

Analysis of adherence and factors affecting insulin therapy outcomes in outpatients with Diabetes Mellitus

Surya Dwiyatna¹, Budi Suprapti^{2,3}, Wenny Putri Nilamsari², Cahyo Wibisono Nugroho^{4,5}, Shafira Muti Ardiana¹

1 Master of Clinical Pharmacy Program Department of Pharmacy Practice, Universitas Airlangga, Surabaya, Indonesia

2 Department of Pharmacy Practice, Faculty of Pharmacy, Universitas Airlangga, Campus C UNAIR, Mulyorejo, Surabaya 60115, Indonesia

3 Department of Pharmacy, Teaching Hospital of Universitas Airlangga, Mulyorejo, Surabaya, 60115, Indonesia

4 Department of Internal Medicine, Teaching Hospital of Universitas Airlangga, Campus C UNAIR, Mulyorejo, Surabaya 60115, Indonesia

5 Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Corresponding author: Budi Suprapti (budi-s@ff.unair.ac.id)

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Abstract

Background: Insulin is an effective diabetes treatment for outpatients with Diabetes Mellitus (DM) to maximize medication therapy. However, the level of insulin adherence is still low. This study aims to analyze adherence, glycemic control, and factors that influence the achievement of insulin therapy in Type 2 Diabetes Mellitus (T2DM) outpatients.

Methods: This study was a cross-sectional study conducted on T2DM outpatients. Adherence to Refills and Medications Scale (ARMS) and Diabetes Knowledge Questionnaire (DKQ) were used to assess patients' adherence and knowledge of insulin use. Multiple logistic regression tests were carried out to measure the effect of factors on adherence and insulin therapy outcomes.

Results: Of the 141 patients adherence to insulin treatment was found to be 33.3%. Patients who achieved glycemic control assessed by Glycosylated Haemoglobin (HbA1c), Fasting Blood Glucose (FBG), and Two hours of Postprandial Blood Glucose (2hPPBG) were 36.2%, 39%, and 43.3%. The duration of insulin use had a significant effect on adherence (p-value 0.013) and 2hPPBG target (p-value 0,049), while other factors had no significance.

Conclusion: Adherence to insulin therapy and glycemic control targets were found to be low. The duration of insulin use was associated with medication adherence and insulin therapy outcomes.

Keywords

Adherence, insulin, therapeutic outcomes, type 2 DM

Introduction

Diabetes Mellitus is included in the group of non-communicable diseases (NCDs) that are of concern to the global community and is one of the top ten causes of death in the world. According to the International Diabetes Federation (IDF), there is an increase in the prevalence of people with diabetes mellitus globally, reaching 10.8% (537 million people) in 2021 and it is estimated that this number will increase to 700 million people in 2045 (IDF 2021, 2022). Indonesia ranked 5th in the world in 2021 with the number of DM patients reaching 19.5 million (IDF 2021). A common problem in type 2 DM is failure to adhere to treatment. This causes diabetes to be ranked second in terms of low adherence to treatment out of 17 chronic diseases, and the second leading cause of hospitalization (Singh and Snekalatha 2022).

In evaluating the achievement of glycemic control targets in patients with type 2 DM, a study by Suprapti et al. reported that in 240 outpatient DM patients, only 20.8% of patients achieved glycemic control targets, 75.1% did not achieve therapeutic targets, and 4.1% experienced side effects of hypoglycemia (Suprapti et al. 2017). In line with this study, a study by Nasruddin et al., also reported that out of 249 patients with type 2 DM, only 4.4% of patients managed to achieve glycemic control (Nasruddin et al. 2021). These studies show that the number of patients who have not succeeded in achieving glycemic control targets is still quite high.

The impact of medication non-adherence in type 2 DM patients can lead to various DM complications, morbidity, mortality, and increased health costs. Based on 2016 national health insurance (JKN) data, 576 million US dollars were spent on direct medical costs, with 56% of this spent on hospitalization costs (Hidayat et al. 2022). The costs incurred per year for individuals with complications are two times higher than for individuals without complications; at least one chronic complication is diagnosed in 52% of DM patients, and 13.6% of deaths are due to uncontrolled DM (Liu et al. 2018). Therefore, the main goal of DM therapy is to perform tight glycemic control in patients to prevent or delay the development of long-term microvascular and macrovascular complications (Navarro-pérez et al. 2018; Dipiro et al. 2020).

Insulin is an effective diabetes treatment, both to overcome acute hyperglycemia conditions and to maximize treatment therapy. However, the level of adherence to insulin use, especially in Indonesia, is still low (Maifitrianti et al. 2020; July et al. 2022). Patient-related barriers have been reported to account for about 30% of the factors contributing to the failure to achieve insulin therapy (Nasruddin et al. 2021). One of them is medication adherence which is still not optimal and is a serious problem, especially in developing country populations. It causes as much as 45% of patients with type 2 DM to fail to achieve targeted glycemic control (Polonsky and Henry 2016; Singh and Snekalatha 2022).

Medication non-adherence is a complex health problem. The World Health Organization (WHO) defined

adherence as the degree to which the person's behavior corresponds with the agreed recommendations from a health care source. Medication non-adherence has multifactorial causes that need to be understood before interventions can be planned to improve medication adherence. According to WHO, there are several factors that can affect medication non-adherence and WHO classifies them into five categories: socioeconomic, health care system, health condition-related, therapy-related, and patient-related (Lam and Fresco 2015). Other references stated that medication adherence and glycemic control outcomes are influenced by several factors, including patient factors, environmental factors, clinical factors, and health system factors (Cheng et al. 2019; Wibowo et al. 2022). The medication adherence itself will also affect the outcome of glycemic control. Low adherence to treatment will make glycemic control difficult to achieve (Horii et al. 2019). This study aims to analyze the influence of patient factors (socio-demographic characteristics and patient knowledge) and clinical factors (duration of illness, comorbidities, regimen complexity, polypharmacy, and side effects) on adherence and treatment outcomes.

Materials and methods

This study was a cross-sectional study conducted at a hospital in Surabaya from May to July 2023. The selection of research samples was carried out using a purposive sampling method. Data collection of research samples was enabled through direct interviews with patients and searches of patients' medical records. The inclusion criteria in this study were type 2 DM outpatients with an age range ≥ 18 years, with or without comorbidities, who had received any type of insulin therapy, either basal, bolus, or premixed insulin for ≥ 2 months before the study was conducted, either in a single form or in combination with other drugs, have HbA1c, FBG, and 2hPPBG data, and who were willing to participate in the study by signing informed consent. The exclusion criteria were type 2 DM outpatients with stage 5 chronic renal failure complications and type 2 DM outpatients with cognitive impairment or other conditions that did not allow them to be interviewed and fill out the questionnaire.

This study collected data on the sociodemographic and clinical characteristics of patients obtained from direct patient interviews and patient medical records. Treatment adherence was assessed using the ARMS questionnaire (The Adherence to Refill and Medication Scale) and patient knowledge about diabetes was assessed using the DKQ (Diabetes Knowledge Questionnaire) questionnaire which has been validated from previous studies (Kripalani et al. 2009; Larasati et al. 2019; July et al. 2022; Zairina et al. 2022). The ARMS questionnaire has 2 indicators divided into 12 items and is calculated using a 4-way Likert type scale. The total score of the ARMS questionnaire is 12 with the categories of adherence ($=12$), and non-adherence (>12). DKQ is a scale measuring the level of patient knowledge containing 24 questions. The answer

options are correct, incorrect and don't know. Assessment was done based on the number of correct items answered by the subject with the correct answer given a value of one while the wrong answer or not knowing was given a value of zero. The level of knowledge was categorized as high if the score was 17–24, medium 10–16, and low 0 – 9 (Alexandra Gracia et al. 2001; Larasati et al. 2019). The achievement of insulin therapy is measured by the values of HbA1c, FBG, and 2hPPBG, with the criteria of HbA1c < 7%, FBG 80–130 mg/dl, and 2hPPBG < 180 mg/dl (Soelistijo 2021).

The independent variables in this study consisted of age (years), gender (male or female), BMI (underweight < 18.5 kg/m², normal weight 18.5–25 kg/m² or overweight > 25 kg/m²), occupation status (working or not working), education level (primary, secondary, tertiary), level of knowledge (low, medium, high), duration of DM (less or more than five years), comorbidities (present or not), suspected adverse drug events (ever or not), polypharmacy (less or more than five drugs), regimen complexity (less or more than 23), type of insulin (single or combination with OAD), duration of insulin use (less or more than five years), and adherence. The dependent variables were adherence and insulin therapy outcomes.

Statistical analysis used the SPSS version 24 statistical program for Windows. Descriptive statistics were used to describe patient characteristics, medication adherence, and prevalence of insulin therapy outcomes. Responses to categorical variables were displayed using frequency counts, means and percentages. Multivariate analysis of multiple logistic regression was analyzed simultaneously to see the effect of sociodemographic factors, knowledge, and clinical characteristics of patients on adherence and insulin therapy outcomes. Multivariate analysis of this study presents the odds ratio (OR), regression coefficient, 95% confidence interval (CI), and p value, where $p < 0.05$ represents the significance level of the tested data.

This study has received approval from the ethics committee of Universitas Airlangga Teaching Hospital Surabaya and was declared ethically sound based on the certificate of passing ethical review number 063/KEP/2023.

Results

In this study, out of 141 patients who met the inclusion criteria, the average age of respondents was 55 years old with most respondents being female, overweight, in secondary education, and unemployed, dominated by housewives. Respondents on average had suffered from DM for ≤ 5 years, had comorbidities, used polypharmacy drugs, obtained high regimen complexity, used single insulin, and reported having experienced suspected adverse drug events (Table 1).

Table 2 shows that out of 141 patients, patients who did not adhere to treatment had a higher percentage, characterized by an ARMS score of more than 12, compared to patients who adhered to treatment.

Table 1. Patient characteristics.

Patient Characteristics	Amount (n)	Percentage (%)
Genders		
Male	47	34
Female	94	66
Ages		
≥ 18–30 years old	2	1,4
31–40 years old	8	5,7
41–50 years old	25	17,7
51–60 years old	69	48,9
> 60 years old	37	26,2
Body Mass Index (BMI)		
Normal weight	59	41,8
Overweight	78	55,3
Underweight	4	2,8
Level of education		
Primary	36	25,5
Secondary	79	56,1
Tertiary	26	18,4
Occupation status		
Working	54	38,3
Not Working	87	61,7
Level of knowledge		
High (17–24)	29	20,6
Moderate (10–16)	95	67,4
Low (1–9)	17	12,0
Duration of DM		
≤ 5 years	75	53,2
>5 years	66	46,8
Comorbidities		
Present	115	81,6
None	26	18,4
Suspected adverse drug events (ADE)		
Ever	40	28,4
Never	101	71,6
Polypharmacy		
< 5 drugs	69	48,9
≥ 5 drugs	72	51,1
Regimen Complexity		
High complexity (≥ 23)	72	51,1
Low complexity (< 23)	69	48,9
Duration of insulin use		
≤ 5 years	119	84,4
> 5 years	22	15,6
Types of comorbidities		
Hypertension	93	66
Hyperlipidemia	69	49
Gout	34	24,1
Dyspepsia	5	3,5
Asthma	1	0,7
Types of suspected adverse drug events		
Hypoglycemia	18	12,8
Gastrointestinal disorders	11	7,8
Urticaria	7	5
Cephalgia	2	1,4
Weight gain	2	1,4
Type of insulin regimens		
Single insulin	94	66,7
Combination with Oral Antidiabetic (OAD)	47	33,3

Table 2. Assessment results of adherence to insulin use in patients with Type 2 DM based on the ARMS questionnaire (n = 141).

Adherence Assessment	Number of Patients (n)	Percentage (%)
Adherence Categories		
Adhere (= 12)	47	33,3
Not adhere (> 12)	94	66,7

Table 3 shows that the number of patients who have successfully achieved the target of insulin therapy is still smaller than the patients who have not succeeded in achieving the target. The results of the blood glucose test of patients in this study revealed that the average HbA1c value was 8.0%, the average FBG was 172.4 mg/dl and the average 2hPPBG was 219.6 mg/dl.

Table 3. Insulin therapy outcomes.

Categories of Insulin Therapy Outcomes	Number of Patients (n)	Percentage (%)
HbA1c		
Target achieved (< 7%)	51	36,2
Target not achieved (\geq 7%)	90	63,8
Fasting blood glucose (FBG)		
Target achieved (80–130 mg/dl)	55	39,0
Target not achieved (> 130 mg/dl)	86	61,0
Two hours of postprandial blood glucose (2hPPBG)		
Target achieved (\leq 140 mg/dl)	61	43,3
Target not achieved (> 140 mg/dl)	81	56,7

Table 4 shows that in this study each group category on the analyzed independent variables showed a relatively similar pattern of adherence and achievement of insulin therapy, where almost all groups showed non-adherence and had not succeeded in achieving the target glycemic control.

Multivariate analysis (multiple logistic regression) in Table 5 showed that patient factors (gender, age, BMI, education level, and occupation), clinical factors (DM duration, comorbidities, drug side effects, polypharmacy, and regimen complexity), and type of insulin regimen did not have a significant influence on adherence and insulin therapy outcomes. Meanwhile, the duration of insulin use had a significant influence on adherence (p-value 0.013; odd ratio 0.160; CI 95% 0.038–0.675) and 2hPPBG insulin therapy outcomes (p-value 0.049; odd ratio 3.252; CI 95% 1.005–10.518) but did not have a significant influence on HbA1c and FBG insulin therapy outcomes.

Table 4. Descriptive analysis results.

Variable	Patients' Adherence		Insulin Therapy Outcomes					
			HbA1c ⁽³⁾		FBG ¹		2hPPBG ²	
	Adhere n (%)	Not adhere n (%)	Achieved n (%)	Not achieved n (%)	Achieved n (%)	Not achieved n (%)	Achieved n (%)	Not achieved n (%)
Ages								
\leq 30 years old	1 (50,0)	1 (50,0)	1 (50,0)	1 (50,0)	0 (0,0)	2 (100,0)	1 (50,0)	1 (50,0)
31–40 years old	4 (50,0)	4 (50,0)	3 (37,5)	5 (62,5)	3 (37,5)	5 (62,5)	3 (37,5)	5 (62,5)
41–50 years old	8 (32,0)	17 (68,0)	8 (32,0)	17 (68,0)	8 (32,0)	17 (68,0)	12 (48,0)	13 (52,0)
51–60 years old	23 (33,3)	46 (66,7)	28 (40,6)	41 (59,4)	28 (40,6)	41 (59,4)	28 (40,6)	41 (59,4)
> 60 years	11 (29,7)	26 (70,3)	11 (29,7)	26 (70,3)	16 (43,2)	21 (56,8)	17 (45,9)	20 (54,1)
Genders								
Male	16 (34,0)	31 (66,0)	21 (44,7)	26 (55,3)	22 (46,8)	25 (53,2)	22 (46,8)	25 (53,2)
Female	31 (33,0)	63 (67,0)	30 (31,9)	64 (68,1)	33 (35,1)	61 (64,9)	39 (41,5)	55 (58,5)
BMI								
Normal weight	20 (33,9)	39 (66,1)	18 (30,5)	41 (69,5)	18 (30,5)	41 (69,5)	22 (37,3)	37 (62,7)
Underweight	1 (25,0)	3 (75,0)	1 (25,0)	3 (75,0)	1 (25,0)	3 (75,0)	2 (50,0)	2 (50,0)
Overweight	26 (33,3)	52 (66,7)	32 (41,0)	46 (59,0)	36 (46,2)	42 (53,8)	37 (47,4)	41 (52,6)
Level of Education								
Primary	11 (30,6)	25 (69,4)	12 (33,3)	24 (66,7)	17 (47,2)	19 (52,8)	19 (52,8)	17 (47,2)
Secondary	27 (34,2)	52 (65,8)	30 (38,0)	49 (62,0)	28 (35,4)	51 (64,6)	34 (43,0)	45 (57,0)
Tertiary	9 (34,6)	17 (65,4)	9 (34,6)	17 (65,4)	10 (38,5)	16 (61,5)	8 (30,8)	18 (69,2)
Occupation Status								
Working	19 (35,2)	35 (64,8)	18 (33,3)	36 (66,7)	28 (33,3)	36 (66,7)	21 (38,9)	33 (61,1)
Not Working	28 (32,2)	59 (67,8)	33 (37,9)	54 (62,1)	37 (42,5)	50 (57,5)	40 (46,0)	47 (54,0)
Level of knowledge								
High	10 (34,5)	19 (65,5)	10 (34,5)	19 (65,5)	11 (37,9)	18 (62,1)	12 (41,4)	17 (58,6)
Moderate	33 (34,7)	62 (65,3)	31 (32,6)	64 (67,4)	35 (36,8)	60 (63,2)	41 (43,2)	54 (56,8)
Low	4 (23,5)	13 (76,5)	10 (58,8)	7 (41,2)	9 (52,9)	8 (47,1)	8 (47,1)	9 (52,9)
Duration of DM								
\leq 5 years	24 (32,0)	51 (68,0)	30 (40,0)	45 (60,0)	31 (41,3)	44 (58,7)	33 (44,0)	42 (56,0)
> 5 years	23 (34,8)	43 (65,2)	21 (31,8)	45 (68,2)	24 (36,4)	42 (63,6)	28 (42,4)	38 (57,6)
Comorbidities								
Present	38 (33,0)	77 (67,0)	39 (33,9)	76 (66,1)	47 (40,9)	68 (59,1)	53 (46,1)	62 (53,9)
None	9 (34,6)	17 (65,4)	12 (46,2)	14 (53,8)	8 (30,8)	18 (69,2)	8 (30,8)	18 (69,2)
Duration of insulin use								
\leq 5 years	44 (37,0)	75 (63,0)	44 (37,0)	75 (63,0)	45 (37,8)	74 (62,2)	48 (40,3)	71 (59,7)
> 5 years	3 (13,6)	19 (86,4)	7 (31,8)	15 (68,2)	10 (45,5)	12 (54,5)	13 (59,1)	9 (40,9)
Suspected adverse drug events								
Ever	11 (27,5)	29 (72,5)	14 (35,0)	26 (65,0)	16 (40,0)	24 (60,0)	18 (45,0)	22 (55,0)

Variable	Patients' Adherence		Insulin Therapy Outcomes					
			HbA1c ⁽³⁾		FBG ¹		2hPPBG ²	
	Adhere n (%)	Not adhere n (%)	Achieved n (%)	Not achieved n (%)	Achieved n (%)	Not achieved n (%)	Achieved n (%)	Not achieved n (%)
Never	36 (35,6)	65 (64,4)	37 (36,6)	64 (63,4)	39 (38,6)	62 (61,4)	43 (42,6)	58 (57,4)
Polypharmacy								
< 5 drugs	24 (34,8)	45 (65,2)	29 (42,0)	40 (58,0)	26 (37,7)	43 (62,3)	31 (44,9)	38 (55,1)
≥ 5 drugs	23 (31,9)	49 (68,1)	22 (30,6)	50 (69,4)	29 (40,3)	43 (59,7)	30 (41,7)	42 (58,3)
Regiment complexity								
High complexity	24 (33,3)	48 (66,7)	20 (27,8)	52 (72,2)	28 (38,9)	44 (61,1)	29 (40,3)	43 (59,7)
Low complexity	23 (33,3)	46 (66,7)	31 (44,9)	38 (55,1)	27 (39,1)	42 (60,9)	32 (46,4)	37 (53,6)
Types of insulin regiments								
Single insulin	30 (31,9)	64 (68,1)	35 (37,2)	59 (62,8)	35 (37,2)	59 (62,8)	42 (44,7)	52 (55,3)
Combination with OAD	17 (36,2)	30 (63,8)	16 (34,0)	31 (66,0)	20 (42,6)	27 (57,4)	19 (40,4)	28 (59,6)
Adherence								
Adhere			19 (40,4)	28 (59,6)	19 (40,4)	28 (59,6)	22 (46,8)	25 (53,2)
Not adhere			32 (34,0)	62 (66,0)	36(38,3)	58 (61,7)	39 (41,5)	55 (58,5)

1FBG: Fasting Blood Glucose ; 22hPPBG : Two hours of Postprandial Blood Glucose; 3HbA1c : Glycosylated Haemoglobin.

Table 5. Multivariate analysis of factors influencing insulin use adherence and achievement of insulin therapy in type 2 DM outpatients.

Variable	Adherence Of Patients			Insulin Therapy Outcomes								
	p-value	Odd ratio	CI 95%	HbA1c			FBG			2hPPBG		
				p-value	Odd ratio	CI 95%	p-value	Odd ratio	CI 95%	p-value	Odd ratio	CI 95%
Ages	0.924			0.313			0.955			0.856		
≤ 30 years old		1			1			1			1	
31–40 years old		0.381	0.012–11.701		2.799	0.091–86.315		>1000	0.000		0.462	0.015–14.00
41–50 years old		0.255	0.011–6.067		2.475	0.105–58.590		>1000	0.000		0.806	0.035–18.588
51–60 years old		0.272	0.012–6.396		4.602	0.192–110.3		>1000	0.000		0.463	0.020–10.710
> 60 years		0.262	0.011–6.304		1.617	0.067–39.284		>1000	0.000		0.450	0.019–10.655
Genders	0.700			0,055			0.136			0.358		
Male		1			1			1			1	
Female		0.835	0.334–2.087		0.396	0.153–1.022		0.510	0.211–1.236		0.664	0.277–1.591
BMI	0.933			0.430			0.244			0.612		
Normal weight		1			1			1			1	
Underweight		0.742	0.062–8.912		0.842	0.067–10.563		0.904	0.080–10.183		1.423	0.167–12.092
Overweight		1.107	0.494–2.481		1.685	0.746–3.806		1.930	0.879–4.234		1.467	0.681–3.162
Level of Education	0.676			0.523			0.625			0.311		
Primary		1			1			1			1	
Secondary		1.323	0.510–3.432		1.794	0.643–5009		0.637	0.255–1.593		0.579	0.237–1.417
Tertiary		0.824	0.232–2.934		1.306	0.334–5.098		0.792	0.225–2.790		0.401	0.111–1.445
Occupation Status	0.375			0.387			0.114			0.214		
Working		1			0.669	0.270–1.662		0.503	0.214–1.179		0.590	0.256–1.356
Not Working		1.471	0.628–3.446		1			1			1	
Level of knowledge	0.621			0.084			0.610			0.858		
High		2.202	0.450–10.766		0.279	0.062–1.258		0.680	0.152–3.031		0.845	0.198–3.612
Moderate		1.638	0.437–6.147		0.248	0.072–0.851		0.558	0.171–1.820		1.133	0.351–3.659
Low		1			1			1			1	
Duration of DM	0.130			0.427			0.329			0.504		
≤ 5 years		1			1			1			1	
> 5 years		1.900	0.827–4.366		0.695	0.283–1.705		0.652	0.276–1.538		0.749	0.321–1.748
Comorbidities	0.823			0.270		0.646–4.767	0.688			0.257		
Present		1			1			1			1	
None		0.889	0.318–2.484		1.754	0.646–4.767		0.814	0.298–2.223		0.557	0.202–1.532
Duration of insulin use	0.013			0.834			0.367			0.049		
≤ 5 years		1			1			1			1	
> 5 years		0.160	0.038–0.675		1.145	0.324–4.050		1.711	0.533–5.496		3.252	1.005–10.518
Suspected adverse drug events	0.283			0.605			0.262			0.463		
Ever		1			1			1			1	
Never		1.641	0.664–4.056		0.790	0.324–1.929		0.613	0.260–1.443		0.732	0.318–1.685

Variable	Adherence Of Patients			Insulin Therapy Outcomes								
	p-value	Odd ratio	CI 95%	HbA1c			FBG			2hPPBG		
				p-value	Odd ratio	CI 95%	p-value	Odd ratio	CI 95%	p-value	Odd ratio	CI 95%
Polypharmacy	0.292			0.999			0.768			0.737		
< 5 drugs		1			1			1			1	0.112–22.113
≥ 5 drugs		0.233	0.016–3.496		>1000	0.000		1.488	0.106–20.901		1.572	
Regiment complexity	0.282			0.999			0.650			0.499		
High complexity		4.241	0.304–59.071		<0.001			0.551	0.042–7.219		0.411	0.031–5.410
Low complexity		1			1	0		1			1	
Types of insulin regimens	0.316			0.827			0.755			0.748		
Single insulin		1			1			1			1	
Combination with OAD		1.569	0.650–3.786		0.905	0.370–2.216		1.144	0.491–2.664		0.872	0.378–2.012
Adherence				0.458			0.807			0.548		
Adhere					1.315	0.639–2.707		1.093	0.534–2.237		1.241	0.613–2.511
Not adhere					1			1			1	

¹FBG: Fasting Blood Glucose; ²hPPBG : Two hours of Postprandial Blood Glucose; ³HbA1c : Glycosylated Haemoglobin.

Discussions

This study reported that most patients were female, over 50 years old, overweight, with secondary education background, were unemployed (housewives), had a moderate level of knowledge, tend to not adhere, and had not succeeded in achieving glycemic targets (Table 1). Several previous studies have reported that women with type 2 DM tend to have low adherence and poorer glycemic control than men due to differences in glucose homeostasis, treatment response, psychological factors, obesity, and lack of physical activity that lead to uncontrolled triglyceride and total cholesterol lipid levels that can aggravate diabetes conditions in women (Pathak and Pathak 2012; Duarte et al. 2019; Xie et al. 2020; Kautzky-willer et al. 2023). In addition, low adherence and poor glycemic control also tend to occur in housewives. This may occur because housewives do not have adequate time to undergo treatment and change their lifestyle (Alcalde-Rabanal et al. 2018).

DM patients of older age, especially geriatrics, tend to have low adherence because geriatrics are prone to experiencing Frailty Syndrome, which is characterized by decreased physical abilities such as decreased walking speed and visual function, as well as decreased cognitive abilities, which prevent patients from undergoing treatment properly. In addition, glycemic control in geriatric patients tends to be poor due to the combined effects of increased insulin resistance and impaired pancreatic function with increasing age (Kirkman et al. 2012; Bonikowska et al. 2022).

A study by Boye et al. reported patients with type 2 DM who were overweight (obese) were twice as likely to have low medication adherence compared to individuals without obesity. Obesity is often associated with a poor lifestyle. The study also reported that 67.1% of patients who were obese were likely to have HbA1c values ≥ 7 or $\geq 8\%$. Hyperinsulinemia and insulin resistance are closely associated with obesity (Wagai and Romshoo 2020; Boye et al. 2021, 2022).

The relationship between low education level and low treatment adherence in patients with type 2 diabetes was reported in the study of Kassahun et al. Patients with low education levels tend to have negative attitudes towards diabetes and poor self-care behaviors. Patients with low education also tend to have poor glycemic control compared to patients with higher education levels (Kassahun et al. 2016). Non-adherence to treatment can also occur in patients who have a good level of knowledge because of forgetfulness and polypharmacy (Haskani et al. 2022).

This study also reported that most of the patients with DM duration of less than five years, a history of comorbidities, polypharmacy (more than five drugs), and high regimen complexity tended to be non-adherent and have poor glycemic control. Patients diagnosed with DM for less than five years are usually still in denial, lack acceptance, and refuse to change their behavior and lifestyle (Cheng et al. 2019). In addition, non-adherence medication in patients with type 2 DM will increase threefold in the presence of comorbidities. Comorbidities contribute to increasing the number of medications, thereby increasing regimen complexity. High regimen complexity is associated with poor glycemic control (Ab Rahman et al. 2022; Sahoo et al. 2022).

Polypharmacy and high regimen complexity also contribute to low adherence and poor glycemic control in DM patients. The high rate of polypharmacy among the diabetic population is due to the coexistence of chronic conditions. One of the studies found 86% of DM patients had at least one chronic condition (Lee et al. 2017; Alwhaibi et al. 2018; Maifitrianti et al. 2020). In addition, DM patients with high levels of regimen complexity were found to be six times non-compliant and more likely to have HbA1c values above 7.0%. High regimen complexity is associated with the presence of comorbidities that contribute to increase the number of medications (Ayele et al. 2019; Ab Rahman et al. 2022).

Patients who have experienced adverse drug events (ADEs) tend to be non-adherent to treatment. However, in this study, the suspected ADEs experienced by patients tended to be low. It proves that the use of insulin in patients is relatively safe and causes harmful side effects rarely. Most of the patients in this study were given single insulin to reduce the risk of hypoglycemia and other side effects due to the combination of insulin with OADs. Patients will be susceptible to Hypoglycemia if they delay eating or eat small amounts (Vos et al. 2016).

The prevalence of adherence to insulin treatment in this study was found to be low. This is in line with research in several countries such as Malaysia, France, Iran, and Brazil with compliance rates of 8.43%, 39%, 28.8%, and 27.8% respectively (Nasruddin et al. 2021). In Indonesia itself, a previous study also reported a low level of adherence to insulin use, which was only 7.4% (Agrimon 2014; July et al. 2022). Based on the results of the ARMS questionnaire, the most common cause of non-adherence is the forgetfulness factor. This factor is included in the category of unintentional non-adherence. The ways to overcome unintentional non-adherence include optimizing family support, using compensatory strategies such as using alarm clocks, medicine boxes, reducing regimen complexity and location of taking medication, and using technology-based strategies such as reminder messages and electronic pill boxes (Delamater 2006; Pratiwi et al. 2023).

The insulin therapy outcomes of patients in this study were still very low. However, in this study, there was no effect of patient adherence on the achievement of insulin therapy targets. This is in line with the study of Feldman et al. who reported that poor glycemic control is not mediated by low adherence, but rather caused by other factors such as age and disease duration (Feldman et al. 2014; Wambui et al. 2016). Different results were found in the Sendekie et al. study which reported that patients who had high treatment adherence tended to have good glycemic control (Sendekie et al. 2022). The factors that influence the achievement of glycemic control in DM patients besides patient factors, clinical factors, and treatment adherence are lifestyle factors (diet, physical activity, smoking habits), psychological conditions (depression, anxiety, and stress), and the presence of complications (chronic diseases) suffered by patients (Alduwayhis et al. 2022; Suprapti et al. 2023).

Based on multivariate analysis in this study, one of the predictors which has a significant influence on insulin adherence was the duration of insulin use. Patients with more than 5 years of insulin use had lower adherence than patients with less than 5 years of insulin use (p-value 0.013; odd ratio 0.160; CI 95% 0.038–0.675). However, patients with more than 5 years of insulin use tended to be more successful in achieving 2hPPBG targets than patients with less than 5 years of insulin use (p-value 0.049; odd ratio 3.252; CI 95% 1.005–10.518), but this did not affect HbA1c and FBG values. These results suggest that

therapeutic success is not only associated with adherence but also needs comprehensive approaches to improve insulin therapy adherence and outcomes as described above. In previous studies, patients with more than five years of insulin use were found to be less adherent. The experience of side effects, complications, polypharmacy, regimen complexity, physical limitations, fear of hypoglycemia, and psychological factors such as depression, anxiety, and decreased cognitive abilities will affect patient compliance (Farsaei et al. 2014; Kalra et al. 2018)

Patients with chronic diseases such as diabetes often become non-adherent when they do not have unpleasant symptoms. A study by Jimmy and Jose reported that 77% of patients showed a high level of adherence to their treatment regimen when the treatment was designed to cure the disease. However, when treatment has to be carried out over a long time, the adherence rate drops drastically to around 50% for both prevention and cure (Jimmy and Jose 2011; Feldman et al. 2014; Wambui et al. 2016; Sendekie et al. 2022).

Interviews of all patients in the study were conducted by the same researcher and blood glucose checks were conducted at the same time as the interview. This was done to ensure that the data collection process remained consistent, so that the adherence and blood glucose data obtained were the latest data from patients. In addition, this study can be the basis for designing interventions to improve patient adherence to insulin use, as well as optimizing the achievement of insulin therapy in patients with type 2 DM. The limitation of this study is that it has been conducted only in one spot of observation.

Adherence to insulin in this study is still low. Hence further research is recommended on improving medication adherence such as offering more education to patients and their families and using some support tools.

Conclusion

The level of insulin adherence and glycemic control targets in type 2 DM outpatients is not optimal. The factor that influences adherence and achievement of insulin therapy in this study is the duration of insulin use. A comprehensive approach is needed to improve therapeutic outcomes including education related to understanding disease, drugs, diet, distress management, and increasing the role of family in DM management.

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