

## RELATION OF MEDICATION ADHERENCE TO THE INCIDENCE OF COMPLICATIONS IN TYPE 2 DIABETES MELLITUS PATIENTS

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### ABSTRACT

**Objective:** The prevalence of diabetes mellitus continues to increase worldwide, followed by the incidence of complications, which ends up causing morbidity and mortality in patients. There were many factors related to the incidence of complications in diabetes mellitus. Patient's adherence to their medication is considered to have an impact on the complications in diabetic patients.

**Methods:** The study was conducted on 68 patients with a cross-sectional method with consecutive sampling. Statistical analysis was done using the Chi-square and Fisher's exact test.  $p < 0.05$  was considered statistically significant. Patients were interviewed using a demographic data questionnaire and medication adherence rating scale - 5 (MARS-5). Other data and diagnosis of complications were collected through medical records. The epidemiological analysis was carried out using the prevalence ratio.

**Results:** There were 47 (69.1%) patients with type 2 diabetes mellitus (T2DM) hospitalized due to complications, and 56 (82.4%) patients have poor adherence to treatment. There was a significant relationship between treatment adherence and the incidence of complications in diabetes mellitus patients with  $p = 0.001$  and it was found that there was a risk of 3.14 times in patients who have poor adherence to be hospitalized due to complications.

**Conclusion:** Treatment adherence affects the incidence of complications in patients with T2DM.

**Keywords:** Diabetes mellitus, Medication adherence, Complication, Medication adherence rating scale-5.

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### INTRODUCTION

Diabetes mellitus has become a global epidemic whose prevalence has continued to increase in recent years. According to the World Health Organization, there was an increase in the prevalence of diabetes mellitus from 4.7% or 108 million people in 1980 to 8.5% or 422 million people in 2014. The International Diabetes Federation estimates that the number of people with diabetes worldwide in 2045 will reach 700 million people, a 51% increase from 2019 which amounted to 463 million. There were 1.6 million deaths worldwide due to diabetes mellitus in 2016. As many as 87% of these deaths occurred in low- and middle-income countries. This causes diabetes mellitus to be in the seventh position in the world as the leading cause of death [1-6].

The increasing prevalence of diabetes mellitus is caused by population growth, increasing age, unhealthy diet, and lifestyle, as well as obesity which is currently also a global epidemic. As the prevalence increases, the risk of complications in diabetes mellitus patients will also increase. Acute complications of type 2 diabetes mellitus (T2DM) such as diabetic ketoacidosis, hyperglycemia hyperosmolar state, and hypoglycemia. Blindness, kidney failure, heart attack, stroke, and amputation of the lower extremities are the chronic microvascular complications caused by diabetes mellitus. Cardiovascular complications and stroke are the main causes of morbidity and mortality in T2DM patients worldwide, accounting for 70% of deaths in diabetics. Chronic kidney disease is major comorbidity found in Asian countries, in which more than 50% of kidney failure caused by diabetes mellitus [7-12].

Good blood sugar control is the key to diabetes mellitus management for patients and their families and medical personnel. To achieve blood sugar targets, the patient adherence to the prescribed medication is required. According to research, adherence to the treatment of chronic

disease patients has only reached 50%, this is thought to affect the incidence of complications in diabetes mellitus patients. Previous researches showed that there was low medication adherence in people with diabetes mellitus [13-19]. There were limited studies about medication adherence in relation to complications in patients with T2DM in Indonesia, especially in Bali. This study aims to determine the association between treatment adherences to the incidence of complications in patients with T2DM at Wangaya Hospital.

### METHODS

#### Research design

The method used in this study was the analytic observational method with a cross-sectional approach. In patients with a history of diabetes mellitus and at least 6 months on medication of oral anti-diabetic regimens and insulin were interviewed and asked to fill the medication adherence rating scale - 5 (MARS-5) questionnaire. This MARS-5 was translated to Bahasa Indonesia and already granted permission to use by the originator of the questionnaire, Professor Robert Horne. Data about complications were taken from the diagnosis in the medical records. This research granted an ethical clearance from the hospital's ethics committee: 028/IV/KEP/RSW/2020.

#### Population and sample of the study

The study was held at inpatient wards of Wangaya Hospital, Denpasar, Bali, Indonesia. We obtained a total of 68 patients with T2DM which fulfilled the inclusion and exclusion criteria as research participants. The inclusion criteria are patients with T2DM, with at least 6 months on medication: Either oral anti-diabetic or insulin, uncooperative patient or patients with a disability can be included by interviewing the patient's family (age >18 years old) who know the patient course of the disease and has assisted the patient in taking the medication. We

exclude patients which used herbal or traditional medicine, pregnant patients, and patients that not willing to participate.

#### Variables and data sources

Demographic characteristics such as age, sex, education, work, and marital status were included in the study. Other variables included were duration of T2DM diagnosis (<5 years or ≥5 years), regimen of therapy (oral anti-diabetic or insulin), drug administration (independent; by the patient him/herself, or dependent; need assistance from family member to give the medicine), comorbidity, and blood sugar level when admitted to the hospital (<200 mg/dL or ≥ 200 mg/dL), complications, and medication adherence (good adherence = MARS-5 score 25, or poor adherence = MARS-5 score of 5–24).

#### Data analysis

The patients or the family of the patients that are knowledgeable of the patient's disease and medication habit were interviewed and requested to fill the MARS-5 questionnaire. Data on complications were taken from the diagnosis in the medical records. The association of medication adherence and complication incidence was analyzed using Fisher exact test, while the relationship between other factors (such as age, sex, education, work, marital status, duration of diagnosis, the regiment of therapy, drug administration, comorbidity, and blood sugar level) and complication incidence was analyzed using the Chi-square test. Both tests were performed with SPSS version 21, with a confidence interval of 95% and \*p<0.05 considered statistically significant.

#### RESULTS

From 68 samples, the patient demographic characteristics showed that the mean age of the patients was 58.6 with a standard deviation of

10.329. The patient age data were tested by the Kolmogorov-Smirnoff test with a result of  $p = 0.200$ , which means that the data were normally distributed. There were 40 (58.8%) male patients and 28 (41.2%) female patients. A total of 53 patients were married (77.9%), and 15 patients (22.1%) were unmarried/widowed/divorced. According to the latest education, there were 14 (20.6%) patients who did not attend school, 23 (33.8%) patients graduated from elementary school, 11 (16.2%) patients graduated from junior high school, 12 (17.6%) patients attended senior high school, and 8 (11.8%) of university graduate patients. Thirty-three (48.5%) patients had diagnosed T2DM for <5 years, and 35 (51.5%) patients had diagnosed diabetes mellitus for more than 5 years.

The number of patients who did not work and work was 39 (57.4%) and 29 (42.6%), respectively. There were 47 patients (69.1%) who took oral anti-diabetic drugs and 21 people (30.9%) who used insulin. There were 46 patients (67.6%) who used drugs independently and 22 patients who are dependent and needed help in administering the drug (32.4%).

Comorbidity was found in 43 (63.2%) patients and complications in 47 (69.1%) patients. Blood sugar levels at the time of admission to the hospital were divided into two groups, the group with blood sugar levels <200 mg/dl was obtained by 23 people (33.8%) and in patients with blood sugar levels ≥200 mg/dL as many as 45 people (66.2%). Twelve patients (17.6%) showed good treatment adherence (MARS-5 =25), while 56 patients (82.4%) had poor treatment adherence (Table 1).

Based on the results of statistical analysis using the Chi-square and Fisher's exact test, it was found that treatment adherence had a relation with the

**Table 1: Demographic characteristic of the sample**

Variable	n (%)	Mean±SD	Median (min:max)
Age		58.6±10.329	59.5 (38:85)
Sex			
Men	40 (58.8)		
Women	28 (41.2)		
Marital status			
Unmarried/widowed/divorced	15 (22.1)		
Married	53 (77.9)		
Education			
Uneducated	14 (20.6)		
Primary school	23 (33.8)		
Junior high School	11 (16.2)		
Senior high School	12 (17.6)		
University	8 (11.8)		
Duration of T2DM diagnosis			
<5 years	33 (48.5)		
≥5 years	35 (51.5)		
Work			
Working	29 (42.6)		
Not working	39 (57.4)		
Therapy regimen			
Oral anti-diabetic	47 (69.1)		
Insulin	21 (30.9)		
Drug administration			
Independent	46 (67.6)		
Dependent	22 (32.4)		
Comorbid			
Yes	43 (63.2)		
No	25 (36.8)		
Complication			
Yes	47 (69.1)		
No	21 (30.9)		
Blood sugar when admitted to hospital			
<200 mg/dL	23 (33.8)		
≥200 mg/dL	45 (66.2)		
Medication adherence (MARS-5)			
Poor adherence	56 (82.4)		
Good adherence	12 (17.6)		

Sample size: 68. MARS: Medication adherence rating scale, T2DM: Type 2 diabetes mellitus

incidence of complications that led to the patient being hospitalized with  $p=0.001$ . Other factors such as gender, marital status, education, duration of diagnosis, occupation, types of the regimen used, method of administration of drugs, comorbid, and blood sugar at admission did not have a significant relationship with the incidence of complications ( $*p>0.05$ ).

The epidemiological analysis showed prevalence ratio (PR) = 3.14, which means that patients with poor adherence to treatment (MARS score 5<25) had 3.14 times the risk of experiencing complications when compared to patients who had good adherence (MARS score 5=25). The analysis results are shown in Table 2.

## DISCUSSION

Complications in diabetes mellitus patients, both acute and chronic, are very common with disease progression, the influence of other factors such as comorbidities, and poor glycemic control. Several previous studies have obtained different results regarding the factors that influence the incidence of complications in patients with diabetes mellitus. A study by Abejew *et al.* found that age, type of treatment regimen, and type of diabetes affected the incidence of complications. The study found the prevalence of hospitalized patients with complications of diabetes mellitus as much as 48.6% of the total sample. However, there was no significant relationship found between the patients' adherence and the incidence of complications [11]. According to a study from Singapore, the prevalence of diabetes mellitus patients with complications was 171 people out of a total of 382 patients or about 44.7%. It was found that there was no relationship between complications and treatment adherence [20]. A study conducted at a *Puskesmas* (Government's Public Health Center) in Yogyakarta, Indonesia, reported low adherence to the medication, at 57% of the total sample [21].

In this study, we found an incidence of complications in 47 (69.1%) samples. Poor adherence to treatment was found in 56 (82.4%)

patients. The factor that influences the incidence of complications is the patient's adherence, with  $p=0.001$ , with 3.14 times risk in patients with poor adherence to develop complications that caused them to be admitted to the hospital, while factors such as age, type of regimen, and duration of diagnosis do not have a significant relationship. Research by Simpson *et al.* stated that there was a relationship between adherence to treatment and the incidence of new complications in diabetes mellitus patients, with the risk of complications incidence of 0.8 (protective) in the adherent group. Good medication adherence is linked to good glycemic control. Meanwhile, poor adherence results in poor clinical outcomes and a decrease in the patient's quality of life [22-24].

Sex (gender) and patient education level had no association with the incidence of complications, but males who did not comply with treatment were found to have 1.35 times the risk of developing complications. This is compatible with the previous research. Marital status also has no relationship with the incidence of complications in this study. Besides, it was reported that comorbidity or chronic disease did not affect the incidence of complications in T2DM patients in both this study and previous studies [11,20].

The number of T2DM patients treated at the wards Wangaya Hospital during the research period was 122 people, but 54 of them did not meet the inclusion or exclusion criteria. Consisting of patients who were newly diagnosed with T2DM when they were admitted to the hospital, patients who had just started diabetes mellitus therapy (<6 months of therapy), patients who used traditional (herbal) medicine, patients who had never taken medication since their diagnosis, and some of which are not willing to be interviewed.

Many of the patients interviewed admitted to not being adherent to treatment (MARS-5 score = 5-24) for various reasons, such as there are no symptoms, forget to take medication, take medication only they think,

**Table 2: The relationship between variable and complication incidence (n=68)**

Variable	With complication	Without complication	p-value	PR*
Age				
≥60 years	23 (67.7)	11 (32.4)	0.793	0.96
<60 years	24 (70.6)	10 (29.4)		
Jenis Kelamin				
Pria	29 (72.5)	11 (27.5)	0.471	1.13
Wanita	18 (64.3)	10 (35.7)		
Marital status				
Unmarried/widowed/divorced	13 (86.7)	2 (4.6)	0.122	1.35
Married	34 (64.2)	19 (16.4)		
Education				
Lower education (Uneducated–primary school)	25 (67.6)	12 (32.4)	0.762	0.95
Higher education (Junior high school–university)	22 (71)	9 (29)		
Duration of T2DM diagnosis				
<5 years	24 (68.6)	11 (31.4)	0.920	0.98
≥5 years	23 (69.7)	10 (30.3)		
Work				
Working	21 (72.4)	8 (27.6)	0.612	1.09
Not working	26 (66.7)	13 (33.3)		
Therapy regimen				
Oral anti-diabetic	31 (66)	16 (34)	0.399	0.87
Insulin	16 (76.2)	5 (6.5)		
Drug administration				
Independent	31 (67.4)	15 (32.6)	0.656	0.93
Dependent	16 (72.7)	6 (27.3)		
Comorbid				
Yes	28 (65.1)	15 (34.9)	0.349	0.86
No	19 (76)	6 (24)		
Medication adherence (MARS-5)				
Poor adherence	44 (78.6)	12 (21.4)	0.001	3.14
Good adherence	3 (25)	9 (75)		
Blood sugar when admitted to hospital				
<200 mg/dL	30 (66.7)	15 (33.3)	0.541	0.9
≥200 mg/dL	17 (73.9)	6 (26.1)		

\*PR: Prevalence ratio. Sample size: 68. MARS: Medication adherence rating scale, T2DM: Type 2 diabetes mellitus

there was a worsening of their condition, fear to injure their kidneys, and other organs as a side effect of prolonged drug use and have no health insurance. This reflects the low knowledge and understanding of diabetes mellitus patients about their disease. The impact of this is non-adherence to treatment and ultimately leads to complications in the patient which aggravates the patient's condition. A qualitative study conducted by Rezaei *et al.* reported that the patient's distrust of medical explanations, the experience of the disease, life records, and economic problems are the causes of disruption to the treatment adherence in patients with diabetes mellitus [25,26].

Likewise, a study by Mandpe *et al.* which stated that patient knowledge of diabetes was closely related to treatment and was associated with lower complications [27]. Factors such as fear of weight gain, the incidence of hypoglycemia, and rejection or "denial" up to the incidence. Depression in the patient at diagnosis is also a factor in poor condition of the patient's treatment [28-31].

## CONCLUSION

From this study, we can conclude that there is a significant relationship between patient's adherence to treatment and the incidence of complications, with the risk of developing complications is higher in the poor adherence group. There are still a lot of patients with presumably poor knowledge of diabetes and diabetic medication. This factor affects adherence in patients with T2DM. Adequate education should be done when the patients first diagnosed with T2DM to prevent the incidence of complications in T2DM patients.

## Study Limitation

The small sample size is the limitation of this research. Recall bias may occur at the time of conducting interviews. A larger sample study and more resources are needed for the sake of future researches.

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## AUTHORS' CONTRIBUTIONS

Putu Dewinta Darmada was responsible for the research planning, research design, data collection and management, literature review, logical interpretation of the result, and writing the manuscript. Dewi Catur Wulandari contributed to research supervision, advising, reviewing, and approving the manuscript for publication.

## CONFLICTS OF INTEREST

The authors reported that there were no conflicts of interest in this research.

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