

NORA WULANDARI -  
MEDICATION ADHERENCE  
ASSESSMENT  
AMONG PATIENTS WITH TYPE  
2 DIABETES MELLITUS  
TREATED POLYTHERAPY IN  
INDONESIAN COMMUNITY  
HEALTH CENTER: A CROSS

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# Medication Adherence Assessment Among Patients with Type 2 Diabetes Mellitus Treated Polytherapy in Indonesian Community Health Center: A Cross Sectional-Study

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## ABSTRACT

**Background:** Type 2 diabetes mellitus (T2DM) is a chronic disease where most of the patients usually need polytherapy. This could affect their medication adherence (MA). However, other complex factors may also associate with MA, which are important to identify. **Aim:** The purpose of this study was to evaluate the MA of patients with T2DM who received polytherapy and to identify other factors that can affect the MA. **Materials and Methods:** This was a cross-sectional study conducted in seven community health centers in Jakarta with HbA<sub>1c</sub> representing their MA level. Poor controlled blood glucose with Hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) of  $\geq 7\%$  is indicated to have low MA. All characteristics were collected to identify factors that are potentially associated with low MA. The univariate analysis tests were used to analyze factors that potentially associate with low MA. Multiple logistic regression analysis was performed in the factors to find their relationship with low MA. **Results:** The study obtained 143 patients with a female dominance (67.8%) and mean  $\pm$  standard deviation (SD) age of  $59.53 \pm 9.251$  years. Approximately 75.5% of the patients had low MA (HbA<sub>1c</sub>  $\geq 7$ ). Univariate analysis found that duration of T2DM significantly ( $P = 0.047$ ) related to MA, where patients with T2DM of less than or equal to 5 years tended to have low MA. Logistic regression showed that patients with T2DM less than or equal to 5 years ( $P = 0.015$ , odds ratio = 1.206, 95% confidence interval = 1.216–8.014) were associated with low MA. **Conclusion:** Patients with the duration of T2DM less than or equal to 5 years surprisingly were susceptible to have low MA. Low MA was not affected by polytherapy.

**KEYWORDS:** Medication adherence, polytherapy, type 2 diabetes mellitus

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## INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder with a maximum number of patients. In 2017, the prevalence of diabetics worldwide was 425 million, and it is estimated that in 2045, people with diabetes will reach 693 million. People with diabetes in Indonesia ranks sixth in the world along with China, India, the United States, Brazil, and Mexico, with an estimated number of people with diabetes of 10 million, and it is expected to increase to 16.7 million people in 2045.

In high-income countries, approximately 7%–12% of all people with diabetes are estimated to have type 1 diabetes, 87%–91% are estimated to have type 2 diabetes, and 1%–3% are estimated to have other types of diabetes.<sup>[1]</sup> The prevalence of DM is based on a

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doctor's diagnosis in the population older than or equal to 15 years in Daerah Khusus Ibukota (DKI) special capital district Jakarta, occupying the highest position of all provinces in Indonesia.<sup>[2]</sup>

Poor glycemic control is a significant contributor to the high rates of morbidity and mortality of patient with type 2 diabetes mellitus (T2DM).<sup>[3]</sup> One of the key factors related to glycemic control in patient with T2DM is medication adherence (MA). Some studies reported that suboptimal glycemic control is found in patient with low MA.<sup>[4,5]</sup> Medication adherence (MA) is commonly used to define the level of compliance to which patients in following the medication prescribed by their health providers. Poor adherence with medication will cause long-term complications that increase morbidity and mortality and increase health costs.<sup>[6]</sup>

Poor MA is linked to nonpatient factors such as lack of integrated care in many health-care system and clinical inertia among health-care professionals, patient demographic factors, critical patients belief about their medications, and perceive patients burden regarding obtaining and taking their medications.<sup>[7]</sup> Some studies reported the complexity and convenience of therapy associated with MA. Reduced tolerance to medication, frequency of medication more than twice a day.<sup>[8]</sup>

Polypharmacy and/or polytherapy are prevalent in adults with diabetes, especially in individuals with chronic conditions. Polypharmacy and/or polytherapy are one of the factors that influence the adherence of the patients to their medications. Patients who take two drugs or less have a lower risk of lower MA than patients who take more than two drugs.<sup>[9]</sup> One study in 2017 showed that of the 382 patients with T2DM who received polypharmacy, 57.1% had low adherence.<sup>[10]</sup> Nevertheless, we hypothesized that other factors could affect MA and associate to the low MA in patients with T2DM in Indonesia.

Therefore, the primary purpose of this study was to evaluate the MA of patients with T2DM who received polytherapy. This study also aimed to identify factors that affect patient's MA, which is represented by glycemic control of the patients.

## MATERIALS AND METHODS

This was a cross-sectional study conducted in seven community health centers (CHC) in Jakarta, Indonesia, from February 2019 to July 2019. The ethical approval for this study was obtained from the ethics committee of

the Faculty of Medicine of the University of Indonesia with number: 588/UN2.F1/ETIK/PPM.00.02/2019.

The inclusion criteria of this study included patients with T2DM who were on at least two antidiabetics (ADs) and aged older than or equal to 18 years, of both genders, could speak and understand Indonesian, patients who were on all type of ADs, patients with T2DM with or without comorbidities, patients who were followed up at the site in at least two visits over a minimum period of 6 month. Meanwhile, patients with T2DM who were pregnant, patients who were on dietary control alone, or had intellectual or cognitive impairment as stated in their medical record were excluded from this study.

Data were collected concurrently where potential subjects were screened by the trained research assistants and health worker in the CHC for enrollment eligibility into this study. They were recruited on a monthly gathering of the Chronic Disease Management Program (PROLANIS) in each CHC. Patients who met the requirements were asked to be the study subject by signing a participation agreement or informed consent and given information in advance. A structured questionnaire to obtain factors, which potentially affected MA such as sociodemographic (age, gender, education, and occupation) and clinical characteristics (duration of T2DM, other chronic diseases, complication, number of ADs, and regular daily drug), was given to patients, and then blood was taken to measure HbA<sub>1c</sub> level by trained health workers who were responsible in each CHC.

The data collected were recapitulated and analyzed. A univariate analysis was carried out to measure the frequency of each characteristic. MA assessment was based on the results of HbA<sub>1c</sub> examination with a controlled blood glucose (HbA<sub>1c</sub>) level greater than or equal to 7%, indicated as low MA and vice versa.<sup>[11]</sup> The Kolmogorov–Smirnov test was performed to measure the normality of the data. A *P* value >0.05 was considered statistically significant, which means that the data were nonparametric. The univariate analysis with the Mann–Whitney *U* test was carried out on numerical data that were not normally distributed, whereas for categorical data that were not normally distributed, chi-square test and Fisher's exact test were used. The data that were significantly related in the univariate analysis were used to perform multivariate tests using multiple regression logistic tests, with the relationship reflected by odds ratios (ORs) (95% confidence intervals [CIs]). A *P* value of 0.05 was considered statistically significant.

Table 1: Characteristics of the patients

Characteristics	Total	Adherent (HbA <sub>1c</sub> < 7%)	Low MA (HbA <sub>1c</sub> ≥ 7%)	P value
Total	143 (100.0)	35 (24.5)	108 (75.5)	
Age (years)				
Less than 60 years	69 (48.3)	14 (20.3)	55 (79.7)	0.353*
60 years or more	74 (51.7)	21 (28.4)	53 (71.6)	
Mean ± SD = 59.53 ± 9.251				
Min-max = 37-85				
Gender				
Male	46 (32.2)	12 (26.1)	34 (73.9)	0.920*
Female	97 (67.8)	23 (23.7)	74 (76.3)	
Level of education				
Basic	34 (23.8)	7 (20.6)	27 (79.4)	0.434*
Moderate	96 (67.1)	23 (24.0)	73 (76.0)	
High	13 (9.1)	5 (38.5)	8 (61.5)	
Occupation				
Not working	112 (78.3)	26 (23.2)	86 (76.8)	0.505*
Working	31 (21.7)	9 (29.0)	22 (71.0)	
Duration of T2DM				
5 years or less	88 (61.5)	27 (30.7)	61 (69.3)	0.047*
More than 5 years	55 (38.5)	8 (14.5)	47 (85.5)	
Other chronic diseases				
None and one	109 (76.2)	28 (25.7)	81 (74.3)	0.644*
Two and above	34 (23.8)	7 (20.6)	27 (79.4)	
Any complication				
Yes	20 (14.0)	3 (15.0)	17 (85.0)	0.404***
No	123 (86.0)	32 (26.0)	91 (74.0)	
Number of AD				
Two	136 (95.1)	34 (25.0)	102 (75.0)	0.522**
Three	7 (4.9)	1 (14.3)	6 (85.7)	
Number of regular daily drugs				
Up to three	98 (68.5)	26 (26.5)	7 (73.5)	0.130**
Four and more	45 (31.5)	9 (20.0)	3 (80.0)	

\*Chi-square test, \*\*Mann-Whitney *U* test, \*\*\*Fisher's exact test

## RESULTS

A total of 143 patients with T2DM were enrolled in this study. The sociodemographic and clinical characteristics are presented in Table 1.

Sociodemographic characteristics showed mean ± standard deviation (SD) age of patients as 59.53 ± 9.251 years, with a slightly more dominance in elderly patients (≥60 years) (51.7%) and women (67.8%). Most of the patients were categorized into moderate education (67.8%) and who did not work (78.3%).

On the basis of its clinical characteristics, more than half (69.3%) of the patients had been diagnosed with T2DM for less than or equal to 5 years. Most of (76.2%) patients did not have nor had one other chronic disease such as hypertension, hyperlipidemia, hyperuricemia, angina pectoris,

and osteoporosis. As many as 14% of the patients experienced complications in the form of diabetic ulcers and diabetic neuropathy. The use of AD in most patients with T2DM (95.1%) was a combination of two ADs with the use of regular daily drug of up to three drugs.

Of all the characteristics, the duration of T2DM appeared significantly ( $P = 0.047$ ) related to the level of the MA.

## DISCUSSION

We used the HbA<sub>1c</sub> level to represent the MA of the patients, because adherence is the key factor that is significantly affecting glycemic factor of the patients.<sup>[10]</sup> This study found more than three-quarter (75.5%) of the patients with low MA, which is shown by the HbA<sub>1c</sub> level more than or equal to 7% [Table 1]. This result is

**Table 2: Logistic regression test results on factors influencing medication adherence**

Characteristics	Low MA (OR, 95% CI)*	P value
Age (years)	1.907 (0.789–4.606)	0.152
Gender	0.927 (0.352–2.437)	0.877
Level of education	0.575 (0.268–1.236)	0.156
Occupation	1.807 (0.604–5.410)	0.290
Other chronic diseases	1.586 (0.462–5.448)	0.464
Number of AD	2.455 (0.237–25.375)	0.451
Duration of T2DM	3.173 (1.206–8.014)	0.015
Number of regular daily drugs	1.181 (0.387–3.602)	0.743

\*Multiple logistic regression

comparable to other studies in other communities in Indonesia and other developing countries, which found low MA ranging from 52.7% to 79%.<sup>[4,12]</sup>

Age did not show a significant relationship to the MA, with slight dominance in the adult patient who had low MA. Meanwhile, female patients were found to have low MA. These observations did not correspond to some studies, which also showed the adult and female patients tended to have low MA.<sup>[10,13]</sup> Level of education and working activity did not show any significance in the number of patients with low MA, which is also similar to a previous study.<sup>[10]</sup>

This study did not find the number of medications (AD or other) taken daily that affected MA; hence, it did not show an association with low MA. Other studies also found the insufficiency of association between number of regular daily drugs and low MA.<sup>[10,14-16]</sup> Seven combinations of AD were used by the patients in the study, which were insulin and acarbose; metformin and acarbose; metformin and glipalamide; metformin and gliquidone; metformin, gliquidone, and acarbose; metformin and glimepiride; and metformin, glimepiride, and acarbose. Of all these combinations, the combination of metformin and glimepiride reportedly had most patients with low MA. This result was not in accordance with previous studies, which reported that the combination was more effective in glycemic control which should also reflect their MA.<sup>[17]</sup>

This study underlined a significant association between the duration of T2DM and MA [Table 2]. Patients with T2DM duration less than 5 years tend to have low MA ( $P = 0.015$ , OR = 1.206, 95% CI = 1.216–8.014). Another study had a similar finding,<sup>[18]</sup> whereas there were other studies too, which found a lack of association between both.<sup>[19,20]</sup>

*Limitations and strengths:* Though this study measured the MA based on the reliable data of HbA<sub>1c</sub> assessment, it could not identify the reason for low MA. However, this method is fast and convenient at a study site where the HbA<sub>1c</sub> is regularly assessed. This study provided a

better result on MA in glycemic control perspective in Indonesia, especially Jakarta, due to the larger sample that covered seven community health centers in Jakarta.

Although our results did not show a relationship between polytherapy and low MA, health-care professionals must continue to pay attention to patients receiving polytherapy and/or polypharmacy. This is because it is one of the risk factors that affect MA. In this study, we found that the duration of T2DM was associated with a low MA, which unexpectedly showed that patients who had T2DM for less than or equal to 5 years were more at risk of having a low MA; therefore, further investigation of the factors affecting MA was needed in new patients with T2DM for less than 5 years.

## CONCLUSION

This study shows a low increase in MA in patients with T2DM in Jakarta. This is important to be addressed by supporting the growing awareness of adherence to antidiabetic among patients, for example, by giving regular education to the patents. Although the polytherapy was found to be unrelated to MA, a surprising finding showed that patients who experienced T2DM less than or equal to five years were prone to have low MA. Health care providers must continue to strive to improve MA in T2DM patients. This can be done by providing counseling and/or any kind of education to patients at each visit and correctly assessing the MA. In addition, improving the relationship between patients and health workers by providing self-management guidelines, which can be done by patients, can also improve glycemic control and health outcomes. As the implication of polytherapy on MA in patients with chronic disease was an intended problem we wanted to identify in our study, we think pharmacy services such as therapeutic management are needed to optimize drug use therefore the use of drugs can be more efficient. Pharmacist and other health workers can work together to not prescribe or stop unnecessary drugs or drugs that cause problems.

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**Conflicts of interest**

There are no conflicts of interest.

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