

ORIGINAL RESEARCH

RISK FACTORS OF TYPE 2 DIABETES MELLITUS DURATION AND NON-COMPLIANCE WITH MEDICATION TO POOR GLYCEMIC STATUS

Faktor Risiko Durasi Diabetes Melitus Tipe 2 dan Ketidakpatuhan Minum Obat terhadap Status Glikemik Buruk

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ABSTRACT

Background: Type 2 diabetes mellitus is a chronic disease that is still a global health problem. Uncontrolled diabetes mellitus (DM) can result in poor glycaemic status, with factors that affect patients including long-term DM and medication compliance. **Purpose:** This study aimed to determine the risk factors of long-term DM and non-compliance with medication on the poor glycaemic control status of patients with type 2 DM. **Methods:** This type of research used observational analysis with a case-control design. Samples were taken from patients with type 2 DM, with 40 cases and 40 controls. The criteria for sample inclusion were that the patients had a glycosylated hemoglobin level check, were willing to be research respondents, and could communicate well. The exclusion criterion was patients experiencing a drastic decline in health status during the study. The sampling technique used was consecutive sampling. This research was conducted at the Panti Wilasa Citarum Hospital in Semarang City from July to September 2019. The relationship and the risk of long-term DM and adherence to taking medication with glycaemic status were tested using the chi-square test. **Results:** This study showed that a duration of DM >5 years ($p = 0.01$; Odds Ratio (OR) = 3.46; 95% confidence interval [CI] = 1.37 < OR < 8.69) and non-compliance with taking medication ($p = 0.02$; OR = 3.15; 95% CI = 1.25 < OR < 7.93) are risk factors for poor glycaemic status. **Conclusion:** Duration of DM >5 years and non-compliance with taking medication are risk factors for poor glycaemic status in patients with type 2 DM.

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ABSTRAK

Latar Belakang: Diabetes melitus (DM) tipe 2 adalah penyakit kronik yang masih menjadi masalah kesehatan global. Diabetes melitus yang tidak terkontrol dapat berakibat status glikemik menjadi buruk, dengan faktor-faktor yang mempengaruhi diantaranya lama menderita DM dan kepatuhan minum obat. **Tujuan:** Penelitian ini bertujuan untuk menentukan faktor risiko lama menderita DM dan ketidakpatuhan minum obat terhadap status kontrol glikemik buruk pasien DM tipe 2. **Metode:** Jenis penelitian menggunakan observasional analitik dengan desain case control. Sampel diambil dari pasien DM tipe 2 dengan 40 kasus dan 40 kontrol. Kriteria inklusi sampel yakni pasien memiliki pemeriksaan kadar HbA1c, bersedia menjadi responden penelitian, dan dapat berkomunikasi dengan baik. Kriteria eksklusi yakni pasien mengalami penurunan status kesehatan secara drastis saat penelitian berlangsung. Teknik pengambilan sampel menggunakan consecutive sampling. Penelitian ini dilakukan di RS Panti Wilasa Citarum Kota Semarang pada bulan Juli-September 2019. Hubungan dan besar risiko lama menderita DM dan kepatuhan minum obat dengan status glikemik diuji menggunakan chi-square. **Hasil:** Penelitian ini menunjukkan bahwa lama menderita DM > 5 tahun ($p = 0,01$; OR = 3,46; 95% CI = 1,37 < OR < 8,69) dan ketidakpatuhan minum obat ($p = 0,02$; OR = 3,15; 95% CI = 1,25 < OR < 7,93) merupakan faktor risiko status glikemik buruk. **Kesimpulan:** Lama menderita DM > 5 tahun dan ketidakpatuhan minum obat merupakan faktor risiko status glikemik buruk pasien diabetes melitus tipe 2.

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INTRODUCTION

Cases of diabetes mellitus (DM) continue to increase globally. The World Health Organization estimated that there were 422 million adults suffering from diabetes worldwide in 2014. Type 2 DM or type 2 diabetes has the largest percentage of between 90% and 95% of diabetes, with the highest proportion in low- and middle-income countries (WHO, 2019). Type 2 DM or hyperglycemia occurs due to insulin resistance, wherein insulin production is insufficient, so the body is unable to respond fully to sugar levels. This is still a common and serious global health problem, including in Indonesia. In 2015, Indonesia was ranked seventh in the world with a high diabetes prevalence of 10 million cases after China, India, the United States, Brazil, Russia, and Mexico (IDF, 2015).

The prevalence of DM in Indonesia regarding the population aged ≥ 15 years is 10.90% (Soelistijo et al., 2015). According to the diagnosis

of physicians of the population aged ≥ 15 years based on provinces in Indonesia by 2%, and Central Java has above the average prevalence in Indonesia (Ministry of Health RI, 2018). One non-communicable disease that needs to be controlled in Central Java is DM. The proportion of DM regarding all non-communicable diseases ranks second largest at 20.57% after hypertension (Central Java Provincial Health Office, 2019).

Diabetes mellitus cannot be cured, but blood glycemic levels can be controlled. Glycemic control has always been the main therapeutic goal for the prevention of target organ damage and other complications arising from diabetes (Kakade, Mohanty, & Rai, 2018). Poor glycemic control of patients with type 2 DM is a major public health problem and accelerates the development of diabetes complications. Based on pathophysiology, DM complications are classified as microvascular (damage to small blood vessels) and macrovascular (damage to arteries). Diabetes is the leading cause of blindness, end-stage kidney

disease, and stroke, which are common in diabetic patients (Fasil, Biadgo, & Abebe, 2019). Microvascular and macrovascular complications in people with DM who have glycemic control result in higher treatment costs (Waari, Mutai, & Gikunju, 2018).

Glycemic control of DM can be seen from the levels of glycosylated hemoglobin (HbA1c); HbA1c is the main target of glycemic control and guides the strategy for initiating and intensifying treatment for diabetics (Camara et al., 2015). Each 1% reduction in the mean HbA1c has been shown to be associated with a risk reduction of 21% for diabetes-related deaths, 14% for myocardial infarctions, and 37% for microvascular complications (Kibirige, Akabwai, Kampiire, Kiggundu, & Lumu, 2017). According to the American Diabetes Association, the target for long-term glycemic control in patients with diabetes is an HbA1c value of less than 7%. Studies have shown that a significant reduction in mortality and morbidity occurs with an increase in glycemic control. This may be due to the reduction of microvascular complications such as low systemic inflammation by preventing immune dysfunction and protecting the endothelium and mitochondrial ultrastructure and function (Asmelash, Abdu, Tefera, Baynes, & Derbew, 2019).

Uncontrolled DM can often damage organs without being felt by patients. Some of the factors that can increase poor glycemic incidence at patients with DM were the duration of DM, adherence to taking DM medication, physical activity, and treatment control (Mamo, Bekele, Nigussie, & Zewudie, 2019; Nanda, Wiryanto, & Triyono, 2018; Widodo, Tamtomo, & Prabandari, 2016).

Long-term DM can be related to insulin secretion. The longer a person suffers from DM, the more damaged their insulin secretion becomes. Thus, it can cause difficulty in controlling blood sugar levels. Li et al (2018)'s study proved that there is a relationship between the duration of type 2 DM and poor glycemic control of diabetes in patients in diabetes care centers in Ningbo, China ($p < 0.01$).

Control of glycemic levels is the main objective in the treatment of DM. One of the glycemic status controls performed by DM patients is adhering to the treatment of diabetes. Compliance is defined as an attempt to take action according to instructions given by doctors in the form of exercise therapy, diet, medication, and disease control. Adherence to diabetes treatment

can improve blood glucose control and prevent long-term complications (Hashimoto et al., 2019). Diabetes treatment adherence is associated with lower HbA1c levels (Marinho et al., 2018).

Methods of measuring compliance with medication can be done directly and indirectly. The direct method looks at the concentration of drugs in the blood, while the indirect method uses the Morisky Medication Adherence Scale (MMAS)-8 questionnaire given to respondents. This questionnaire is used to assess compliance with taking medication and has been validated by the World Health Organization. Studies conducted by Nanda, Wiryanto, & Triyono (2018) provided evidence of adherence to taking anti-diabetic drugs in female outpatients aged 45–59 years to have a correlation with blood sugar regulation. Research conducted by Purwitaningtyas, Putra, & Wirawan (2015) also showed the relationship of medication adherence with controlling blood sugar levels; uncontrolled blood sugar in patients with DM occurred in patients who did not regularly take medication. This was in contrast to the results of Lin, Sun, Heng, Kwang-Chew, & Chong (2017)'s research, which showed that there is no relationship between medication adherence and glycemic control.

There has been an increase in patients with DM in Semarang City. In 2014, the DM cases amounted to 9,772 and, in 2018, increased rapidly to 48,996 (Semarang City Health Office, 2018). One hospital that has a lot of DM patient visits is Panti Wilasa Citarum Hospital in Semarang City, with 10,923 outpatient visits in 2018. A high number of complications due to poor glycemic status were found in the data of outpatient DM visits which are 1,253 patients in 2017 and increased become 1,531 DM patients with complications in August 2019.

The risk factors for poor glycemic status still need to be investigated. These factors are the duration of DM and medication adherence to glycemic status of patients with type 2 DM. Based on the description of the problem, this study aimed to determine the risk factors of long-term DM and medication adherence for poor glycemic status in patients with type 2 DM at Panti Wilasa Citarum Hospital in Semarang City.

METHODS

The type of research in this study was an observational analysis with a case–control design. Research with this design was carried out by determining in advance which groups had a bad

glycemic status as cases and which groups had a good glycemic status as controls.

The population in this study was all patients with type 2 DM who visited Panti Wilasa Citarum Hospital in Semarang. The sample size in this study was 80 people, with 40 cases (bad glycemic status) and 40 controls (good glycemic status). The inclusion criteria for the selected sample included examining HbA1c levels $>7\%$ for case samples and HbA1c levels $\leq 7\%$ for control samples, willingness to become research respondents, and ability to communicate well. The exclusion criterion of this study was patients experiencing a drastic decline in health status during the study. The sampling in this study used consecutive sampling.

This research was conducted at Panti Wilasa Citarum Hospital in Semarang City by interviewing outpatients with type 2 DM. The time of the data collection was July–September 2019. The primary data were obtained based on interviews, namely independent variables consisting of age, sex, recent education, occupation, duration of DM, and medication adherence. Adherence to medication was measured from the Morisky Medication Adherence Scale questionnaire with eight question items. The assessment of medication adherence was divided into two categories, namely compliant (value ≥ 8) and non-compliant (value < 8). The dependent variable was the glycemic status obtained from laboratory tests of the HbA1c levels of the patients with type 2 DM. The secondary data were the data on the number of patients with type 2 DM in Panti Wilasa Citarum Hospital in Semarang City.

The data were analyzed univariately and bivariately. The univariate analysis described the characteristics of the respondents, i.e., age, sex, recent education, and occupation in the frequency distribution table. The bivariate analysis was done by cross-tabulation between the dependent variable and the independent variable. Test the relationship between duration of DM compliance with medication taking with glycemic status using the chi square test. This study obtained ethical eligibility from the Health Research Ethics Commission of the Faculty of Medicine, University of Diponegoro, Number 412 / EC / KEPK / FK UNDIP / IX / 2019.

RESULTS

Table 1 illustrates that the majority of respondents were female (55.00%). The majority of respondents were aged between 55 and 59 years

(30.00%), with the youngest age being 45 years and the oldest 77 years. Most of the respondents had graduated from high school (43.80%). Regarding occupation, the majority of respondents did not work namely, because they were housewives (41.30%).

Table 1
Frequency Distribution of Respondents

Variable	n	%
Age (years)		
45–49	4	5.00
50–54	15	18.80
55–59	24	30.00
60–64	21	26.30
65–69	9	11.30
70–74	3	3.80
75–79	4	5.00
Gender		
Male	44	55.00
Female	36	45.00
Recent Education		
No School	1	1.30
Elementary school	16	20.00
Middle School	7	8.80
High School	35	43.80
College	21	26.30
Occupation		
Unemployment	6	7.50
Housewife	33	41.30
Retired Government Employees	15	18.80
Military/Police	3	3.80
General employees	13	16.30
Entrepreneur	10	12.50
Total	80	100.00

Table 2 shows that the results of the relationship test with the duration of DM obtained a p-value of 0.01 with an Odds Ratio (OR) value of 3.46 (95% confidence interval [CI] = 1.37–8.69), which meant that there was a relationship between the duration of DM and the glycemic status of patients with type 2 DM. The odds ratio was 3.46 (95% CI = 1.37–8.69), which meant that patients who have type 2 DM for more than five years have a 3.46 times greater risk of experiencing poor glycemic status than patients who have type 2 DM for less than five years. The proportion of patients suffering from DM for more than five years in the case group (62.50%) was greater than that in the control group (32.50%).

In Table 2, the proportion of respondents who were not compliant with taking medication was greater in the case group (57.50%) than in the

control group (30.00%). A drug compliance test was obtained $p = 0.02$, OR = 3.15 (95% CI = 1.25 < OR < 7.93), which meant that there was a relationship between medication adherence and glycemic status in patients with type 2 DM. The odds ratio was 3.15 (95% CI = 1.25–7.93), meaning that patients with type 2 DM who are not adherent to taking medication have a 3.15 times greater risk of experiencing a worse glycemic status than patients with type 2 DM who are adherent to taking medication.

Table 3 shows the non-compliance of the patients in the poor glycemic status group, most of whom (75.00%) would forget to take the drug. The statement of the reason for the non-compliance with medication that was proven to be related to the glycemic status of the patients with type 2 DM was that the patients felt worse when taking anti-diabetic drugs, with a value of $p = 0.03$ ($p < 0.05$). This meant there was a relationship between stopping or reducing the drug because the patients' condition became increasingly uncomfortable and the glycemic status of the patients with type 2 DM.

Table 2
Relationship Between Long-Term Type 2 DM and Compliance with Medication for Glycemic Status

Variable	Glycemic Status				<i>p value</i>	OR (95% CI)
	Poor		Good			
	n	%	n	%		
Long-Term Type 2 DM (years)						
>5	25	62.50	13	32.50	0.01	3.46 (1.37–8.69)
≤ 5	15	37.50	27	67.50		
Compliance with Medication						
No	23	57.50	12	30.00	0.02	3.15 (1.25–7.93)
Yes	17	42.50	28	70.00		
Total	40	100.00	40	100.00		

Table 3
Reasons for Non-Compliance with Medication

Compliance with Medication	Glycemic Status				<i>p value</i>	OR (95% CI)
	Poor		Good			
	n	%	n	%		
Forgot to take medicine						
Yes	30	75.00	26	65.00	0.46	1.62 (0.61–4.25)
No	10	25.00	14	35.00		
Deliberately did not take medicine						
Yes	12	30.00	6	22.50	0.18	2.43 (0.81–7.30)
No	28	70.00	34	77.50		
The condition felt uncomfortable						
Yes	14	35.00	5	12.50	0.03	3.77 (1.21–11.79)
No	26	65.00	35	87.50		
Forgot to bring medicine when traveling						
Yes	19	47.50	19	47.50	1.00	1.00 (0.42–2.41)
No	21	52.50	21	52.50		
Did not take medication yesterday						
Yes	2	5.00	4	10.00	0.67	0.47 (0.08–2.75)
No	38	95.00	36	90.00		
Felt healthy						
Yes	12	30.00	7	17.50	0.29	2.02 (0.70–5.83)
No	28	70.00	33	82.50		
Interrupted by having to take medication						
Yes	16	40.00	12	30.00	0.48	1.56 (0.62 – 3.93)
No	24	60.00	28	70.00		
Total	40	100.00	40	100.00		

DISCUSSION

The Relationship of Long-Term DM with Glycemic Status

This study showed that the proportion of long-term DM of more than five years in the case group (62.50%) was greater than that in the control group (32.50%). In theory, long-term DM is associated with glycemic status. In this study, the results showed that there is a relationship between the length of suffering from DM and glycemic status ($p = 0.01$; $OR = 3.46$; $95\% CI = 1.37-8.69$), which means that patients with type 2 DM >5 years have a 3.46 times greater risk of experiencing poor glycemic status than patients with type 2 DM ≤ 5 years. The results of this study support research from Li et al (2018) that proved that the duration of type 2 DM is associated with poor glycemic control. Every one-year increase in the duration of DM is associated with a 5% reduction in the likelihood of achieving glycemic control targets. A longer diabetes duration negatively affects glycemic control. This happens because of the progressive disruption of insulin secretion over time as a result of beta cell failure. As the disease progresses, most patients require increased pharmacotherapy to maintain glycemic control.

A study conducted by Haghghatpanah, Nejad, Haghghatpanah, Thunga, & Mallayasamy (2018) revealed the same results: A longer duration of diabetes affects glycemic control, perhaps due to a reduction in insulin secretion or excessive insulin resistance in these patients. The same thing was also shown in research by Kayar et al (2017) that found a significant relationship ($p = <0.01$) between poor glycemic control and the duration of disease. Diabetes is a progressive disease, and because glucose levels increase, more drugs are needed to achieve good glycemic control. A longer duration of diabetes is known to be associated with poor glycemic control, and this can be explained by the progressive decrease of insulin secretion over time due to beta cell failure (Badedi et al., 2016). This differs from the research conducted by Ishak, Mohd-Yusoff, Rahman, & Kadir (2017) that found no relationship between the duration of diabetes and glycemic status, with a value of $p = 0.35$.

The Relationship of Medication Compliance with Glycemic Status

There is a relationship between compliance with taking anti-diabetes drugs and poor glycemic status in patients with DM. Respondents who were

not compliant with taking anti-diabetic drugs had a 3.46 times higher risk of experiencing poor glycemic status compared to respondents who were compliant with taking anti-diabetic drugs. The odds ratio showed that the more obedient a patient was in taking anti-diabetic medication, the more their glycemic status would be controlled. The results of this study were in line with those of Alqarni, Alrahbeni, Al Qarni, & Al Qarni (2019), who showed that poor adherence to diabetes medication provides poor glycemic control. A low and optimal HbA1c value has also been found in patients with high MMAS-8 scores (Waari, Mutai, & Gikunju, 2018). The same thing was also shown in research by Nanda, Wiryanto, & Triyono (2018), which provided evidence of adherence to taking oral anti-diabetic drugs in female outpatients aged 45–59 years in Surabaya related to blood sugar regulation. In contrast, the research results of Lin, Sun, Heng, Kwang-Chew, & Chong (2017) showed that there is no relationship between medication adherence and glycemic control.

Based on the test results of the current study that the reasons for the non-compliance of patients to taking drug consumption was because of the condition of patients feeling uncomfortable when taking anti-diabetic drugs (p -value of 0.03). The results of this study were consistent with those of studies conducted in India, wherein one of the most common reasons for not complying with medication was feeling worse (Sajith, Pankaj, Pawar, Modi, & Sumariya, 2014).

The reason some patients felt their condition was getting worse was because they felt side effects when taking anti-diabetic medication. Some patients experienced symptoms such as dizziness, stomach discomfort, and diarrhea. The patients were forced to stop taking medication until they returns to the doctor to complain of the side effects of the drug. Research by Rosyida, Priyandani, Sulistyarini, & Nita (2015) mentioned that patients who stop taking medication or reduce medication due to side effects caused by drugs. The effects are disruptive but not consulted to the doctor so that when the patient drinks less than the recommended dose, the effect does not appear again.

In this study, the majority of respondents consumed oral anti-diabetes drugs, namely metformin and glimepiride. Metformin is an anti-diabetes drug that increases insulin sensitivity but has side effects in the form of digestive tract disorders. Glimepiride is in the sulfonylurea class of drugs to increase insulin secretion by pancreatic

beta cells and has major side effects of hypoglycemia and weight gain (Soelistijo et al., 2015).

Patients' reasons for forgetting to take medication in this study proved to be unrelated to poor glycemic status ($p = 0.46$). The majority of respondents with poor glycemic status by reason of forgetting to take medication (75.00%). Research conducted by Jemal & Abdela (2017) found that factors that cause non-compliance with taking medication are forgetting to take medication, omitting the dose, lack of finances, and long duration of therapy in the case of some DM patients. In research conducted at the Addis Ababa Tikur Anbessa specialty hospital using the Morisky four-item instrument, most patients missed their treatment due to negligence (Tsehay, Engidawork, & Ahmed, 2016).

Forgetfulness is the most common reason for disobedience. In research conducted by Inbaraj, Georg, Kham, & Norman (2016), all respondents who were forgetful were over 40 years old, and half (52.90%) of them were over 60 years old. Forgetting to take medicine can actually be overcome by telling family members to remind them or using a reminder alarm. In this study, the reason for patients forgetting to take medicine was due to decreased memory of the patients due to increasing age; however, the majority of respondents also tried not to forget to take the medication because it had become a routine, so they only forgot to take the medication once a week.

The reason of deliberately not taking medication ($p = 0.18$) was shown to be unrelated to poor glycemic status. The reason for not taking drugs was because the patients did not want to become addicted to drugs. Some respondents were afraid that taking drugs could damage their kidneys. Some patients interspersed type 2 DM treatment with alternative or herbal treatments such as cinnamon and garlic. In this study, the reason of forgetting to bring the drug while traveling ($p = 1.00$) was shown to be unrelated to poor glycemic status. This differed from research by Nanda, Wiryanto, & Triyono (2018) that proved that there is a relationship between patients forgetting to take drugs while traveling and blood sugar regulation with a value of $p = 0.03$. Patients who have a controlled glycemic status feel more responsible for managing their DM. Patients also try not to forget to take medication and bring medicine when traveling, and this makes patients with controlled blood sugar levels more obedient in taking medication.

The reasons for not taking medicine yesterday ($p = 0.67$), i.e., feeling healthy ($p = 0.29$) and disturbed by the need to take medication ($p = 0.48$), were also not proven to be associated with poor glycemic status of patients with type 2 DM. Patients felt bored with having to take mandatory medication every day because they felt disturbed.

Research Limitations

Not all patients had HbA1c examination data from the last three months because it is rare for patients to undergo HbA1c examination. This research would have been better if it were done homogeneously, taking HbA1c data from the last three months.

CONCLUSION

Based on the results of the study, it can be concluded that patients with a poor glycemic status are more non-compliant with taking medication. Duration of DM >5 years and non-compliance with taking medication are risk factors for poor glycemic status in patients with type 2 DM at Panti Wilasa Citarum Hospital in Semarang.

CONFLICT OF INTEREST

The authors declare that no conflict of interest in this study.

AUTHOR CONTRIBUTION

All authors participate actively in this article and are responsible for the content of the article. MGP: Writing- Original draft preparation, Conceptualization Editing, HNHS: Reviewing, Research Supervisor, Conceptualization, Visualization, MSA: Reviewing, Research Supervisor, Methodology, SS: Reviewing, BW: Reviewing.

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