The author reports no conflicts of interest. The author alone is responsible for the content and writing of the article.

REFERENCES

[1] Golden SH, Lazo M, Carnethon M, Bertoni AG, Schreiner PJ, Roux AV, Lee HB, Lyketsos C. Examining a bidirectional association between depressive symptoms and diabetes. Jama. 2008; 299(23): 2751–2759. [CrossRef]

[2] Genuth S. A case for blood glucose control. Adv Intern Med. 1995; 40: 573–623. [CrossRef]

[3] Reichard P, Nilsson BY, Rosenqvist V. The effect of long-term intensified insulin treatment on the development of microvascular complications of diabetes mellitus. N Engl J Med. 1993; 329(5): 304–309. [CrossRef]

[4] Gavard JA, Lustman PJ, Clouse RE. Prevalence of depression in adults with diabetes: an epidemiological evaluation. Diabetes Care. 1993; 16(8): 1167–1178. [CrossRef]

[5] Wing RR, Marcus MD, Blair EH, Epstein LH, Burton LR. Depressive symptomatology in obese adults with type II diabetes. Diabetes Care. 1990; 13(2): 170 – 172. [CrossRef]

[6] Jacobson AM, De Groot M, Samson JA. The effects of psychiatric disorders and symptoms on quality of life in patients with type I and type II diabetes mellitus. Qual Life. 1997; 6(1): 11–20. [CrossRef]

[7] Hanninen JA, Takala JK, Keinanen-Kiukaanniemi SM. Depression in subjects with type 2 diabetes: predictive factors and relation to quality of life. Diabetes Care. 1999; 22(6): 997–998. [CrossRef]

[8] Gary TL, Crum RM, Cooper Patrick L, Ford D, Brancati FL. Depressive symptoms and metabolic control in African-Americans with type 2 diabetes. Diabetes Care. 2000; 23(1): 23–29. [CrossRef]

[9] Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes: impact of depressive on adherence, function, and costs. Arch Intern Med. 2000;160(21):3278-3285. [CrossRef]

[10] Lin EH, Katon W, Von Korff M, Rutter C, Simon GE, Oliver M, Ciechanowski P, Ludman EJ, Bush T, Young B. Relationship of depression and diabetes self-care, medication adherence, and preventive care. Diabetes Care. 2004; 27(9): 2154–2160.

[11] Culbertson FM. Depression and gender- An international review. Am Psychol. 1997; 52(1): 25-31. [CrossRef]

[12] A li S, Stone MA, Peters JL, Davies MJ, Khunti K. The prevalence of co-morbid depression in adults with type 2 diabetes: a systematic review and meta-analysis. Diabet Med. 2006; 23(11): 1165-1173. [CrossRef]

[13] Eren I Erdi O, Ozcankaya R. Relationship between blood glucose control and psychiatric disorders in type II diabetic patients. Türk Psikiyatri Derg. 2003; 14(3): 184-191.

[14] Hillary R Bogner, Knashawn H Morales, Heather F de Vries, Anne R Cappola. Integrated management of Type 2 diabetes mellitus and depression treatment to improve medication adherence: A randomized controlled trial. Ann Fam Med. 2012; 10(1):15-22. [CrossRef]