Original article

Poor Glycemic Control: Prevalence and Risk Factors Among Patients with Type 2 Diabetes Mellitus in Northeast State of Peninsular Malaysia

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Abstract:

Background: Poor glycemic control remains an on-going public health concern worldwide. With the increasing prevalence of diabetes mellitus in Malaysia, good control of blood glucose level is paramount to avert life-long complications of diabetes mellitus. Hence, this study aimed to determine the prevalence of poor glycemic control and its associated factors to assist clinicians in achieving good glycemic control among diabetic patients. ***Materials and Methods:*** A comparative cross-sectional study between groups of good glycemic control and poor glycemic control patients was conducted among type 2 diabetes mellitus (T2DM) patients who fulfilled study criteria in Pasir Puteh district, Kelantan, a northeast state of Peninsular Malaysia. Eligible samples registered in the National Diabetes Registry from 1st January 2019 until 31st December 2019 were recruited into the study. Descriptive statistics, simple and multiple logistic regressions were used for data analysis. ***Results:*** The prevalence of patients with poor glycemic control in Pasir Puteh district was 79.6%% (95% CI: 0.78, 0.81). Multivariable analysis using multiple logistic regression revealed age, duration of diabetes, cigarette smoking, presence of hypertension and presence of dyslipidaemia were the significant factors associated with poor glycemic control among T2DM patients in Pasir Puteh district with an adjusted odds ratio (AOR) of 0.93 (95%CI:0.91, 0.94); p<0.001), AOR 1.19 (95%CI:1.14, 1.25; p<0.001), AOR 2.75 (95%CI:1.52, 4.97; p=0.001), AOR 2.19 (95%CI:1.32, 3.62; p=0.002) and AOR 2.16 (95%CI:1.45, 3.21; p<0.001) respectively. ***Conclusion:*** This study provided important criteria for clinicians to improve management of diabetes mellitus and optimize glycemic control based on the pinpointed significant risk factors.

Keywords: Type 2 diabetes mellitus, poor glycemic control, associated factors, Kelantan, Malaysia.

Introduction

Diabetes mellitus is one of non-communicable diseases that developed over a long period of time. It is a condition when one has an elevated blood sugar levels with disruption of carbohydrate, fat and protein metabolism. It may be due to failure of pancreas to excrete insulin (type 1) or inability of body cells to react to insulin (type 2). It also could happen during pregnancy due to hormonal changes (gestational diabetes)[1,2].

Worldwide, the prevalence of type 2 diabetes mellitus (T2DM) is more than 6% across all continents. World Health Organization (WHO) in their work on Global Report on Diabetes has illustrated trend of diabetes prevalence. Across all class of income group countries, high income group has shown small range of increment compared to lower, lower-middle and upper-middle income group. Nonetheless, countries across all income group has shown an increasing trend since 1980,

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with upper-middle income group has the highest prevalence in 2014 at more than 8%[2].

In Malaysia, a National Health Morbidity Survey (NHMS) conducted in 2015 found that 17.5% of adults aged 18 years and above has T2DM with 8.3% are known to have diabetes while 9.2% are previously undiagnosed with diabetes[3]. Percentage of those who were unknown to have diabetes is higher than those who were diagnosed might suggest low health seeking behavior among Malaysian that may be contributed by low awareness of diabetes or low accessibility to quality healthcare[4]. Late diagnosis of diabetes mellitus may contribute to poorly controlled diabetes and therefore, might increase risk for complications in diabetes such as retinopathy, nephropathy and cardiomyopathy[5].

In diagnosing diabetes mellitus, glycated hemoglobin (HbA1c) is used as the gold standard measurement[6]. HbA1c test tells the average level of blood sugar over the past 2 to 3 months. According to Malaysia's Clinical Practice Guideline on Management of Diabetes Mellitus, HbA1c of > 6.3% is used to diagnose diabetes mellitus[7]. For those who are newly diagnosed, at younger age, no cardiovascular complication, has low risk of hypoglycemia and has longer life expectancy, the targeted HbA1c is between 6.0 – 6.5%. While those who has comorbidities (such as coronary disease, heart failure, kidney failure and liver dysfunction), prone to hypoglycemia and has shorter life expectancy, an HbA1c range of 7.1 – 8.0% is aimed. Those who are not in both categories, the target A1c is 6.6-7.0%. Therefore, patients with an HbA1c level of more than the range in the individualized group is considered to have poor glycemic control[7].

Factors that are associated with poor glycemic control are modifiable and non-modifiable factors such as younger age (<50 years old)[8], female, overweight, longer duration of diagnosis, had more diabetic complications, hypertension and dyslipidemia[9,10]. Therefore, it is important to manage diabetes as a whole by tackling modifiable risk factors such overweight and obesity.

Timely treatment of patients with poor glycemic control is critical to prevent its dangerous complications. Besides, uncontrolled diabetes mellitus is highly associated with increased susceptibility to certain infections such as tuberculosis and skin infections due to impaired host immunity[11-14]. Knowing the predisposing factors for poor glycemic control can be effective in controlling diabetes mellitus and avert the life-long complications. Therefore, this study is aimed to estimate the prevalence of patients with poor glycemic control and determine its associated factors among T2DM patients in Pasir Puteh district, Kelantan.

Materials and Methods

From 15th December 2019 until 15th January 2020, we conducted a comparative cross-sectional study in eight primary healthcare facilities in the district of Pasir Puteh, Kelantan, a northeast state of Peninsular Malaysia. The clinics involved were Pasir Puteh Health Clinic, Selising Health Clinic, Cherang Ruku Health Clinic, Jeram Health Clinic, Gaal Health Clinic, Banggol Pak Esah Health Clinic, Gong Kulim Health Clinic and Sungai Petai Health Clinic[15].

The reference populations were all T2DM patients in Pasir Puteh district, and the study samples were all T2DM patients who fulfilled study inclusion and exclusion criteria in the eight selected health clinics. The inclusion criteria were T2DM patients who actively underwent diabetes clinic follow-up for at least 3 visits at any of the eight recruited health clinics until 31st December 2019. T2DM patients who died or lost to diabetes clinic follow-up were excluded from the study.

The sample size was calculated for each variable of associated factors for poor glycemic control among T2DM patients using power and sample size calculation software[16], as well to compare two independent proportions. The largest estimated sample for each group was 341 using the proportion of patients with good glycemic control by the factor of hypertension (0.34)[17], an estimated proportion of 0.24, 5% type 1 error, 80% power and additional of 10% missing data. Therefore, the total sample size required is 682 T2DM patients. We employed simple random sampling for subject recruitment from the total T2DM patients in Pasir Puteh district which fulfilled the study criteria.

Data were collected from National Diabetes Registry; an online database for diabetes mellitus

under the governance of Ministry of Health Malaysia[18], and recorded in patient's pro forma. The retrieved information for independent variables included socio-demographic characteristics (age, gender) and clinical characteristics (duration of diabetes mellitus; cigarette smoking status; presence of comorbidities such as hypertension and dyslipidaemia; presence of diabetic complications such as retinopathy, nephropathy, diabetic foot ulcer, cerebrovascular disease and cardiovascular disease). The dependent variable was the diabetic control status either good control or poor control of diabetes mellitus. The HbA1c level of patients which served as indicator of glycemic control status was retrieved from the Dynamic Management System, an online database for clinical laboratory findings. In this study, good glycemic control is defined as HbA1c level ≤6.5%. Meanwhile, HbA1c level beyond 6.5% is considered as poor glycemic control[7].In this study, hypertension in diabetic patient is defined as systolic blood pressure of >140 mmHg and/or diastolic blood pressure of >90 mmHg[7]. Dyslipidaemiain diabetic patient is defined as levels of either LDL>2.6mmol/L, HDL≤1.0 mmol/L, or triglycerides ≥1.7mmol/L[7].

Statistical Analysis

We used SPSS Statistics (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp) for data entry and analysis. Descriptive statistics with mean and standard deviation (SD), frequency and percentages were calculated. Simple and multiple logistic regression analysis were used to determine factors associated with poor glycemic control among T2DM patients. All significant variables with a p-value <0.25 from univariable analysis and clinically important variables were chosen for multiple logistic regression analysis. A p-value<0.05 was considered statistically significant.

Results

From the National Diabetes Registry, as of 31st December 2019, there were a total of 1780 diabetic patients who fulfilled the study criteria in Pasir Puteh primary healthcare facilities. The prevalence of patients with poor glycemic control were 79.6% (95% Confidence Interval (CI): 0.78, 0.81) or 1417 out of 1780 patients. Out of 1780 patients,

341 samples were randomly selected for each of the comparison group in accordance to sample size calculation.

Socio-demographically, the mean (±SD) age for T2DM patients with poor glycemic control was 59.87 (±9.77) years old. Majority of T2DM patients with poor glycemic control were female and non-smoker. As for duration of diabetes since diagnosis, the mean (±SD) duration for T2DM patients with poor glycemic control was 7.42 (±5.22) years.

As for complications in T2DM patients, majority of those with poor glycemic control had no retinopathy, no nephropathy, no diabetic foot ulcer, no cerebrovascular disease and no cardiovascular disease. For comorbidities, majority of patients with poor glycemic control had hypertension and dyslipidaemia. Details are summarized in Table 1.

In the univariable analysis, age, duration of diabetes, smoking status, presence of nephropathy, hypertension and dyslipidaemia were the statistically significant and clinically important factors selected for multivariable analysis. Details are summarized in Table 2.

Multivariable analysis using multiple logistic regression revealed age, duration of diabetes, cigarette smoking, presence of hypertension and presence of dyslipidaemia were the significant factors associated with poor glycaemic control among T2DM patients in Pasir Puteh district with an adjusted odds ratio (AOR) of 0.93 (95%CI:0.91, 0.94); p<0.001), 1.19 (95%CI:1.14, 1.25; p<0.001), 2.75 (95%CI:1.52, 4.97; p=0.001), 2.19 (95%CI:1.32, 3.62; p=0.002) and 2.16 (95%CI:1.45, 3.21; p<0.001) respectively. Details are shown in Table 3.

Discussion

The prevalence of patients with poor glycaemic control in Pasir Puteh district was 79.6% (95% CI: 0.78, 0.81) which is higher than the prevalence reported by Eid, Mafauzy (2003) among T2DM patients on follow up at Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan which was 73%[19]. Besides, a study in one of the health clinics in Sarawak also reported lower prevalence of patients with poor glycemic control which was only 38% out of 1031 patients on diabetic clinic follow up[20]. Similarly, another local study done in

Tampin district, Negeri Sembilan reported lower prevalence of poor glycemic control (66.4%) in relative to our finding[21]. Due to high prevalence of patients with poor glycemic control in Pasir Puteh district in relative to other studies of local settings, it justified the need for our inferential study to be done to delve the risk factors for poor glycemic control in the setting of Pasir Puteh district.

Age is one of the significant factors associated with poor glycemic control in this current study. It is found that older patient has lower risk of having poor glycemic control (AOR: 0.93; 95%CI: 0.91, 0.94; p<0.001). It is congruent to another local nationwide study in 2015 which reported that young-old and middle-old age group was a significant predictor of poor glycemic control as compared to those of age beyond 80 years old[22]. Studies from other international settings reported similar findings[23,24]. A South Korean study has found important factors that influenced older adult's view on glycemic control. Through qualitative exploration, they found that older adults considered 'positive attitude and self-confidence' are important in achieving good glycemic control besides technical coaching from medical staff[25]. Therefore, empowering the elderly to self-manage their health condition could be a turning point in management of diabetes. Detailed information must be given to them such as advices on healthy diet, physical activity and medication compliance.

Duration of diabetes mellitus plays a substantial role as well. We found that patient with longer duration of diabetes has higher risk of having poor glycemic control (AOR: 1.19; 95%CI: 1.14, 1.25; p<0.001). Similar finding was observed in another local study in the state of Johor, Malaysia[26]. Longer T2DM duration is related to progressive loss of pancreatic beta cell function which subsequently will cause poor glycemic control regardless of treatment regime[27]. Besides that, it is also postulated that "metabolic memory" plays important role in the development of macro- and microvascular complication in later life[28]. Those who has longer episode of hyperglycemia has poorer outcome. Hyperglycemia will lead to oxidative stress that causes harm to endothelial epithelium of blood vessels. If the insult left uninterrupted, the damage to the endothelium will be irreversible. Therefore, intensive intervention at early stage of disease has protective effect to the development of complications[24,28,29].

We also found significant association between cigarette smoking with poor glycemic control. Patient who smoke cigarette has 2.75 higher odds of having poor glycemic control. This finding is similar with a Swedish study which reported cigarette smoking is independently associated with poor glycemic control[30]. An Australian study had suggested that there is an association between cigarette smoking and diabetes. Those who is a carrier of C-allele gene in CYP1A1 enzyme (a detoxification enzymes of polycyclic aromatic hydrocarbons (PAH) which is a toxin component produced by cigarette smoking) and who is also a smoker, has more than two times the risk of having diabetes. This enzyme not only detoxify PAHs but also plays a role in intracellular oxidative metabolism. When the enzyme is affected by the toxins from cigarette smoking, it could lead to disturbances in intracellular oxidative metabolism that further affect insulin-related metabolic abnormalities in diabetes[31]. Therefore, cigarette smoking could disturb CYP1A1 enzyme function and hence further affecting the control of diabetes.

Apart from that, our study found that patients with dyslipidaemia were more likely to have poor glycemic control (AOR: 2.16; 95%CI: 1.45, 3.21; p<0.001 respectively). Similarly, a study in Montenegro reported that low level of high-density lipoprotein cholesterol (HDL-c) was found to be the independent predictor of higher HbA1c (AOR: 0.44, 95%CI: 0.20–0.67, p=0.039), and increase in HDL-c by 1 mmol/L reduced the probability of higher HbA1c by 56%[32]. It is postulated that lipid-related genetic loci may affect glycemic metabolism, suggesting potentially causal relationship between genetically determined low HDL-c or high triglycerides levels and increased risk of T2DM[33]. Interestingly, a study done in a Malaysian teaching hospital found that hypertensive patients with dyslipidaemia who were prescribedstatin showed higher A1c levels regardless of diabetes status[34]. Therefore, focus should be given to diabetic patients who are on statin. If controlling glucose level in these patients is difficult, it is best to replace statin with other lipidlowering medications to achieve better glycemic control.

Another statistically significant determinant for poor glycemic control was presence of hypertension in which hypertensive patients were more prone to have poor glycemic control (AOR: 2.19; 95%CI: 1.32, 3.62; p=0.002). This finding is consistent with few studies which also echoed the association of hypertension with glycemic control[22,35]. Hypertension and T2DM usually co-exist. The prevalence of hypertension in T2DM is higher than that in the general population. At the age of 75 around 60% of patients with T2DM are hypertensive[36].The pathophysiological mechanisms explaining the association between blood pressure and incidence of T2DM are not clearly understood, but several postulations were proposed. High blood pressure was shown to induce microvascular dysfunction, which may contribute to the pathophysiology of diabetes development and impairment in blood glucose control[37]. Besides, endothelial dysfunction which is related to insulin resistance is also strongly linked with hypertension, and biomarkers of endothelial dysfunction were found to be independent predictors of impaired blood glucose regulation[38].

Limitation of the study: As for the study limitation, we did not include family history of T2DM and diabetic treatment regime as part of the studied factors. These two factors are among the well-known significant predictors for poor glycemic control as reported by few Malaysian studies previously[21,39,40].

Conclusion and Recommendations

In conclusion, poor glycemic control among T2DM patients is quite prevalent in Pasir Puteh district. Younger age, longer duration of diabetes mellitus, cigarette smoking, presence of hypertension and dyslipidaemia were the significant risk factors for poor glycemic control. Hence, it is recommended that focus on diabetic care and education should be given to all groups of patients, not necessarily to elderly group only as our study reported that younger population was more prone towards poor glycemic control. Our study also revealed the link between longer duration of diabetes with poorer glycemic outcome, thus, it is imperative for us to manage diabetes optimally for patients who are diagnosed with diabetes mellitus at a very young age as they will have diabetes for quite a long time.

Diabetes educators or counselors in clinics should educate young diabetic patients on the importance of medication adherence and healthy lifestyle in order to achieve good glycemic control.

Besides that, all diabetic patients who smoke cigarette should be referred to Quit Smoking Clinic to help them with cigarette smoking cessation. Smoking cessation would reduce the likelihood of getting poor glycemic control among T2DM patients. Co-morbidities in diabetic patients such as hypertension and dyslipidaemia should be controlled optimally. Equal priority should be given to both blood glucose control and co-morbidities during follow-up session as failure to optimize blood pressure and lipid level would lead to failure in glycemic control. Blood pressure should be monitored regularly during each diabetes follow-up session while lipid levels should be checked every 6 months in diabetic patients to achieve optimal management of co-morbidities and good glycemic control[7].

Table 1: Socio-demographic and clinical characteristics of T2DM patients in accordance to glycemic control outcomes (n=682).

Characteristics	Frequency (%)	
	Poor glycemic control (n=341)	Good glycemic control (n=341)
Age (years)*	59.87 (±9.77)	64.87 (±10.60)
Duration of diabetes (years)*	7.42 (±5.22)	4.83 (±4.22)
Gender		
Male	97 (28.4)	98 (28.7)
Female	244 (71.6)	243 (71.3)
Cigarette smoking		
No	289 (84.8)	315 (92.4)
Yes	52 (15.2)	26 (7.6)
Retinopathy		
Absent	325 (95.3)	331 (97.1)
Present	16 (4.7)	10 (2.9)
Nephropathy		
Absent	291 (85.3)	307 (90.0)
Present	50 (14.7)	34 (10.0)
Diabetic foot ulcer		
Absent	336 (98.5)	339 (99.4)
Present	5 (1.5)	2 (0.6)
Cerebrovascular disease	337 (98.8)	335 (98.2)
Absent		
Present	4 (1.2)	6 (1.8)
Cardiovascular disease	334 (97.9)	333 (97.7)
Absent		
Present	7 (2.1)	8 (2.3)
Hypertension		
Absent	54 (15.8)	79 (23.2)
Present	287 (84.2)	262 (76.8)
Dyslipidaemia		
Absent	75 (22.0)	133 (39.0)
Present	266 (78.0)	208 (61.0)

*Mean (±SD)

Table 2: Factors associated with poor glycemic control among T2DM patients in Pasir Puteh district by simple logistic regression (n=682).

Factors	β	S.E.	Wald statistics (df)	Crude OR (95% CI)	p-value
Age (years)	-0.05	0.008	36.40 (1)	0.95 (0.93, 0.97)	<0.001
Duration of diabetes (years)	0.12	0.02	43.43 (1)	1.13 (1.09, 1.17)	<0.001
Gender					
Male				1.00	
Female	-0.01	0.17	0.01 (1)	0.93 (0.73, 1.41)	0.932
Cigarette smoking					
No				1.00	
Yes	0.78	0.25	9.44 (1)	2.18 (1.22, 3.58)	0.002
Retinopathy					
Absent				1.00	
Present	0.49	0.41	1.41 (1)	1.63 (0.73, 3.64)	0.234
Nephropathy					
Absent				1.00	
Present	0.44	0.24	3.44 (1)	1.55 (0.98, 2.47)	0.064
Diabetic foot ulcer					
Absent				1.00	
Present	0.93	0.84	1.21 (1)	2.52 (0.49, 13.09)	0.271
Cerebrovascular disease					
Absent				1.00	
Present	-0.41	0.65	0.40 (1)	0.66 (0.19, 2.37)	0.527
Cardiovascular disease					
Absent				1.00	
Present	-0.14	0.52	0.07 (1)	0.87 (0.31, 2.43)	0.794
Hypertension					
Absent				1.00	
Present	0.47	0.20	5.78 (1)	1.60 (1.09, 2.35)	0.016
Dyslipidaemia					
Absent				1.00	
Present	0.82	0.17	22.79 (1)	2.27 (1.62, 3.17)	<0.001

Table 3: Factors associated with poor glycemic control among T2DM patients in Pasir Puteh district by multiple logistic regression (n=682).

Factors	β	S.E.	Wald statistics (df)	Adjusted OR (95% CI)	*p*-value
Age (years)	-0.08	0.01	64.13 (1)	0.93 (0.90, 0.94)	<0.001*
Duration of diabetes (years)	0.18	0.02	60.42 (1)	1.19 (1.14, 1.25)	<0.001*
Cigarette smoking					
No				1.00	
Yes	1.01	0.30	11.11 (1)	2.75 (1.52, 4.97)	0.001*
Nephropathy					
Absent				1.00	
Present	-0.33	0.29	1.34 (1)	0.72 (0.41, 1.26)	0.717
Hypertension					
Absent				1.00	
Present	0.78	0.26	9.31 (1)	2.19 (1.32, 3.62)	0.002*
Dyslipidaemia					
Absent				1.00	
Present	0.77	0.20	14.32 (1)	2.16 (1.45, 3.21)	<0.001*

*p-value <0.05

No multicollinearity and no interaction found.

Hosmer Lemeshow test, p-value=0.174

Classification table 70% correctly classified.

Area under Receiver Operating Characteristics (ROC) curve was 76.6%.

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