Factors related to medication adherence in patients with type 2 diabetes based on the MARS-10 scale

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Abstract

Introduction: Medication adherence directly affects glycemic control and clinical outcomes. Factors related to medication adherence tend to be complex due to interactions between medication, patients, and healthcare professionals. **Objectives:** To investigate medication adherence rate and factors related to medication adherence in patients with type 2 diabetes. **Subjects and Methods:** A cross-sectional study was conducted, interviewing 394 patients at the Internal Medicine Clinic, Hue University of Medicine and Pharmacy Hospital, from July 2022 to July 2023, using the MARS-10 questionnaire. **Results:** The medication adherence rate was 81.7%. Factors associated with medication adherence included HbA1c target (p = 0.025), reminders from healthcare professionals (p = 0.028), and monthly follow-up visits (p = 0.027). **Conclusion:** Measures are needed to enhance counseling and education to remind patients about medication use and glycemic control at home.

Keywords: *type 2 diabetes, MARS-10, medication adherence.*

1. INTRODUCTION

In 2021, the International Diabetes Federation (IDF) highlighted the continuous increase in the number of diagnosed diabetes patients globally and affirmed this as a societal challenge [1]. In addition to increased mortality, diabetes can lead to poor physical and mental health [2]. The chronic nature of diabetes requires patients to take lifelong medication, with increasing complexity of drug regimens over time [3]. To prevent the development of life-threatening complications related to diabetes, glycemic control is essential. To achieve this goal, patients should be encouraged to adhere to treatment regimens, make lifestyle changes, and follow clinicians' recommendations [3]. Besides, there are many factors related to medication adherence. Factors relating to patients, healthcare providers, and medications interact complexly [4]. Therefore, research evaluating medication adherence and related factors is important in diabetes treatment.

The WHO has clearly accepted that there is no "gold standard" for measuring medication adherence behavior [5, 6, 7]. However, it is recognized that the use of questionnaires is the basic psychometric standard for assessing specific behaviors related to health issues, allowing for better prediction of treatment adherence behavior [7]. MARS is a self-reported scale of non-adherence behavior that is non-threatening and non-judgmental, which can lead to honest answers, and is used in a variety of long-term conditions. It is a general tool that can be used to assess any prescribed medication, regardless of health status. Medication adherence means that patients actively monitor and make adaptive adjustments in various aspects of diabetes management to control blood glucose and reduce the likelihood of complications. These include: home glucose monitoring (blood or urine); adjusting food intake, especially carbohydrates, to meet daily needs and match available insulin; taking medication (insulin or oral hypoglycemic agents); regular physical activity; foot care; regular medical follow-up visits and other behaviors (i.e., oral care, appropriate clothing, etc.) that may vary depending on the type of diabetes [6]. Currently, in Vietnam, studies evaluating medication beliefs using the MARS scale in type 2 diabetes patients are very few and have not been widely published like studies on other scales. Studies on medication adherence using the MMAS-8 scale have inconsistent results. The MARS-10 scale adds missing aspects, reaffirms the value of other scales, and also helps identify individual patient concerns to move towards practical interventions [5, 8]. At present, in Vietnam, studies using MARS-10 are limited, so this study was conducted with the

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following objectives:

1) To survey the general characteristics of outpatients with type 2 diabetes at Hue University of Medicine and Pharmacy Hospital.

2) To investigate medication adherence rate factors related to medication adherence in patients with type 2 diabetes based on the MARS-10 scale.

2. SUBJECTS AND METHODS

2.1. Study Subjects

The study subjects were patients diagnosed with type 2 diabetes who attended the Internal Medicine outpatient clinic at Hue University of Medicine and Pharmacy Hospital from July 2022 to December 2022.

Inclusion criteria: 18 years of age or older, diagnosed with type 2 diabetes, prescribed diabetes medication for 3 months or more, able to understand and speak Vietnamese, and willing to participate in the study.

Exclusion criteria: Patients taking medications that affect blood glucose levels: glucocorticoids, contraceptives, drugs toxic to pancreatic beta cells, HIV medications, certain blood pressure medications (thiazides, propranolol, atenolol) [9, 10] pregnant women, patients with conditions affecting verbal communication or memory, such as mental illness or Alzheimer's disease.

2.2. Research Method

Study design: Cross-sectional descriptive study

Sample size:

Sample size calculation was performed using the formula for estimating a single proportion to estimate the minimum sample size:

$$n = Z^2_{1-\alpha/2}\frac{p(1-p)}{d^2}$$

Where:

n: number of type 2 diabetes patients needed for the study

p: proportion of patients with medication adherence. We chose p = 0.5 to obtain the largest sample size.

d: relative error, the allowable difference between the proportion obtained from the sample and the proportion of the population. Typically, the value of d is taken between 0.05 and 0.1. In this study, we took d = 0.05.

With a 95% confidence level, Z(1 - α/2) = 1.96.

The minimum sample size was 385 patients. The actual sample size obtained was 394.

Sampling method:

Convenient sampling method. Data were collected from the most easily accessible patients through direct contact.

2.3. Data Collection

Step 1: Patient Selection

Any patient who came to the clinic and met the study criteria was selected; patients who came for repeat visits during the data collection period were only interviewed once.

Step 2: Information Collection

- Patients were explained the content and purpose of the study to understand and decide whether to participate. If the patient agreed to participate, the interview continued.

- Patients were asked for information in the questionnaire about demographic, socio-economic, lifestyle characteristics and relevant information, disease characteristics, and the questions in the MARS-10 scale.

- HbA1c results, fasting blood glucose levels, and prescribed medications were recorded from the medical records. Missing data were collected from the electronic medical records.

During the interview, the researcher did not give the questionnaire to the subjects to fill out themselves. The researcher read the questions for the subjects to think and provide their answers. If the subjects did not understand the question, the question was reread, the MARS-10 questions could be explained more clearly, or the patient's family members could be asked (about lifestyle) for more accurate information.

Step 3: Data Processing and Analysis

Evaluation Criteria

Treatment target evaluation criteria for HbA1c and FPG were based on ADA 2024 standards: FPG 80 - 130 mg/dL (4.4 - 7.2 mmol/L) and HbA1c < 7% (53 mmol/mol) for non-pregnant adults, with individualized treatment targets [11].

The MARS-10 scale is a method for assessing medication adherence indirectly through self-reporting [12]. It is a multidimensional tool consisting of 3 parts: (Questions 1 - 4) describe medication adherence behavior; (Questions 5 - 8) attitudes, perspectives, and beliefs about medication use; (Questions 9 - 10) the impact of side effects on adherence [13]. The MARS-10 scale was translated into Vietnamese according to the translation principles of Cha Kim and Erlen in 2007 [14] by three language experts from the research team. After consensus, the Vietnamese translation was sent to several healthcare professionals for feedback, and a pilot interview was conducted with 30 patients to adjust and complete the official questionnaire. The MARS-10 scale measures the level of adherence

with 10 yes/no questions. The first six questions (questions 1 - 6), question 9, and question 10 are scored as "No = 1" and "Yes = 0," while questions 7 and 8 are scored as "No = 0" and "Yes = 1" [15]. The total MARS-10 score ranges from 0 to 10. Patients with a total MARS-10 score ≤ 5 are considered poor or non-adherent, while a MARS score ≥ 6 is considered good adherence [13].

2.4. Data Processing Method

Data were processed using SPSS software. For our analysis, we used the median and interquartile range to describe continuous MARS-10 scores, as the data were not normally distributed. We described discrete variables using percentages. To compare these variables, we used chi-squared tests and considered a p-value of less than 0.05 to be statistically significant. Any variables with a significant p-value were then included in a multivariable logistic regression model to identify factors associated with medication adherence.

2.5. Research Ethics

This study was approved by the Scientific Council and the Ethics Committee in Biomedical Research of Hue University of Medicine and Pharmacy (No. H2022/235). The study was conducted with the voluntary participation of patients.

3. RESULTS

3.1 Characteristics of the Study Subjects

The study included 394 outpatients with type 2 diabetes with the following characteristics:

Table 1. Characteristics of the Study Subjects

Characteristic		Number (n)	Percentage (%)
Age	34 - 59	112	28.4%
	≥ 60	282	71.6%
Gender	Male	159	40.4%
	Female	235	59.6%
Occupation	Intellectual	12	3.0%
	Manual Labor	21	5.3%
	Other	120	30.5%
	At home. retired	241	61.2%
Education Level	High school or below	348	88.3%
	Above high school	46	11.7%
Living Situation	Living alone	375	95.2%
	Living with relatives	19	4.8%
Duration of Disease	< 5 years	120	30.5%
	≥ 5 years	274	69.5%
Comorbidities	No	371	94.2%
	Yes	23	5.8%
Treatment Regimen	1 oral medication	93	23.6%
	2 oral medications	119	30.2%
	3 oral medications	29	7.4%
	Oral and injection combination	123	31.2%
	Injection only	30	7.6%
Smoking	Yes	14	3.6%
	No	380	96.4%
Alcohol Consumption	Yes	11	2.8%
	No	383	97.2%
Exercise	Regular (> 5 times/week)	271	68.8%
	Occasional (3 - 5 times/week)	56	14.2%
	None (less than 3 times/week)	67	17.0%

Diet	Yes	346	87.8%
	No	48	12.2%
Glucose Monitoring at Home	Regular (> 2 times/week)	56	14.2%
	Occasional (1 - 2 times/week)	43	10.9%
	None/rarely	295	74.9%
Monthly Diabetes Check-ups	Yes	387	98.2%
	No	7	1.8%
Reminders from Healthcare Professional	Regular	249	63.2%
	Occasional	84	21.3%
	None	61	15.5%
Satisfaction with Healthcare Services	Yes	308	78.2%
	Neutral	71	18.0%
	No	15	3.8%
FPG Target*	Achieved	190	48.2%
	Not achieved	204	51.8%
HbA1c Target	Achieved	213	54.1%
	Not achieved	181	45.9%

**FPG (Fasting Plasma Glucose)*

The elderly patient group accounted for 71.6% of the total, with 59.6% being female. The proportion of patients not working (at home, retired) was 61.2%. Patients with a duration of diabetes diagnosis of 5 years or more accounted for 69.5% of the group. The majority had comorbidities. The combined oral and injection treatment regimen had the highest proportion at 31.2%. Only 14.2% regularly monitored their blood glucose and nearly 40% of patients are not regularly reminded by medical staffs about taking their medication. The numberof patients who achieved the HbA1c and the fasting blood glucose treatment target was about 50%.

3.2. Medication Adherence and Associated Factors

Table 2. Results of the MARS-10 Questionnaire Survey

Question (N=394)	Yes (%)	No (%)
1. Do you ever forget to take your medication?	136 (34.5)	258 (65.5)
2. Are you careless at times about taking your medicine?	70 (17.8)	324 (82.2)
3. When you feel better. do you sometimes stop taking your medicine?	35 (8.9)	359 (91.1)
4. Sometimes if you feel worse when you take the medicine. do you stop taking it?	16 (4.1)	378 (95.9)
5. I take my medicine only when I am sick.	20 (5.1)	374 (94.9)
6. It is unnatural for my mind and body to be controlled by medicine.	288 (73.1)	106 (26.9)
7. My thoughts are clearer on medication.	320 (81.2)	74 (18.8)
8. By staying on medication. I can prevent getting sick.	361 (91.6)	33 (8.4)
9. I feel weird. like a zombie. on medication.	34 (8.6)	360 (91.4)
10. Medication makes me feel tired and sluggish.	48 (12.2)	346 (87.8)
Average score of MARS-10 (Median	**8.09 ± 1.83**	
Adherence (score ≥ 6)	322 (81.7%)	
Non-adherent (score ≤ 5)	72 (18.3%)	

The results yielded an average score of 8.09 ± 1.83, and the rate of patient medication adherence was 81.7%.

Table 3. The relationship between variables and medication adherence

Characteristic		Number (n)	Percentage (%)		p
			Yes n (%)	No n(%)	
Age	34-59	112 (28.4%)	90 (80.4%)	22 (19.6%)	0.658
	≥ 60	282 (71.6%)	232 (82.3%)	50 (17.7%)	
Gender	Male	159 (40.4%)	130 (81.8%)	29 (18.2%)	0.988
	Female	235 (59.6%)	192 (81.7%)	43 (18.3%)	
Occupation	Intellectual	12 (3.0%)	8 (66.7%)	4 (33.3%)	0.110
	Manual Labor	21 (5.3%)	14 (66.7%)	7 (33.3%)	
	Other	120 (30.5%)	98 (81.7%)	22 (18.3%)	
	At home. retired	241 (61.2%)	202 (83.8%)	39 (16.2%)	
Education Level	High school or below	348 (88.3%)	285 (81.9%)	63 (18.1%)	0.809
	Above high school	46 (11.7%)	37 (80.4%)	9 (19.6%)	
Living Situation	Living alone	375 (95.2%)	18 (94.7%)	1 (5.3%)	0.220
	Living with relatives	19 (4.8%)	304 (81.1%)	71 (18.9%)	
Duration of Disease	< 5 years	120 (30.5%)	97 (81.5%)	22 (18.5%)	0.955
	≥ 5 years	274 (69.5%)	224 (81.8%)	50 (18.2%)	
Comorbidities	No	371 (94.2%)	18 (78.3%)	5 (21.7%)	0.587
	Yes	23 (5.8%)	304 (81.9%)	67 (18.1%)	
Treatment Regimen	1 oral medication	93 (23.6%)	76 (81.7%)	17 (18.3%)	**0.044**
	2 oral medications	119 (30.2%)	106 (89.1%)	13 (10.9%)	
	3 oral medications	29 (7.4%)	25 (86.2%)	4 (13.8%)	
	Oral and injection combination	123 (31.2%)	94 (76.4%)	29 (23.6%)	
	Injection only	30 (7.6%)	21 (70.0%)	9 (30.0%)	
Smoking	Yes	14 (3.6%)	10 (71.4%)	4 (28.6%)	0.298
	No	380 (96.4%)	312 (82.1%)	68 (17.9%)	
Alcohol Consumption	Yes	11 (2.8%)	7 (63.6%)	4 (36.4%)	0.122
	No	383 (97.2%)	315 (82.2%)	68 (17.8%)	
Exercise	Regular (> 5 times/week)	271 (68.8%)	221 (81.5%)	50 (18.5%)	0.365
	Occasional (3-5 times/week)	56 (14.2%)	49 (87.5%)	7 (12.5%)	
	None (less than 3 times/week)	67 (17.0%)	52 (77.6%)	15 (22.4%)	
Diet	Yes	346 (87.8%)	283 (81.8%)	63 (18.2%)	0.927
	No	48 (12.2%)	39 (81.2%)	9 (18.8%)	
Glucose Monitoring at Home	Regular (> 2 times/week)	56 (14.2%)	48 (85.7%)	8 (14.3%)	0.629
	Occasional (1 - 2 times/week)	43 (10.9%)	36 (83.7%)	7 (16.3%)	
	None/rarely	295 (74.9%)	238 (80.7%)	57 (19.3%)	
Monthly Diabetes Check-ups	Yes	387 (98.2%)	321 (82.9%)	66 (17.1%)	< 0.001
	No	7 (1.8%)	1 (14.3%)	6 (85.7%)	

Reminders from Healthcare Professional	Regular	249 (63.2%)	210 (84.3%)	39 (15.7%)	0.002
	Occasional	84 (21.3%)	72 (85.7%)	12 (14.3%)	
	None	61 (15.5%)	40 (65.6%)	21 (34.4%)	
Satisfaction with Healthcare Services	Yes	308 (78.2%)	258 (83.8%)	50 (16.2%)	0.097
	Neutral	71 (18.0%)	54 (76.1%)	17 (23.9%)	
	No	15 (3.8%)	10 (66.7%)	5 (33.3%)	
FPG Target*	Achieved	190 (48.2%)	163 (85.8 %)	27 (14.2%)	0.044
	Not achieved	204 (51.8%)	159 (77.9 %)	45 (22.1%)	
HbA1c Target	Achieved	213 (54.1%)	189 (88.7 %)	24 (11.3%)	< 0.001
	Not achieved	181 (45.9%)	133 (73.5%)	48 (26.5%)	

**FPG (Fasting Plasma Glucose)*

Medication adherence of the patient was significantly associated with a treatment regimen (p = 0.044), monthly diabetes check-ups (p < 0.001), reminders from a healthcare professional (p = 0.002), FPG target (p = 0.044), and HbA1c target (p < 0.001).

Table 4 . Multivariate logistic regression analysis

Characteristics		OR (CI 95%)	p
Treatment Regimen	1 oral medication	1	0.2
	2 oral medications	1.1 (0.4 - 3.4)	
	3 oral medications	0.5 (0.2 - 1.4)	
	Oral and injection combination	0.4 (0.1 - 1.6)	
	Injection only	0.8 (0.3 - 2.1)	
Reminders from Healthcare Professional	None	1	0.028
	Occasional	2.4 (1.2 - 4.8)	
	Regular	0.9 (0.4 - 1.8)	
HbA1c Target	Achieved	1	0.016
	Not achieved	0.4 (0.2 - 0.8)	
Monthly Diabetes Check-ups	No	1	0.015
	Yes	15.6 (1.7 - 12.1)	
FPG Target	Achieved	1	0.664
	Not achieved	0.9 (0.4 - 1.7)	

Multivariate logistic regression results showed that several factors were significantly associated with medication adherence. Patients who were reminded by healthcare professionals were more likely to have an adherence level higher than the remaining group. Patients who had regular monthly diabetes check-ups were 15.6 times more likely to have good medication adherence. Patients who achieved HbA1c treatment goals were 2.5 times more likely to have better adherence than those who had an uncontrolled target value.

4. DISCUSSION

4.1. Characteristics of the Study Subjects

Among the 394 patients participating in the study, the majority were 40 years old and above. This was consistent with the characteristics of type 2 diabetes patients, whose age of onset was usually over 40 years old [16]. Patients over 60 years of age accounted for the highest proportion (71.6%), similar to the studies by Nguyen Thieu Anh at Thieu Hoa General Hospital in 2019 (52.5%) [17]. The proportion of diabetes in men and women differed (40.4% and 59.6%, respectively). This rate was different from the studies of Tran Thi Thuy Nhi at the same Hue University of Medicine and Pharmacy Hospital in 2019, where men were 31.3% and women were 68 .7% [18], both of which had a higher rate of women than men. This difference may be due to the complicated Covid-19 epidemic situation in 2020 - 2021, besides, it may be due to different inclusion and exclusion criteria of the sample. The percentage of patients staying at home (housewives and retired) was the highest at 61.2%, a figure that

was completely reasonable because of the average age of diabetic patients in the study.

In the study, the mean duration of type 2 diabetes mellitus was 8.4 ± 6.1 years, and the proportion of diabetic patients with at least one comorbidity was 94.2%. Diabetes mellitus is associated with chronic complications that affect almost every part of the body. In addition, it is associated with a significantly increased rate of several debilitating microvascular complications such as nephropathy, retinopathy, and neuropathy, and macrovascular complications such as atherosclerosis and stroke [19]. At the time of the study, the FPG concentration of the study subjects was quite high, with an average of 8.8 ± 3.5 mmol/L, and only 48.2% of the patients achieved the FPG target. The average HbA1c was 8 ± 1.8% with 54.1% of the patients achieving the HbA1c target. Besides FPG, glycated hemoglobin (HbA1c), initially discovered by Rahbar et al. in 1969, has also been recommended as a diagnostic and treatment monitoring tool for diabetes [20]. Previous studies have demonstrated that HbA1c is less variable among individuals and better predicts both microvascular and macrovascular complications [21, 22].

The research recorded groups of oral diabetic medicines and insulin were used in the treatment with ingredients: biguanide (metformin), sulfonylurea (gliclazide, glimepiride), DPP-4 inhibitor (saxagliptin, sitagliptin, linagliptin, vidagliptin), SGLT-2 inhibitor (dapagliflozin) and insulin (short-acting, long-acting, mixed). All of these are recommended by ADA 2023 and the Ministry of Health in 2020, to increase the effectiveness of type 2 diabetes treatment, reduce unwanted effects and treatment costs [10, 23]. In this study, monotherapy regimens accounted for 23.6%, of which metformin accounted for the majority and more than half of the patients used combination regimens. Each antidiabetic medicine has different benefits on cardiovascular risk factors and adverse drug reactions. Achieving the level of glycemic control is the most important goal to prevent cardiovascular complications in patients with type 2 diabetes [24].

4.2. Medication Adherence and Associated Factors

In the study, the mean score of the MARS-10 scale was 8.1 ± 1.8. A detailed discuss at the responses indicates varied patient perspectives on their treatment. While a majority of patients demonstrated positive behaviors towards taking their medication, with over 64.5% achieving the maximum score in this domain.. Only 20.3% of patients achieved the maximum score (4 points) in assessing patient beliefs and attitudes about medication. Notably, a significant portion, 73.1%, agreed with the statement, "It is unnatural for my mind and body to be controlled by medicine," highlighting a potential internal conflict despite high overall adherence. Furthermore, there were 12.2% of patients with unusual symptoms when using treatment drugs, indicating that side effects, though not predominant, are a tangible concern for a subset of the patient population.

The results showed that the rate of medication adherence was 81.7% and non-adherence was 18.3%. This result was similar to that reported in the Wells Joshua study in 2021 in South London, which reported an adherence rate of 83.8% [25] and was not significantly different from the study by Abdulaziz Aflakseir in an outpatient clinic in Shiraz, Iran in 2011 which was 87% [26]. However, our study had a higher adherence rate than the study by Rakhi Mishra in 2020 in a University Hospital in Uttarakhand, India where 155 (56%) patients had poor adherence and 122 (44%) had good adherence [27].

The study used the chi-square test to evaluate the independence of factors affecting medication adherence of patients with type 2 diabetes in the study. Among them, the factors were: treatment regimen ($p = 0.044$), monthly diabetes check-ups ($p < 0.001$), reminders from healthcare staff ($p = 0.002$), FPG goals ($p = 0.044$), and HbA1c target ($p < 0.001$), which were statistically significantly associated with the level of patient adherence. Then, multivariate logistic regression analysis was conducted, and the variables HbA1c target, reminders from healthcare staff, and monthly diabetes check-ups were statistically significantly related to medication adherence ($p < 0.05$).

The group of patients who were reminded by health staff had a higher rate of adherence than the remaining group. Specifically, those who received occasional reminders were 2.4 times more likely to be adherent than those who received no reminders (OR = 2.4, $p = 0.028$). This underscores the crucial role of provider-patient communication.Antoinette M. Schoenthaler et al. (2012) pointed out that the quality of treatment instructions and reminders to patients were factors affecting treatment adherence and effectiveness [30]. Luis-Emilio García-Pérez et al. also recommend that there was a dramatic relationship among the level of compliance with the interaction between health workers and diabetic patients. In which, the doctor having a good relationship with the patient and frequent reminders were related to increased adherence and treatment

effectiveness [3]. The most striking finding was the impact of regular follow-up. Patients who attended monthly diabetes check-ups were 15.6 times more likely to have good medication adherence compared to those who did not (OR = 15.6, p = 0.015). This is consistent with the findings of Myriam Jaam and colleagues, who also reported a positive correlation between regular medical appointments and medication adherence [31].

Furthermore, achieving clinical targets was significantly associated with adherence. Patients who achieved their HbA1c treatment goals were 2.5 times more likely to have better adherence than those with uncontrolled HbA1c levels (calculated as 1/0.4, from OR = 0.4, 95% CI [0.2 - 0.8], p = 0.016). This suggests a potential positive feedback loop, where patients who see tangible results from their treatment are more motivated to continue adhering to their medication regimen. While the FPG target was significant in the initial chi-square test, its significance was not maintained in the multivariate analysis (p = 0.664), indicating that the HbA1c target is a more robust predictor of long-term

5. CONCLUSION

The findings of our study indicate that counselling for patients on self-management of medication adherence and reminding patients to have regular monthly diabetes check-ups affect treatment effectiveness directly. Health care professionals should take appropriate measures to enhance medication adherence and treatment belief for outpatients.

LIMITATION

The MARS-10 scale is not a scale specifically for diabetic patients, and it seems to limit studies in Vietnam that use MARS-10 to measure medication adherence in type 2 diabetic patients. Our study only evaluated the association between medication adherence and FPG control or HbA1c target without other criteria such as blood lipid index and blood pressure.

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