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Oral Antidiabetic Utilization and Various Factors as an Indicator for HbA1c Control Among Patients with Type 2 Diabetes

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Abstract

Background: Diabetes mellitus requires aggressive long-term therapy to decrease morbidity and mortality. Non-adherence to oral antidiabetic therapy represents a barrier to treatment that could lead to the deterioration of patient health. This study aimed to develop an indicator for predicting glycemic control among patients with type 2 diabetes. **Methods:** This unmatched case-control study recruited 110 patients from the Primary Health Care center in Palembang City. The chi-square test was used for certain variables, and multivariate analysis was performed using unconditional logistic regression to assess the effects of different variables after considering certain sociodemographic and economic characteristics as potential confounding variables. **Results:** The results revealed no statistically significant association of sociodemographic and economic variables (sex, age, education, and employment) with glycemic control. Family history of diabetes, duration of diabetes, body mass index, adherence, monitoring, therapy, and comorbidity were associated with glycemic control. **Conclusions:** Continuous education of primary care physicians is one way of improving skills for managing hyperglycemic patients. However, the challenge in treating patients with type 2 diabetes is to shift the main criterion from a disease-oriented to patient-centered approach in the context of patients' circumstances. Additionally, our developed indicator can be used as a screening test for assessing glycemic.

Keywords: antidiabetic, HbA1c, indicator, utilization

Introduction

Diabetes mellitus (DM) is associated with diseases such as heart disease, stroke, and kidney failure. Diabetes requires aggressive long-term therapy to decrease the morbidity and mortality resulting from complications. Glycemic control in diabetes is a "biomedical goal." However, comprehensive management must encompass both biomedical and biopsychosocial aspects. Several studies have identified patient adherence to treatment as an important biopsychosocial aspect.^{1,2} Non-adherence is a barrier to successful treatment that may worsen the health status of the patient, leading to errors in future treatments.¹ Non-adherence or non-compliance is the main cause of poor glycemic control among patients with type 2 diabetes. The prevalence of non-adherence is high among patients with diabetes, consequently increasing treatment costs.¹ As an example, non-adherence is believed to increase healthcare costs in the US by \$100 billion per year.²

The World Health Organization identified non-adherence as a multifactorial problem caused by the interplay of variables in the five following areas: (1) the patient, (2) the condition, (4) the type of therapy prescribed, (4) socio-economic factors, and (5) health system-related factors.³

A study in Nigeria identified financial constraints as the most common cause of non-adherence cited by patients with type 2 diabetes.⁴ Meanwhile, a separate study surveyed older adults in the Netherlands with type 2 DM who demonstrated greater adherence with social support and routine medication-taking behaviors.⁵ Unfortunately, these determinants have differed in various studies. Several studies have examined medication adherence in patients with diabetes around the world.³ However, few studies have been conducted in Indonesia. Additionally, few studies have examined the association of various factors with treatment adherence using indicators of outcome such as hemoglobin A1c (HbA1c). For these reasons, we sought to develop an indicator for predicting glycemic control among patients with type 2 diabetes with knowing oral antidiabetic drug utilization and the various factors that associated. These findings may clarify the association of poor glycemic control with comorbidity among patients and provide insights into the successful management of this chronic illness in the future.

Methods

This research was conducted from August 2017 to November 2017, and 110 patients (55 cases and 55

controls) were randomly selected from the Primary Health Care center in Palembang City. Patients were informed that personal information would be protected. The study was approved by Health Research Review Committee of Mohammad Hoesin Central General Hospital and Faculty of Medicine Sriwijaya University with Ethical Approval Certificate Number: No.61/kepkrsmhfkunsri.

The inclusion criteria for the case group were a diagnosis of type 2 DM by a general practitioner or internist, willingness to participate in the study, provision of informed consent, HbA1c $\geq 7\%$ or ≥ 53 mm/mol based on laboratory data for at least 3 months, and oral antidiabetic drug use for at least 3 months. Meanwhile, patients in the control group had HbA1c levels of less than 7% or 53 mm/mol. Pregnant female patients, patients using insulin for the treatment of DM, and non-domiciled patients in Palembang City were excluded from the study. Sociodemographic, disease, and comorbidity data were measured using standard methods. HbA1c levels were measured using a laboratory standard. Body mass index (BMI) is calculated as the weight (kg) divided by height (m). Standing height is measured using a stadiometer bar, without shoes, with shoulders in a relaxed position and arms hanging freely, and recorded to the nearest 0.1 cm. Body weight is measured when wearing light clothing without shoes on a digital electronic weighing scale (TD 150, range 4-150 kg). Body mass index (BMI) is then calculated as the weight (kg) divided by height (m²). Adherence was assessed using the 8-item Morisky Medication Adherence Scale (MMAS-8). For each item of the MMAS-8, a score of 1 was given for a positive answer (i.e., yes), whereas a score of 0 was given for a negative answer (i.e., no). The final score is tabulated as the sum of the scores of the eight items, with scores ≥ 3 indicating non-adherence.^{3,6} The eight items of MMAS-8 are presented in Table 1, with alternate answer of Never; Once in a while; Sometimes; Usually; All the time.

All variables (even if originally continuous such as Age, Body Mass Index and time since diagnosis with diabetes

were categorized in dichotomous variables - Age (<45 years/ ≥ 45 years), Body Mass Index (obese/normal), time since diagnosis (<3 years/ ≥ 3 years), monitoring (routine/not routine), drug standard therapy (monotherapy/combination), comorbidity (moderate/severe), education (primary/middle school/high school), employment (formal/informal/unemployed), and family history (yes/no).

Data analysis. Data analysis was conducted using STATA ver. 15.0 (College Station, Texas 77845 USA). The significance level was set as two-sided *p* value < 0.05. The chi-square test and contingency coefficient test were used for certain variables. Multi-variate analysis was performed using unconditional logistic regression to assess the effects of different variables after considering certain sociodemographic and economic characteristics as potential confounding variables. Data are presented as odds ratio with 95% confidence intervals to illustrate the association between variables and outcome, i.e., glycemic control.

Results

The study found that there were significant association of family history of diabetes, body mass index, time since diagnosis of diabetes, blood glucose monitoring, standard therapy type, adherence, and comorbidity with oral antidiabetic drug utilization (*p* < 0.05) (Table 2). The total of 57.1% family history were uncontrolled DM. Patients who obese were higher compared to patient with normal body mass index with total 68% people in uncontrolled DM. The gender, age, education, and employment showed no significant association with oral antidiabetic drug (Table 2).

After conducting multivariate analysis with logistic regression (Table 3), the following formula was devised to predict the risk of treatment non-adherence:

$$\text{Logit Glycemic Control} = -0.708 + 1.20 (\text{family history}) + 1.74 (\text{BMI}) - 1.89 (\text{time since diagnosis}) - 1.50 (\text{monitoring}) + 1.38 (\text{drug standard therapy}) - 1.28 (\text{adherence}) + 2.16 (\text{comorbidity}).$$

Table 1. The 8-item morisky medication adherence scale

Item
1 Do you sometimes forget to take your medicine?
2 People sometimes miss taking their medicines for reasons other than forgetting. Thinking over the past 2 weeks, were there any days when you did not take your medicine?
3 Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it?
4 When you travel or leave home, do you sometimes forget to bring along your medicine?
5 Did you take all your medicines yesterday?
6 When you feel like your symptoms are under control, do you sometimes stop taking your medicines?
7 Do you ever feel hassled about sticking to your treatment plan?
8 How often do you have difficulty remembering to take all your medicine?

Table 2. Association of various factors with glycemic control in patients with type 2 diabetes mellitus (DM)

Variables	Uncontrolled DM (Case)		Controlled DM (Control)		<i>p</i>
	Number (n = 55)	Percent (%)	Number (n = 55)	Percent (%)	
Sex					
Male	24	47.1	27	52.9	0.702
Female	31	52.5	28	47.5	
Age					
<45 years	8	72.7	3	27.3	0.204
≥45 years	47	47.5	52	52.5	
Education					
Primary	7	77.8	2	22.2	0.098
Middle school	27	42.9	36	57.1	
High school	21	55.3	17	44.7	
Employment					
Formal	17	58.6	12	41.4	0.384
Informal	14	53.8	12	46.2	
Unemployed	24	43.6	31	56.4	
Family history of diabetes					
Yes	44	57.1	33	42.9	0.037*
No	11	33.3	22	66.7	
Body mass index					
Obese	17	68.0	8	32.0	0.041*
Normal	38	44.7	47	55.3	
Time Since Diagnosis of Diabetes					
<3 years	28	60.9	18	39.1	0.034*
≥3 years	27	42.2	37	57.8	
Monitoring					
Routine	42	60.0	28	40.0	0.010*
Not routine	13	32.5	27	67.5	
Standard drug therapy					
Monotherapy	23	39.7	35	60.3	0.036*
Combination	32	61.5	20	38.5	
Adherence					
Good	29	63.0	17	37.0	0.033*
Poor	26	40.6	38	59.4	
Comorbidity					
Moderate	18	36.0	32	64.0	0.013*
Severe	37	61.7	23	38.3	

*Chi-square test, *p* < 0.05.**Table 3.** Multivariate analysis of factors associated with glycemic control

Variables	B	Sig.	Exp(B)	95% CI	
				Lower	Upper
Family history	1.203	0.030	3.33	1.13	9.85
Body mass index	1.743	0.009	5.71	1.55	21.10
Duration of diabetes	-1.888	0.002	0.15	0.05	0.49
Standard drug Therapy	1.376	0.018	3.96	1.27	12.40
Adherence	-1.282	0.018	0.28	0.09	0.80
Monitoring	-1.503	0.010	0.22	0.07	0.69
Comorbidity	2.156	0.000	8.63	2.67	27.94
Constant	-.708	0.308	0.49		

*Reference: 1= Yes; 0 = No

Discussion

The analysis found no associations of age, gender, education, and employment with oral antidiabetic drug utilization, in line with ² findings of the Hill-Briggs study, which observed no correlation between gender and level of adherence to diabetes medications among African-Americans.^{6,7} However, these findings differ from those of previous study, who found that patients with more strenuous work schedules had higher inclinations toward non-compliance.⁸ Adherence is a key issue, especially for chronic illnesses such as DM. Non-adherence results in elevation of blood sugar levels and subsequent microvascular and macrovascular complications.^{9,10} In the study, family history of diabetes was examined for each patient's mother and father. An association between family history and HbA1c levels was indicated. This association was largely explained for the association of parental history of diabetes with a longer duration of diabetes.¹⁰

In this observational study, we found an association between adherence and glycemic control (HbA1c). The results indicated that early adherence has a profound effect on glycemic control. Better adherence was associated with better responses to and the durability of metformin monotherapy as well as metformin and sulfonyleurea combination therapy. Because medication adherence represents a complex series of patient behaviors rather than a single construct, the cumulative glycemic burden experienced by patients with diabetes over time could be substantially lowered by adherence behaviors established early in the course of diabetes.¹¹⁻¹⁴ The potential reasons for poor glycemic control include high carbohydrate food consumption, a lack of physical activity, and a lack of knowledge about diabetes and its treatment.¹⁵ In Palembang City, the main food staple in the community is *pempek*, which consists of a mixture of fish and sago. Consumption of this local specific food is presumed to have resulted in high carbohydrate consumption among patients with diabetes in this study.

The finding of an association of time since diagnosis diabetes with glycemic control was in line with the previous study, who identified a correlation between the duration of DM and glycemic control (HbA1c). In their study, each 1-year increase in the duration of DM was associated with a 5% reduction in the likelihood of achieving glycemic control.¹⁵ Therefore, with disease progression, most patients require an increase in pharmacotherapy to maintain glycemic control.^{16,17} In general, patients with type 2 diabetes start pharmacotherapy with metformin, but treatment with more than one oral antidiabetic drug might be needed to maintain glycemic control. A number of studies have indicated that adherence decreases as the number of drugs increases.^{20,21}

Another important variable that can predict glycemic control among patients with type 2 diabetes is comorbidity.

In this research, we found that comorbidity had a highly significant association with glycemic control. The time since diagnosis of diabetes has been as an independent risk factor for comorbidity, as it is highly correlated with the number of complications and severity disease.^{20,21} This study had several limitations. First, this was a retrospective study with a small sample size, and the risk of recall bias cannot be dismissed. Second, patients using insulin were excluded. Third, other variables with potential associations with glycemic control were not measured, including regimen complexity, medication beliefs, and other human and economic factors. Future research should focus on the interplay between adherence to insulin and other antidiabetic therapies with follow-up observation.

Conclusions

Our findings identified several factors associated with uncontrolled diabetes, including family history, body mass index, time since diagnosis of diabetes, blood glucose monitoring, standard therapy type, adherence level, and comorbidity. Continuous education of primary care physicians is one way of improving skills for managing ⁷perglycemic patients. However, the challenge in treating patients with type 2 diabetes in the face of increasing comorbidity is to shift the main criterion from a disease-oriented to patient-centered approach in the context of patients' circumstances. Additionally, our developed indicator can be used as a screening test for assessing glycemic control in an effort to reduce the cost of health care and medical complications associated with DM.

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Conflict of Interest Statement

The authors declared ⁴no conflict of interest.

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