Original Research

Evaluation of medication adherence among Lebanese diabetic patients

Lara MROUEH D, Dana AYOUB Maya EL-HAJJ , Sanaa AWADA Samar RACHIDID,

Salam ZEIN[®], Amal AL-HAJJE[®].

Received (first version): 18-Jun-2018 Accepted: 22-Oct-2018 Published online: 4-Dec-2018

Abstract

Background: Diabetes type 2 is considered one of the main public health concerns. Lack of adherence to treatment leads to poor therapeutic outcome, poor glycemic control, and high risk for developing diabetes complications.

Objectives: The aim of this study is to evaluate adherence to oral antidiabetic medication in Diabetes type 2 Lebanese patients, and to evaluate factors leading to low adherence.

Methods: A cross-sectional study was conducted in outpatients endocrinology clinics of two hospitals and four private clinics located in Beirut-Lebanon. Data was collected using a well-structured questionnaire by trained pharmacists. Adherence level was measured by the Lebanese Medication Adherence Scale (LMAS-14). Bivariate and multivariate analyses were conducted using SPSS version 20.

Results: Overall, 245 patients were included in the study with the majority being females (54.3%) and obese (47.8%). Only 29% of the participants had controlled glycemia (HbA1c <7%) with 31.8% of subjects had high adherence to their medication compared to 68.2% with low adherence. Increased working hours/day was associated with a decrease in adherence to oral antidiabetic medication (OR=0.31; 95% CI 0.11:0.88; p=0.029). Other factors significantly associated with decreased adherence to treatment were forgetfulness, high drug costs, complex treatment regimens, experiencing side effects, and perception of treatment inefficacy. Postponing physician office visits also decreased the probability of being adherent to oral antidiabetic medication (OR=0.36; 95% CI 0.15:0.86; p=0.022). Skipping or doubling the dose in case of hypo/hyperglycemia and the sensation of treatment burden also decreased medication adherence (OR=0.09; 95% CI 0.02:0.34; p=0.001, and OR=0.04; 95% CI 0.01:0.13; p<0.001 respectively).

Conclusions: Adherence to oral antidiabetic medication is low for Lebanese patients, which leads to a poor glycemic control and increases the diabetes complications. Intervention programs including patient education strategies are essential to improve medication adherence.

Keywords

Medication Adherence; Treatment Adherence and Compliance; Diabetes Mellitus, Type 2; Risk Factors; Multivariate Analysis; Cross-Sectional Studies; Lebanon

INTRODUCTION

Diabetes type 2 (DM2) is considered one of the main public health concerns, and its prevalence is increasing at an alarming rate worldwide. According to the International Diabetes Federation's latest report, the global prevalence of diabetes is estimated to be 8.8%, and predicted to increase by 54% worldwide between 2010 and 2030. The World Health Organization (WHO) estimates that Diabetes will be the seventh leading cause of death by 2030.

The American Diabetic Association (ADA) considers

Lara MROUEH. PharmD. Clinical and Epidemiological Research Laboratory, Faculty of Pharmacy, Lebanese University. Beirut (Lebanon). laramroueh@outlook.com

Dana AYOUB. PharmD. Clinical and Epidemiological Research Laboratory, Faculty of Pharmacy, Lebanese University. Beirut (Lebanon). danaayoub@hotmail.com

Maya EL-HAJJ. PhD. Clinical and Epidemiological Research Laboratory, Faculty of Pharmacy, Lebanese University. Beirut (Lebanon). hajj_maya@hotmail.com Sanaa AWADA. PharmD, PhD. Clinical and Epidemiological

Research Laboratory, Faculty of Pharmacy, Lebanese University. Beirut (Lebanon). sanaa3a@hotmail.com

Samar RACHIDI. PharmD, PhD. Clinical and Epidemiological Research Laboratory, Faculty of Pharmacy, Lebanese University. Beirut (Lebanon). samar.rachidi@outlook.com

Salam ZEIN. PharmD, PhD. Clinical and Epidemiological Research Laboratory, Faculty of Pharmacy, Lebanese University. Beirut (Lebanon). salamzein@hotmail.com

Amal AL-HAJJE. PharmD, PhD. Clinical and Epidemiological Research Laboratory, Faculty of Pharmacy, Lebanese University. Beirut (Lebanon). amalkeh@hotmail.com

glycemic control as an important strategy for managing DM2.⁴ Glycosylated hemoglobin (HbA1c) is the most reliable method and the main target to control glycemia and prevent complications.⁵ The treatment target set by ADA for HbA1c is less than 7%.⁴ A high value of HbA1c (7% or over) indicates a poor diabetes control, leading to severe complications such as cardiovascular disease, neuropathy, retinopathy, nephropathy, and lower limb amputations.^{6,7}

A study done in the United States found that 12.9% of diabetic patients had poor glycemic control and did not achieve the control target HbA1c⁸ compared to a larger number of diabetic patients in Saudi Arabia, Lebanon, Jordan, and Libya (32.1%, 31.8%, 30%, and 20.2% respectively).⁹⁻¹²

The WHO defines adherence as the extent to which a patient's behavior in medication intake, diet follow up, and performing lifestyle changes, agrees with health care provider recommendations. In developed countries, WHO estimates adherence to long-term therapy for chronic diseases to be around 50%. Adherence to diabetes treatment is very variable and may range from 1.4 to 88%. A great progress has been made in the treatment of DM2 with the development of new therapeutic classes. However, a lack of adherence to treatment leads to a poor therapeutic outcome, a poor glycemic control, a high risk for developing diabetes complications, and an increased hospitalization and death rates. In a study conducted



on diabetic patients in Malaysia, 53% of patients were found to have low adherence¹⁸ and 72% of patients had poor glycemic control.¹⁹ Nevertheless, several studies have shown a positive association between adherence and glycemic control.^{20,21}

Numerous factors influence treatment adherence, including demographic characteristics, socioeconomic status, duration of disease, class of drug prescribed, presence of comorbidities, polypharmacy, patienthealthcare provider relationship, occurrence of adverse events, perception of inefficacy, drug cost, forgetfulness, and presence of psychological factors, specifically depression. 22

In Lebanon, there is a shortage of studies evaluating adherence to antidiabetic medication. Therefore, the main objective of this study is to evaluate adherence to oral antidiabetic medication for DM2 Lebanese patients, and to evaluate factors leading to low adherence.

METHODS

Study design

An observational cross-sectional study was conducted in outpatient endocrinology clinics of two tertiary care hospitals and four private endocrinology clinics located in Beirut, Lebanon between April 1st, 2017 and July 30th, 2017.

The sample size in this cross-sectional study was calculated using the following formula²³:

$$n = Z^{2} * p(1-p)/d^{2}$$

where Z is the standard normal variate (Z=1.96 when confidence interval is 95%), p is the expected proportion of outcome in the population (based on other studies), and d is the precision. 23

Based on a study done on Lebanese patients with chronic diseases, 17% were highly adherent²⁴, so a minimal sample size of 217 patients was necessary.

Lebanese adult outpatients (>18 years), diagnosed with DM2 by an endocrinologist and have been taking at least one oral antidiabetic medication (biguanides, sulfonylureas, meglitinides, thiazolidinediones, dipeptidyl peptidase 4 inhibitors, alpha-glucosidase inhibitors and sodium-glucose co-transporter 2 inhibitors) for at least 6 months were included in this study. Excluded subjects were patients less than 18 years of age, patients with diabetes type 1, patients on insulin therapy only, pregnant women, and patients with memory disorders or intellectual disability.

Data collection

Data was collected using a well-structured questionnaire which was developed based on a literature review. The questionnaire was presented in Arabic language to facilitate its comprehension and was filled by trained pharmacists. It was tested on 20 patients to evaluate their understanding of the questions and to do the necessary modifications. These patients were not included in the final sample.

The questionnaire contained data about sociodemographic characteristics, lifestyle information such as physical

activity defined by at least 30 minutes of moderateintensity exercise on most days of the week²⁵, health status, patient disease status, medication-related characteristics, medication adherence using a Lebanese Medication Adherence Scale (LMAS-14), patient's relationship with the healthcare providers, and information about the patient's attitudes, behaviors, knowledge, and motivation towards his illness and treatment.

The clinics were visited by patients coming from different Lebanese regions. For each patient visiting the clinics included in the study, interviewers checked the patient's file to confirm the diagnosis of DM2 and to check the inclusion criteria. An oral consent was obtained from each patient to participate in the study. Accurate data on the patient's medical and medication history was recorded from the patient's file. The value of HbA1c of each patient was taken from the recent lab test performed within less than 1 month, brought in with the patient. A controlled HbA1c in DM2 patients is defined as being below 7%.5 Patients were asked about past medication history and over-the-counter (OTC) drugs containing sugar such as cough syrups and some vitamins. Certain acute hyperglycemic medications such as glucocorticoids, and some chronic drugs such as thiazide diuretics, and atypical antipsychotics were also recorded.5

The LMAS-14

Adherence to oral antidiabetic medication was evaluated using the fourteen-item LMAS-14. This instrument is a new Lebanese scale to measure medication adherence by considering socio-economic and cultural factors related to the Lebanese culture. It was validated by Lebanese hypertensive patients and can be used to assess adherence to treatment in chronic diseases. ²⁶ The LMAS-14 contains 14 Likert scale questions with four answers each (coded from zero (less adherence) to three (high adherence)). Score can range from zero (lowest adherence) to 42 (highest adherence). LMAS assesses occupational factors including forgetfulness during busy periods (intensive work or travel), if the patient was invited to lunch or dinner, if some food items were prohibited during treatment period because of possible food-medication interaction, and delay in buying a new pills box when the old one is over. It also assesses psychological factors including experiencing any secondary effects or feeling clinically better or worse with a change in behavior when the laboratory exams are improved. Annoyance factors are also included in LMAS-14 such as frustration from taking a lot of pills, boredom of chronic treatment, and experience of some side effects. Finally, economical factors are assessed in LMAS-14 including health insurance coverage of medication cost, and expensive medication.

Each patient's score was calculated to assess adherence to medication. Patients were classified into adherent or non-adherent using a cut-off point of 38 as in previous studies. Sensitivity and specificity of LMAS-14 were respectively 82.9% and 36.9%. ²⁶

Data analysis

All data were analyzed using SPSS version 20. Bivariate and multivariate analyses (logistic regression) were done. A confidence interval of 95% and a p-value <0.05 were



Table 1. Description of the study population (N=245)
Variables	n (%)
Sex	
Females	133 (54.3)
Body mass index (BMI) ¹ Underweight (BMI<18.5 kg/m ²)	1 (0.4)
Onderweight (BMI<18.5 kg/m) Normal weight (BMI≥18.5 kg/m²)	1 (0.4) 36 (14.7)
Overweight (BMI≥25 kg/m²)	91 (37.1)
Obese (BMI≥30 kg/m²)	117 (47.8)
Education level	, ,
Illiterate	87 (35.5)
Elementary	74 (30.2)
Intermediate/ Secondary	56 (22.9)
University	28 (11.4)
Occupation	120 (40)
Unemployed Employed/Self-employed	120 (49) 111 (45.3)
Retired	14 (5.7)
Working hours/ day	1.(3.7)
0	134 (54.7)
<8h	13 (5.3)
>8h	98 (40)
Medical Insurance	177 (72.2)
Smoking	
Yes	96 (39.2)
No	124 (50.6)
Ex-smoker	25 (10.2)
Physical activity Recommendation of diet by physician	85 (34.7)
Follow-up of diet	237 (96.7)
No/Sometimes	195 (79.6)
Yes	50 (20.4)
Family history of diabetes	160 (65.3)
Intake of chronic hyperglycemic medication	41 (16.7)
Intake of acute hyperglycemic medication (OTC)	80 (32.7)
HbA1c (%)	
Uncontrolled (≥7%)	174 (71)
Controlled (<7%)	71 (29)
Type of Comorbidities	454 (64.6)
Hypertension	151 (61.6)
Dyslipidemia Respiratory diseases (Asthma or COPD ²)	147 (60) 9 (3.7)
Congestive heart failure/Angina/ Arythmia	40 (16.3)
Kidney disease	19 (7.8)
Hepatic disease	3 (1.2)
Gastrointestinal disease	11 (4.5)
Other Comorbidities (uricemia, anemia,	, ,
osteoporososis, thyroid/nervous disease)	101 (41.2)
Pharmacological class of oral antidiabetic	
medication	
Biguanides	216 (88.2)
Sulfonylureas	126 (51.4)
DPP-4 inhibitors	96 (39.2)
Thiazolidinediones SGLT2 inhibitors	14 (5.7) 11 (4.5)
Meglitinides	8 (3.3)
Alpha-glucosidase inhibitors	2 (0.8)
Combination	91 (37.1)
1	· · · · · · · · · · · · · · · · · · ·

¹ World Health Organization (WHO). Global Database on Body Mass Index.

considered to get a statistically significant result. The dependent variable for logistic regression was the dichotomized adherence score (based on a cut-off point=38). Only variables having p-value<0.2 in the bivariate analysis were included in the multivariate analysis.

RESULTS

A total of 245 patients who met the inclusion criteria were included in this study, with an average age of 59.32 years (SD=10.77). More than half of the patients (54.3%) were females. Age difference was not significant between males (60.59 years; SD 11.22) and females (58.25 years; SD 10.304) with a p-value=0.09. The majority of the patients were either overweight (37.1%) or obese (47.8%). Most of the patients were illiterate (35.5%) and unemployed (49%). Around half of the population (50.6%) was nonsmokers. Only 34.7% were physically active and 20.4% followed the diet recommended by their physician properly. One hundred sixty patients (65.3%) had a family history of diabetes. The mean duration of diabetes was 9.03 years (SD 8.01) and was accompanied with comorbidities in 86.5% of the cases. The most common comorbidity was hypertension (61.6%) followed by dyslipidemia (60%). Almost 63% of patients regularly measured their HbA1c. The mean HbA1c was 7.90% (SD 1.63). Good glycemic control (HbA1c<7) was achieved in only 29% of participants. The total number of medications taken per day by the patients was 5.21 (SD 2.76). The most common class of oral antidiabetics taken was biguanides (88.2%) followed by sulfonylureas (51.4%) (Table 1).

After classification of LMAS-14 score into two classes, 31.8% of patients had a high adherence (score≥38) and 68.2% had low adherence (score<38) following dichotomization using a cut-off point 38.

Bivariate analysis

Among socio-demographic factors, only working hours/day had a significant influence on medication adherence (p=0.001).

Concerning lifestyle characteristics, among patients who follow up the diet recommended by their physician, most of them were adherent to their oral antidiabetic medication (30.8%) while 15.6% were non-adherent (p=0.006). Moreover, among patients who do not consume beverages containing sugar, 85.9% of them were adherent (p=0.01).

Among patients who had an uncontrolled HbA1c level, 75.4% of the patients were non-adherent to their oral antidiabetic medication (p=0.025). Concerning patient's health status, the presence of comorbidities had no significant effect on medication adherence. However, the presence of respiratory disease (Asthma or Chronic Obstructive Pulmonary Disease) was associated with a decrease in medication adherence (p=0.041) (7.8% were non-adherent while 1.3% were adherent).

Taking sulfonylureas was also a significant factor (p=0.026) affecting adherence. From the patients who knew the names of their antidiabetic drugs, 52.6% were adherent while 37.7% were not (p=0.029), and among patients who did not understand their treatment regimen, 20.5% were adherent while 34.1% were not (p=0.03). Among patients who postponed their physician office visits, 53.9% were non-adherent while 29.5% were adherent (p<0.001), and finally among patients who visited their physicians annually or every few years, 32.9% and 14.4% were non-adherent, while 23.1% and 5.1% were adherent (p=0.026), respectively.

²COPD: Chronic Obstructive Pulmonary Disease

Table 2. Factors associated with adherence score using a dichoton	nized scale		
Variables	n (%) Non-adherent (<38)	n (%) Adherent (≥38)	p-value
Working hours/ day			0.001
0	97 (58.1)	37 (47.4)	
< 8h	3 (1.8)	10 (12.8)	
> 8h	67 (40.1)	31 (39.7)	
Follow up of diet			0.006
No/ Sometimes	141 (84.4)	54 (69.2)	
Yes	26 (15.6)	24 (30.8)	
Consumption of beverages with sugar			0.010
No	118 (70.7)	67 (85.9)	
Yes	49 (29.3)	11 (14.1)	0.005
HbA1c	426 (75.4)	40 (64 5)	0.025
Uncontrolled (≥ 7%)	126 (75.4)	48 (61.5)	
Controlled (< 7%)	41 (24.6)	30 (38.5)	2 2 4 4
Respiratory disease (Asthma or COPD)	454 (02.2)	77 (00 7)	0.041
No	154 (92.2)	77 (98.7)	
Yes Sulfonylureas	13 (7.8)	1 (1.3)	0.026
Suironyiureas	73 (43.7)	46 (59)	0.026
Yes	94 (56.3)	32 (41)	
Knowledge of the drugs' names by the patient	J -1 (JU.J)	J2 (41)	0.029
Some of them/ No	104 (62.3)	37 (47.4)	0.023
Yes	63 (37.7)	41 (52.6)	
The patient understood his treatment regimen	05 (57.7)	41 (32.0)	0.030
No	57 (34.1)	16 (20.5)	0.030
Yes	110 (65.9)	62 (79.5)	
Postponing physician office visits	=== (====)	()	< 0.001
No	77 (46.1)	55 (70.5)	10.002
Yes	90 (53.9)	23 (29.5)	
Frequency of physician office visits		- (/	0.026
Every month	15 (9)	8 (10.3)	
Every 3 to 6 months	73 (43.7)	48 (61.5)	
Every year	55 (32.9)	18 (23.1)	
Every few years (> 2 years)	24 (14.4)	4 (5.1)	
Experience of side effects			0.002
No	94 (56.3)	60 (76.9)	
Yes	73 (43.7)	18 (23.1)	
In case of hypo/hyperglycemia, patient skips/doubles the dose			< 0.001
No	115 (68.9)	72 (92.3)	
Yes	52 (31.1)	6 (7.7)	
In fasting states, patient skips taking his medication			0.012
No	136 (81.4)	73 (93.6)	
Yes/ Sometimes	31 (18.6)	5 (6.4)	
Following healthcare provider instructions			< 0.001
No/ Sometimes	73 (43.7)	16 (20.5)	
Yes	94 (56.3)	62 (79.5)	
Main reason for discontinuing treatment		_ ,	< 0.001
Forgetfulness	55 (32.9)	5 (6.4)	
High cost	41 (24.6)	11 (14.1)	
Complexity of treatment regimen	11 (6.6)	3 (3.8)	
Experience of unwanted side effects	22 (13.2)	1 (1.3)	
Perception of inefficacy	10 (6)	1 (1.3)	
No discontinuation of treatment	28 (16.8)	57 (73.1)	.0001
The patient feels his treatment is inconvenient and a burden	74 (42 5)	70 (00 7)	< 0.001
No	71 (42.5)	70 (89.7)	
Yes	96 (57.5)	8 (10.3)	0.047
Number of comorbidities	Mean = 2.072	Mean = 1.705	0.047
Total number of medications/ day	Mean = 5.503	Mean = 4.590	0.016
Number of antidiabetic medication / day	Mean = 1.898	Mean = 1.667	0.041

Experiencing side effects lead patients to be less adherent (p=0.002). Among the patients who had experienced side effects, 43.7% were non-adherent while 23.1% were adherent. On the other hand, stopping medication in case of hypo/hyperglycemia and fasting were also significant factors for non-adherence, p<0.001 and p=0.012, respectively. Moreover, forgetfulness, high drug cost,

complex treatment regimens, and perception of treatment inefficacy had a significant association with poor medication adherence (p<0.001) (Table 2).

Multivariate analysis

Results of logistic regression showed that increased working hours/day was associated with a decrease in



Table 3. Results of the binary logistic	regression using the dichotomized LMAS a	s the dependent variable		
Variables		Adjusted Odds Ratio (Exp-beta)	95% Confidence Interval	p-value
Working hours/ day	<8h vs 0h	1.537	0.548; 4.310	0.414
	>8h vs 0h	0.307	0.106; 0.884	0.029
Main reason for discontinuing treatment (Reference group: not discontinuing)	Forgetfulness	0.023	0.006; 0.084	<0.001
	High cost	0.202	0.067; 0.608	0.004
	Complexity of treatment regimen	0.065	0.012; 0.359	0.002
	Experience of unwanted side effects	0.022	0.002; 0.214	0.001
	Perception of inefficacy	0.072	0.007; 0.786	0.031
Postponing physician office visits		0.358	0.149; 0.860	0.022
Follow-up of diet		2.555	0.986 ; 6.618	0.053
In case of hypo/hyperglycemia, the patient skips/doubles the dose		0.087	0.022 ; 0.344	0.001
The patient feels his treatment is inconvenient and a burden		0.042	0.014; 0.125	<0.001

Dependent variable: dichotomized LMAS. Omnibus test p-value<0.001/Hosmer-Lemeshow test p-value=0.831. Nagelkerke R^2 =0.654/Overall predicted percentage = 85.3%.

Variables excluded from the model: Age, Gender, BMI, Physical activity, Consumption of beverages with sugar, Controlled/Uncontrolled HbA1C, Number of comorbidities, Presence of COPD/Asthma, Taking sulfonylureas, Intake of acute hyperglycemic medication (OTC), Knowledge of the drugs' names by the patient, Frequency of physician office visits, The patient understood his treatment regimen, Experience of side effects, Presence of diabetes complications, Number of antidiabetic medication/day, Number of medications/day, Skipping doses in fasting states, Following healthcare provider instructions.

adherence to oral antidiabetic medication (OR=0.31; 95%CI 0.11:0.88; p=0.029). Forgetfulness, high drug cost, complex treatment regimens, experiencing side effects, and perception of inefficacy were significantly associated with a decrease in the level of adherence (p<0.001, p=0.004, p=0.002, p=0.001, and p=0.031 respectively). Postponing physician office visits significantly decreased the probability of being adherent to oral antidiabetic medication (OR=0.36; 95%CI 0.15:0.86; p=0.022). Skipping or doubling the dose in case of hypo/hyperglycemia, and sensation of treatment burden were also significantly associated with a decrease in the level of adherence (OR=0.09; 95%CI 0.02:0.034; p=0.001, and OR=0.04; 95%CI 0.01:0.13; p<0.001 respectively) (Table 3).

DISCUSSION

Adherence to oral antidiabetic medication was 31.8% among Lebanese DM2 patients. The adherence rate was similar to studies conducted in China²⁷ and Korea²⁸, greater than that reported in Iraq (29.8%)²⁹, and lower than reports from of other countries, such as Ethiopia (45.9%)²², United States (47.3%)³⁰ and India (60%).³¹ Cultural diversity between countries could explain the difference in adherence levels between different populations. Yet, this difference could also be due to the variation of the methodologies and the different measurement scales used to evaluate adherence.³²

Among the socio-demographic factors, the findings showed that adherence rates were similar in both genders, which was consistent with the results obtained in Malaysia and India. 18,31 Age also had no association with adherence to treatment. However some studies have found an association between age and non-adherence. In a Malaysian study, older age was associated with an increased medication adherence. 18 This study also found a significant association between working hours/day and medication adherence. When the working hours increase (>8h), the probability of being adherent to oral antidiabetic medication decrease. Being at work for a long period of time may prevent the patient from taking his treatment

regularly and attending to his health care professional as recommended. $^{\rm 33}$

Lack of follow up to recommended diet and consumption of beverages containing sugar were also increased among non-adherent patients. Other studies have also found that non-adherence to oral antidiabetic medication also comprised non-adherence to the non-pharmacologic guidelines. Following non-pharmacologic recommendations is crucial in achieving the target HbA1C. This includes a proper diet (low in saturated fat, sodium and carbohydrates, and high in fiber contents), weight loss, and exercise. 4

Among Lebanese DM2 patients, only 29% had achieved the target HbA1c (<7%). This is much lower than that in the United States (87.1%). In this study, patients who had good glycemic control had better adherence to oral antidiabetic drugs compared to those who had poor glycemic control. This coincides with studies done in China²⁷, Ethiopia³⁵, and Libya³⁶ where an inverse association between medication adherence and glycemic control (represented by the value of HbA1C) was reported. 35-37

The duration of diabetes after diagnosis was not found to be associated with adherence among Lebanese DM2 patients. Nevertheless a study conducted in China showed that newly diagnosed patients had a lower adherence to their therapy.²⁷ Newly diagnosed patients may still not be aware of the consequences of missing their treatment and the complications associated with poor glycemic control. Contrariwise, a study done in the United Arab Emirates showed that patients with a longer duration of diabetes were more likely to be non-adherent to their treatment.³⁸ It is suggested that newly diagnosed patients may be more committed to their treatment, but they soon adapt to the disease burden due to the chronic nature of disease.³⁸

The presence of comorbidities was not associated with medication adherence. However, the presence of asthma or COPD was found to reduce adherence in diabetic patients. This can be explained by the use of corticosteroids or long-term beta agonists in the control of these diseases, which may lead to corticosteroids-induced hyperglycemia.



Furthermore, it is suggested that decreased quality of life in the presence of these diseases may decrease motivation to treatment and thus adherence.

Medication related factors, including regimen complexity and multiple daily dosing, were also factors affecting medication adherence. Patients taking more than two drugs were less adherent to treatment.³⁹ This is similar to the results obtained on diabetic patients in Nigeria, Ghana, and Hungaria, where adherence rates decreased as the pill burden increased.³⁹⁻⁴¹ Combination therapy reduces pill burden and dosing frequency, and is a good strategy to improve drug adherence.^{40,42}

Among the different classes of oral hypoglycemics, only sulfonylureas were associated with decreased adherence. Sulfonylureas are particularly associated with an increased risk of hypoglycemia which is perceived as life-threatening by patients. A study conducted in Sweden showed symptomatic hypoglycemia in patients treated by sulfonylureas was associated with non-adherence. Hypoglycemia can negatively affect the quality of life for diabetic patients, and decrease their adherence to treatment.

In this study, it was revealed that patients who experienced side effects to their medication were less adherent to the treatment regimen. This result is in agreement with the findings in United States which reported that side effects of medication is a main factor for low adherence to antidiabetic medication. ³⁰

As for factors related to the patient-provider relationship, patients who visited their physician more frequently and did not postpone their office visits were more adherent to their medication as they were more interested in improving their health status. The physician's communication skills and a good relationship between patients and their healthcare providers are two factors that greatly improve adherence. ^{13,45,46} Communication between physician and patient promotes the patient's knowledge about his treatment and illness condition and thus improves medication adherence. ⁴⁷

Forgetfulness and high cost of drugs were two factors leading to low medication adherence when the motivation or intention exists. This is similar to the findings of several studies in Canada and Nigeria. Several actions are suggested to decrease patient forgetfulness such as getting help from a family member, using pill boxes, putting medication in a place where the patient performs daily activity, and setting medication alarms. Concerning high drug costs, physicians may prescribe generic drugs at lower prices for less fortunate patients. Also a governmental plan should be launched to provide free access to medical services and chronic medications.

No association was found between adherence and education level, similar to studies from Ethiopia, India and Nigeria. This may be due to the fact that the majority of the population were elderly and had poor knowledge concerning their disease or treatment. Low understanding of treatment regimen among diabetic patients was significantly associated with low medication adherence.

This is similar to another study which demonstrated a significant association between medication adherence and patient's knowledge. ¹⁸ To that end, patient education by the health care professional on medication regimen and behavior towards the disease is essential in order to improve adherence and to achieve a controlled level of HbA1c. Health care professionals should be approachable, listen to their patients' concerns, inform their patients about the course of the disease and how to manage side effects. A shared decision making model is reccomended. ⁴⁷

This study is the first study in Lebanon to assess medication adherence among diabetic patients. Numerous factors were found to negatively affect adherence, leading to poor treatment outcomes. However, this study presents several limitations. Self-reporting was used to evaluate adherence so a recall bias may have occurred and patients may have elicited only socially accepted responses. Due to these possibilities it is suggested that adherence was overestimated. Also, being a cross-sectional study, a causal relationship between medication adherence and the various behaviors of the patient is difficult to establish.

CONCLUSIONS

Several factors influence adherence levels in Lebanese DM2 patients including drug discontinuation when fasting and not respecting physician's instructions. This reflects the fact that some patients have their own perceptions which affect their treatment decisions. This issue can be solved by improving patient education and reinforcing the continuity of care by emphasizing patient-physician relationships.

Moreover, forgetfulness, high cost of drugs, complexity of treatment regimen, side effects, and perception of inefficacy are factors that decrease adherence. Resolving these problems involves decreasing the number and the frequency of therapy. Health care providers should also give more attention to medication side effects in chronic diseases that require long-term treatment.

In the absence of any medical insurance or government program for social support, the cost of medications imposes a great burden for many patients. This highlights the need for better social security programs and governmental support to decrease the economic burden of medication and therefore to avoid diabetes complications.

A study on a larger patient size and conducted all over Lebanon is needed to provide stronger evidence about the factors affecting adherence, and to perform better intervention programs.

CONFLICT OF INTEREST

There is no conflict of interest.

FUNDING

Lebanese University.



References

- 1. Lumb A. Diabetes and exercise. Clin Med (Lond). 2014;14(6):673-676. doi: 10.7861/clinmedicine.14-6-673
- 2. International Diabetes Federation. Diabetes Atlas, 7th ed. Belgium: IDF; 2015. ISBN: 978-2-930229-81-2
- 3. Zimmet PZ, Magliano DJ, Herman WH, Shaw JE. Diabetes: a 21st century challenge. Lancet Diabetes Endocrinol. 2014;2(1):56-64. doi: 10.1016/S2213-8587(13)70112-8
- 4. American Diabetes Association. Prevention or delay of type 2 diabetes. Diabetes Care. 2016;39(Suppl 6):36-38.
- 5. Currie C, Peters JR, Tynan, A, Evans M, Heine RJ, Bracco OL, Zagar T, Poole CD. Survival as a function of Hba(1c) in people with type 2 diabetes: a retrospective cohort study. Lancet. 2010;375(9713):481-489. doi: 10.1016/S0140-6736(09)61969-3
- Fowler MJ. Microvascular and Macrovascular Complications of Diabetes. Clin Diabetes. 2008;26(2):77-82. Doi: 10.2337/diaclin.26.2.77
- Qaseem A, Humphrey LL, Sweet DE, Starkey M, Shekelle P. Oral pharmacologic treatment of type 2 diabetes mellitus: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2012;156(3):218-231. doi: 10.7326/0003-4819-156-3-201202070-00011
- 8. Ali MK, Bullard KM, Imperatore G, Baker L, Gregg EW. Characteristics associated with poor glycemic control among adults with self reported diagnosed diabetes. MMWR Suppl. 2012 Jun 15;61(2):32-37.
- Khan AR, Al-Abdul Lateef ZN, Al Aithan MA, Bu-Khamseen MA, Al Ibrahim I, Khan SA. Factors contributing to non-compliance among diabetics attending primary health centers in the Al Hasa district of Saudi Arabia. J Family Community Med. 2012;19(1):26-32. doi: 10.4103/2230-8229.94008
- 10. Noureddine H, Nakhoul N, Galal A, Soubra L, Saleh M. Level of A1C control and its predictors among Lebanese type 2 diabetic patients. Ther Adv Endocrinol Metab. 2014;5(3):43-52. doi: 10.1177/2042018814544890
- 11. Al-Lawati JA, Barakat M, Al-Zakwani I, Elsayed MK, Al-Maskari M, Al-Lawati N, Mohammed AJ. Control of risk factors for cardiovascular disease among adults with previously diagnosed type 2 diabetes mellitus: a descriptive study from a middle eastern arab population. Open Cardiovasc Med J. 2012;6:133-140. doi: 10.2174/1874192401206010133
- 12. Roaeid RB, Kadiki OA. Prevalence of long-term complications among Type 2 diabetic patients in Benghazi, Libya. J Diabetol. 2011;2(3):5.
- 13. World Health Organization (WHO). Adherence to Longterm Therapies: Evidence for Action. Geneva: WHO; 2003.
- 14. Raum E, Kramer HU, Ruter G, Rothenbacher D, Rosemann T, Szecsenyi J, Brenner H. Medication non-adherence and poor glycaemic control in patients with type 2 diabetes mellitus. Diabetes Res Clin Pract. 2012;97(3):377-384. doi: 10.1016/j.diabres.2012.05.026
- 15. Sherifali D, Nerenberg K, Pullenayegum E, Cheng JE, Gerstein HC. The effect of oral antidiabetic agents on A1C levels: a systematic review and meta-analysis. Diabetes Care. 2010;33(8):1859-1864. doi: 10.2337/dc09-1727
- 16. Breitscheidel L, Stamenitis S, Dippel FW, Schoffski O. Economic impact of compliance to treatment with antidiabetes medication in type 2 diabetes mellitus: a review paper. J Med Econ. 2010;13(1):8-15. doi: 10.3111/13696990903479199
- 17. Bundrick Harrison L, Lingvay I. Appointment and medication non-adherence is associated with increased mortality in insulin-treated type 2 diabetes. Evid Based Med. 2013;18(3):112-113. doi: 10.1136/eb-2012-100912
- 18. Ahmad NS, Ramli A, Islahudin F, Paraidathathu T. Medication adherence in patients with type 2 diabetes mellitus treated at primary health clinics in Malaysia. Patient Prefer Adherence. 2013;7:525-530. doi: 10.2147/PPA.S44698
- 19. Firouzi S, Barakatun-Nisak MY, Azmi KN. Nutritional status, glycemic control and its associated risk factors among a sample of type 2 diabetic individuals, a pilot study. J Res Med Sci. 2015;20(1):40-46.
- 20. Egede LE, Gebregziabher M, Hunt KJ, Axon RN, Echols C, Gilbert GE, Mauldin PD. Regional, geographic, and racial/ethnic variation in glycemic control in a national sample of veterans with diabetes. Diabetes Care. 2011;34(4):938-943. doi: 10.2337/dc10-1504
- 21. Rozenfeld Y, Hunt JS, Plauschinat C, Wong KS. Oral antidiabetic medication adherence and glycemic control in managed care. Am J Manag Care. 2008;14(2):71-75.
- 22. Abebe SM, Berhane Y, Worku A. Barriers to diabetes medication adherence in North West Ethiopia. Springerplus. 2014;3:195. doi: 10.1186/2193-1801-3-195
- 23. Charan J, Biswas T. How to calculate sample size for different study designs in medical research? Indian J Psychol Med. 2013;35(2):121-126.
- 24. Al-Hajje A, Awada S, Rachidi S, Zein S, Bawab W, El-Hajj Z, Bou Zeid M, Yassine M, Salameh P. Factors affecting medication adherence in Lebanese patients with chronic diseases. Pharm Pract (Granada). 2015;13(3):590. doi: 10.18549/PharmPract.2015.03.590
- 25. World Health Organization. Physical Activity. Available from: http://www.who.int/mediacentre/factsheets/fs385/en/ (accessed February 23, 2018).
- 26. Bou Serhal R, Pascale S, Wakim N, Issa C, Kassem B, Abou Jaoude L, Saleh N. A New Lebanese Medication Adherence Scale: Validation in Lebanese Hypertensive adults. Int J Hypertens. 2018 May 20;2018:3934296. doi: 10.1155/2018/3934296
- 27. Wang J, Bian RW, Yong-zhen MO. Validation of the Chinese version of the eight-item Morisky medication adherence scale in patients with type 2 diabetes mellitus. J Clin Gerontol Geriatr. 2013;4(4):119-122. doi: 10.1016/j.icgg.2013.06.002
- 28. Lee WY, Ahn J, Kim JH, Hong YP, Hong SK, Kim YT, Lee SH, Morisky DE. Reliability and validity of a self-reported measure of medication adherence in patients with type 2 diabetes mellitus in Korea. J Int Med Res. 2013;41(4):1098-1110. doi: 10.1177/0300060513484433
- 29. Shakor J, Qader S. Drug Adherence among Diabetic and Hypertensive Patients in Association with Demographic and Healthy Behavior. Int J Sci Res. 2012;3(12):1998-2003.



- 30. Gatti ME, Jacobson KL, Gazmararian JA, Schmotzer B, Kripalani S. Relationships between beliefs about medications and adherence. Am J Health Syst Pharm. 2009;66(7):657-664. doi: 10.2146/ajhp080064
- 31. Priyanka T, Lekhanth A, Revanth A, Gopinath C, Babu SC. Effect of Polypharmacy on Medication Adherence in Patients with Type 2 Diabetes mellitus. Indian J Pharm Prac. 2015;8(3):126-132.
- 32. Yassine M, Al-Hajje A, Awada S, Rachidi S, Zein S, Bawab W, Bou Zeid M, El Hajj M, Salameh P. Evaluation of medication adherence in Lebanese hypertensive patients. J Epidemio IGlob Health. 2016;6(3):157-67. doi: 10.1016/j.jegh.2015.07.002
- 33. Lee CS, Tan JHM, Sankari U, Koh YLE, Tan NC. Assessing oral medication adherence among patients with type 2 diabetes mellitus treated with polytherapy in a developed Asian community: a cross-sectional study. BMJ Open. 2017;7(9):e016317. doi: 10.1136/bmjopen-2017-016317
- 34. Anderson RM, Fitzgerald JT, Oh MS. The relationship between diabetes-related attitudes and patients' self-reported adherence. Diabetes Educ. 1993;19(4):287-292. doi: 10.1177/014572179301900407
- 35. Kassahun T, Eshetie T, Gesesew H. Factors associated with glycemic control among adult patients with type 2 diabetes mellitus: a cross-sectional survey in Ethiopia. BMC Res Notes. 2016;9:78. doi: 10.1186/s13104-016-1896-7
- 36. Ashur S, Shah S, Bosseri S, Fah TS, Shamsuddin K. Glycaemic control status among type 2 diabetic patients and the role of their diabetes coping behaviours: a clinic-based study in Tripoli, Libya. Libyan J Med. 2016;11:31086. doi: 10.3402/ljm.v11.31086
- 37. Ashur ST, Shah SA, Bosseri S, Morisky DE, Shamsuddin K. Illness perceptions of Libyans with T2DM and their influence on medication adherence: a study in a diabetes center in Tripoli. Libyan J Med. 2015;10:29797. doi: 10.3402/ljm.v10.29797
- 38. Arifulla M, John LJ, Sreedharan J, Muttappallymyalil J, Basha SA. Patients' Adherence to Anti-Diabetic Medications in a Hospital at Ajman, UAE. Malays J Med Sci. 2014;21(1):44-49.
- 39. Awodele O, Osuolale JA. Medication adherence in type 2 diabetes patients: study of patients in Alimosho General Hospital, Igando, Lagos, Nigeria. Afr Health Sci. 2015;15(2):513-522. doi: 10.4314/ahs.v15i2.26
- 40. Bruce SP, Acheampong F, Kretchy I. Adherence to oral anti-diabetic drugs among patients attending a Ghanaian teaching hospital. Pharm Pract (Granada). 2015;13(1):533
- 41. Hanko B, Kazmer M, Kumil P, Hragyel Z, Samu A, Vincze Z, Zelko R. Self-reported medication and lifestyle adherence in Hungarian patients with type 2 diabetes. Pharm World Sci. 2007;29(2):58-66.
- 42. Laufs U, Rettig-Ewen V, Böhm M. Strategies to improve drug adherence. Eur Heart J. 2011;32(3):264-268. doi: 10.1093/eurhearti/ehg297
- 43. Belsey J, Krishnarajah G. Glycaemic control and adverse events in patients with type 2 diabetes treated with metformin + sulphonylurea: a meta-analysis. Diabetes Obes Metab. 2008;10(Suppl 1):1-7. doi: 10.1111/j.1463-1326.2008.00884.x
- 44. Walz L, Pettersson B, Rosenqvist U, Deleskog A, Journath G, Wandell P. Impact of symptomatic hypoglycemia on medication adherence, patient satisfaction with treatment, and glycemic control in patients with type 2 diabetes. Patient Prefer Adherence. 2014;8:593-601. doi: 10.2147/PPA.558781
- 45. Brown MT, Bussell JK. Medication adherence: WHO cares? Mayo Clin Proc. 2011;86(4):304-314. doi: 10.4065/mcp.2010.0575
- 46. Kelly B, Haskard Z, DiMatteo R. Physician Communication and Patient Adherence to Treatment: A Meta-analysis. Med Care. 2009;47(8):826-834. doi: 10.1097/MLR.0b013e31819a5acc
- 47. Guenette L, Lauzier S, Guillaumie L, Giguère G, Grégoire J, Moisan J. Patients' beliefs about adherence to oral antidiabetic treatment: a qualitative study. Patient Prefer Adherence. 2015;9:413-420. doi: 10.2147/PPA.S78628
- 48. Fadare J, Olamoyegun M, Gbadegesin BA. Medication adherence and direct treatment cost among diabetes patients attending a tertiary healthcare facility in Ogbomosho, Nigeria. Malawi Med J. 2015;27(2):65-70.

