Factors associated with good glycemic control among patients with type 2 diabetes mellitus

Nur Sufiza Ahmad1, Farida Islahudin2, Thomas Paraidathathu2*

1Pharmaceutical Services Division, Ministry of Health Malaysia, Petaling Jaya, Malaysia 2Faculty of Pharmacy, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

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*Correspondence
Thomas Paraidathathu
Tel.: +60-3-92897484
Fax: +60-3-26983271
E-mail address: ptthom@gmail.com

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ABSTRACT
Aims/Introduction: The aim of the present study was to determine the status of glycemic control and identify factors associated with good glycemic control among diabetic patients treated at primary health clinics.

Materials and Methods: A systematic random sample of 557 patients was selected from seven clinics in the Hulu Langat District. Data were collected from patients’ medication records, glycemic control tests and structured questionnaires. Logistic regression analysis was carried out to predict factors associated with good glycemic control.

Results: Variables associated with good glycemic control included age (odds ratio 1.033; 95% confidence interval 1.008–1.059) and duration of diabetes mellitus (odds ratio 0.948; 95% confidence interval 0.909–0.989). Compared with the patients who were receiving a combination of insulin and oral antidiabetics, those receiving monotherapy (odds ratio 4.797; 95% confidence interval 1.992–11.552) and a combination of oral antidiabetics (odds ratio 2.334; 95% confidence interval 1.018–5.353) were more likely to have good glycemic control. In the present study, the proportion of patients with good glycemic control was lower than that in other published studies. Older patients with a shorter duration of diabetes who were receiving monotherapy showed better glycemic control.

Conclusions: Although self-management behavior did not appear to influence glycemic control, diabetic patients should be consistently advised to restrict sugar intake, exercise, stop smoking and adhere to medication instructions. Greater effort by healthcare providers in the primary health clinics is warranted to help a greater number of patients achieve good glycemic control.

INTRODUCTION
The Malaysian Clinical Practice Guidelines (CPG) for type 2 diabetes mellitus has provided a comprehensive approach for diabetes, focusing on treatment strategies1. Current emphasis is on a hemoglobin A1c (HbA1c) target of <6.5% for good glycemic control1. Indeed, the United Kingdom Prospective Diabetes Study (UKPDS) study has also shown that glycemia control prevents death associated with diabetes-related complications2. The study concluded that a 1% reduction in mean HbA1c level was associated with a 12–43% reduction of microvascular and macrovascular complications2. Clearly, an improvement in glycemic control is likely to reduce the risk of diabetic complications. Therefore, diabetic patients are recommended to achieve HbA1c levels as close to normal (<6%) as possible to ensure the risk of disease progression is reduced3. Although the benefits of stringent glycemic control are evident, it has been reported that more than 60% of diabetic patients have been shown to not reach the recommended glycemic control target4.

Several studies have been carried out in Malaysia, involving primary healthcare centers and hospitals. A study in 49 private general practice clinics involving 438 patients with type 2 diabetes mellitus found that just 20% of patients achieved HbA1c levels of <7%, whereas just 11% had fasting blood glucose levels of <6.7 mmol/L2. Similarly, studies in public primary healthcare centers that provide free consultation and free medication found that just 28.8% of diabetic patients had a HbA1c level <7.5%, whereas 61.1% had HbA1c of more than 8%6. Glycemic control in diabetic patients in Jordan was also poor, where 65.1% of patients had poorly controlled HbA1c levels of more
than 7%, and it was significantly associated with a longer duration of the disease and non-adherence to diabetic care\(^7\). In contrast, studies carried out in Germany and Japan have shown that more than 45 and 65%, respectively, of patients with type 2 diabetes mellitus who were treated by general practitioners were able to achieve HbA1c levels of $<7.0\%$\(^8,9\). Thus, results of glycemic control in the local setting and in other developing countries were found to be substantially lower than findings from more developed countries, such as Japan and Germany.

In clinical practice, the recommended glycemic control target is very difficult to achieve. It is important, therefore, to identify factors that influence the outcomes of glycemia in order to improve the quality of diabetic management. Previous work that involved diabetic patients treated by private general practitioners in Kelantan, Malaysia, showed unsatisfactory results\(^5\). More than 80% of the diabetic patients had a body mass index (BMI) of $>23\, \text{kg/m}^2$, just 37.4% adhered to a diabetic diet, 6.9% carried out home glucose monitoring and just 20% had HbA1c levels of $<7\%$\(^5\). Similarly, in diabetic patients seen at the outpatient clinic of a tertiary hospital, more than 73% had poor glycemic control. However, younger female patients and patients newly diagnosed with diabetes had better glycemic control (HbA1c $<7\%$)\(^10\). In contrast, among young diabetics (those diagnosed before 40 years-of-age) with poor glycemic control, access to nurse educators, ethnic background and waist-to-hip ratio were found to be significant predictors of HbA1c\(^6\). Lack of awareness of diabetes and a low rate of self-monitoring of blood glucose levels have also been suggested as probable determinants of glycemic control in Malaysian patients\(^11\). It is apparent, therefore, that diabetic patients in Malaysia who were treated at private clinics and at outpatient clinics of tertiary hospitals did not achieve satisfactory glycemic control. Therefore, the present study was carried out to determine the status of current glycemic control outcomes, and to identify factors that influence good glycemic control among type 2 diabetes mellitus patients in government primary health clinics located in semi-urban and rural locations.

**MATERIALS AND METHODS**

The present cross-sectional survey was carried out within a 7-month period in seven Ministry of Health Primary Health Clinics in Hulu Langat, Selangor, Malaysia. The data were collected from January until July in 2008 at public health clinics that treated patients within the vicinity for various diseases including type 2 diabetes mellitus. Patients attended the clinic at appointed times determined by the healthcare officers for continuous monitoring and consultation of their disease.

Sample size was calculated based on the number of diabetic patients registered in the Hulu Langat District. Based on Krejcie and Morgan's\(^12\) formula for calculating sample size, this gave a calculated sample size of approximately 380 patients. However, a higher number was targeted in order to account for possible exclusions, dropout and the need to carry out subgroup analysis. A total of 557 patients were finally included in the study. Patients included in the study were type 2 diabetes mellitus patients older than 20 years who were receiving ongoing diabetic treatment. These patients must have undergone a HbA1c test within the previous 3 months, and also consented to undergo the test during the study period. Patients with critical illness or severe psychiatric disorders, such as major depression, or eating disorders that rendered them unable to be adherent to regular medication therapy and those unable to answer the questionnaires were excluded. To avoid sampling bias, a systematic random sample (every fifth patient) of type 2 diabetes mellitus patients in the Hulu Langat District was taken from the seven primary health clinics. The participants were informed of the study objective, and were recruited after obtaining informed consent.

The present study was approved by the Medical Research and Ethics committee of the Ministry of Health Malaysia. Data such as age, sex, ethnic, BMI, duration of diabetes mellitus, comorbidities and type of drug used were collected from the patients’ medical records. In the present study, all the patients were interviewed using standard self-reporting questionnaires. The questionnaire was divided into three parts, consisting of patients’ background, medication knowledge and medication compliance questions (MCQ). Patients’ lifestyle activities, such as smoking, alcohol intake and exercise, were also recorded. Patients were also asked whether they restricted their sugar intake.

The MCQ was developed with reference to other validated questionnaires from the self-reporting scale of Morisky et al.\(^13\), Hill-Bone Compliance to High Blood Pressure Therapy Scale\(^14\) and Morisky Medication Adherence Scale\(^15\). The present study questionnaire was adapted from these questionnaires, with minor changes in vocabulary to ensure a better understanding among the local respondents, while maintaining the essence of each question. The MCQ used was prepared in English and Malay. The original English version was translated to Malay, as most of the patients preferred to communicate in Malay. This Malay version of the MCQ was forwarded to a relevant expert in translation at the Language Center, University Kebangsaan Malaysia (UKM) to verify the translation. A total of seven questions were included in the MCQ, from which each respondent’s adherence score was calculated. Validity and reliability tests were carried out for the MCQ. The face and content validity were established by consulting with relevant experts. A reliability test ensured internal consistency and interrater reliability. Internal consistency showed a Cronbach alpha value of 0.782. Each patient underwent an interview by one of two researchers. The Cohen kappa statistic value was 0.787, which is considered an acceptable interrater reliability (between two researchers)\(^16\).

The outcomes of HbA1c were collected from the medical records or from tests carried out during the study period. HbA1c is a measure of the degree to which hemoglobin is glycosylated in erythrocytes, and is expressed as a percentage of...
HbA1c was determined by a high-performance liquid chromatography (HPLC) using Mindray® BS-400 Chemistry Analyzer (Mindray Medical International Limited, Nanshan, Shenzhen, China). The Malaysian CPG for type 2 diabetes mellitus and UKPDS indicate that HbA1c levels lower than 6.5% are considered as good glycemic control1,2.

**RESULTS**

A total of 557 patients were included in the study. Every eligible fifth patient who was approached consented to participate, thus giving a respondent rate of 100%. The present study included 205 men and 352 women with type 2 diabetes mellitus, aged between 30 and 84 years, with a mean (SD) of 55.95 years (9.13 years) and diabetes mellitus duration of 7.8 years (6.21 years). Just 14.7% of the patients had diabetes mellitus only (without any comorbidities), whereas the remaining patients were diagnosed with diabetes and other comorbidities, such as hypertension, dyslipidemia or both.

Approximately 60.3% of the population used a combination of oral antidiabetic drugs, followed by monotherapy (24.4%), and a combination of oral antidiabetics and insulin (15.3%). The patients in the monotherapy group were 6.81-fold more likely to achieve glycemic control compared with those using a combination of insulin and oral antidiabetic drugs. Those using a combination of oral antidiabetic drugs were 2.36-fold more likely than those receiving combination insulin and oral antidiabetic drug therapy to achieve glycemic control. Among the patients receiving monotherapy, more patients receiving sulphonylureas achieved glycemic control, with HbA1c levels lower than 6.5% (41.4%), than those using metformin (37%). However, patients receiving sulphonylureas (n = 29) were fewer than those receiving metformin (n = 100).

For self-management behavior among the patients, 40.8% did not control their diet (sugar intake), 55.3% did not engage in regular exercise and 88.9% did not smoke. Approximately 53.4% of the patients were compliant in taking their medication.

Out of the total of 557 patients, 23.0% (n = 128) had HbA1c levels below 6.5%, which is classified as good glycemic control, whereas the mean (SD) HbA1c level for all 557 patients was 8.04% (2.04%). The proportion of patients with good glycemic control according to demographics and health status of patients, and self-management behavior are shown in Tables 1 and 2. The patients were more likely to have good glycemic control if they were female, Chinese, elderly and had a shorter duration of diabetes mellitus. However, a comparison of patients with good and poor glycemic control showed that good glycemic control was associated with age, duration of diabetes mellitus, drug utilization pattern and adherence to

### Table 1 | Glycemic control by demographics and health status of patients

| Characteristic                        | Good glycemic control n (%) | Poor glycemic control | P-valuea |
|---------------------------------------|-----------------------------|-----------------------|----------|
| Age group                             |                             |                       |          |
| <5 years                              | 76 (27.8)                   | 196 (72.1)            | 0.007*   |
| 5–20 years                            | 49 (19.9)                   | 198 (78.1)            | 0.714    |
| >20 years                             | 3 (7.9)                     | 35 (92.1)             |          |
| BMI                                   |                             |                       |          |
| Normal (18.5–22.9)                    | 15 (19.7)                   | 196 (72.1)            | 0.714    |
| Overweight (23–27.4)                  | 53 (24.3)                   | 118 (78.1)            |          |
| Obese (≥27.5)                         | 60 (22.8)                   | 91 (83.5)             |          |
| Comorbidity                           |                             |                       |          |
| Diabetes mellitus only                | 15 (18.5)                   | 66 (81.5)             | 0.171    |
| Diabetes mellitus and comorbidity     | 113 (23.7)                  | 363 (76.3)            |          |
| Level of education                    |                             |                       |          |
| High education                        | 17 (23.9)                   | 54 (76.1)             | 0.817    |
| Secondary                             | 51 (22.0)                   | 181 (78.0)            |          |
| Primary                               | 48 (24.9)                   | 145 (75.1)            |          |
| Not attending school                  | 12 (19.7)                   | 49 (80.3)             |          |
| Drug utilization pattern              |                             |                       |          |
| Monotherapy                           | 52 (38.2)                   | 84 (61.8)             | <0.0001* |
| Combination of oral antidiabetics     | 68 (20.2)                   | 268 (79.5)            |          |
| Combination of oral antidiabetics and insulin | 7 (8.3)  | 77 (91.7) |          |

aKruskal–Wallis test. *P < 0.05. BMI, body mass index.
medication. Self-management behavior, such as diet and non-smoking, were not associated with good glycemic control.

The results of binary logistic regression analysis to predict whether 11 variable factors; that is, sex, race, BMI, comorbidity, level of education, age, duration of diabetes mellitus, medication knowledge, number of drugs taken, adherence and type of antidiabetic drugs were associated with good glycemic control showed that age, duration of diabetes mellitus and drug utilization pattern were statistically significantly associated with good glycemic control, as shown in Table 3. Each 1-year increase in age and 1-year decrease in duration of diabetes mellitus resulted in a 3.3 and 5.2% increase in odds, respectively, of having good glycemic control. Diabetic patients receiving monotherapy and those receiving a combination of oral antidiabetic drugs were 4.8- and 2.3-fold more likely to have good glycemic control, respectively, compared with patients using a combination of oral antidiabetics and insulin.

**DISCUSSION**

The present study showed that HbA1c levels among diabetic patients in the primary health clinics was not achieved in most patients, and that glycemic control was unsatisfactory. Low levels of glycemic control has been similarly shown in other studies in Malaysia and in other developing countries. Among the reasons that have been suggested for the poor glycemic control are a local diet that is high in carbohydrates, a lack of physical activity, and a lack of knowledge about diabetes and its treatment. Conversely, the better glycemic control seen in Japan and Germany might be because of the higher literacy rate in developed countries, and consequently probably better knowledge about the disease. This is an issue of concern, because the prevalence of diabetes mellitus in Malaysia is increasing, and significant amounts of money are spent each year on antidiabetic drugs while desired glycemic outcomes are not achieved in most patients. Interestingly, in the present study, achieving glycemic control was not associated with sex, race, BMI, family history of diabetes mellitus, diet and comorbidity, although a previous study had found an association between ethnicity and glycemic control. That study found better glycemic control among young Chinese diabetics, and they reported ethnicity as a predictor for good glycemic control.

Although, in the present study, females, overweight/obese patients, and patients with diabetes and hypertension showed slightly higher HbA1c values, they were not statistically significant.

The four variables found to influence the outcome of glycemic control in the present study were age, duration of diabetes mellitus, drug utilization pattern and adherence. This current study showed that for age, an increase in 1 year was associated with a 3% increase in the likelihood of achieving targeted glycemic control. Achievement of glycemic control among patients older than 65 years was higher than among the other age groups. The mean age for those with appropriate glycemic control was 57.7 years, which was higher than the 55.4 years for those who did not achieve the target glycemic control. The results show that older patients had better glycemic control than younger patients. Asian society often has an extended family set-up, and hence younger members of the family might assist in the care of the elderly, including reminding them about their medications. In this extended family set-up, family members might play a role in increasing adherence in elderly patients, and this could have contributed to the better adherence among the older patients. However, no significant association between age groups and achievement of glycemic control was observed in other studies.

The duration of diabetes mellitus was correlated with the outcome of glycemic control (HbA1c). Each 1-year increase in duration of diabetes mellitus was related to a 5% reduction in the odds of achieving target glycemic control. Previous work in

### Table 2 | Good glycemic control and self-management behavior (n = 128)

| Characteristic                  | Good glycemic control n (%) | P-valuea |
|---------------------------------|-----------------------------|----------|
| Diet                            |                             |          |
| Yes                             | 83 (25.2)                   | 0.085    |
| No                              | 45 (19.5)                   |          |
| Exercise                        |                             |          |
| Yes                             | 54 (21.7)                   | 0.291    |
| No                              | 74 (24.0)                   |          |
| Smoking habits                  |                             |          |
| Yes                             | 13 (22.8)                   | 0.562    |
| No                              | 115 (23.0)                  |          |
| Adherence status                |                             |          |
| Yes                             | 71 (27.1)                   | 0.019*   |
| No                              | 57 (19.3)                   |          |

*Kruskal–Wallis test. *P < 0.05.

### Table 3 | Multiple logistic regression analysis determining factors associated with good glycemic control (n = 128)

| Predictor variables               | Odds ratioa | 95% Confidence interval | P-value |
|----------------------------------|-------------|-------------------------|---------|
| Age group (per year)             | 1.033       | 1.008–1.059             | 0.008*  |
| Duration of diabetes mellitus (years) | 0.948 | 0.909–0.989 | 0.012* |
| Adherence status                 | 0.706       | 0.466–1.070             | 0.101   |
| Drug utilization patternb        | 4.797       | 1.992–11.552            | <0.0001*|
| Combination of oral antidiabetics| 2.334       | 1.018–5.353             | 0.045*  |

*P < 0.05. The final model was tested for goodness-of-fit by Hosmer–Lemeshow test, classification table and area under the receiver operating characteristics curve. The dependent variable was good glycemic control; Yes (1), No (0). Odds ratio was the adjusted odds ratio when other predictor variables were controlled. Reference group: a combination of insulin and oral antidiabetics.
Hong Kong has also shown that patients with longer duration of diabetes and more complex treatment regimens were associated with poorer glycemic control\textsuperscript{18}. Additionally, other studies have shown that a longer duration of diabetes was also associated with a higher incidence of hypertension\textsuperscript{10}. A longer duration of diabetes negatively affects glycemic control, possibly because of progressive impairment of insulin secretion over time as a result of \( \beta \)-cell failure\textsuperscript{5}. Therefore, as the disease progresses, most patients require an increase in their pharmacotherapy to maintain glycemic control\textsuperscript{19}.

The drug utilization pattern influenced the outcome of glycemic control. The best glycemic control was achieved by those on monotherapy, followed by those on a combination of oral antidiabetic drugs, followed by those receiving a combination of insulin and oral antidiabetic drugs. This could probably be as a result of the increasing difficulty in taking more than one drug and then the injections, thus also probably affecting adherence. Both sulphonylureas and metformin are widely used as first-line antidiabetic therapy. The popularity of sulphonylureas has decreased, and metformin is now a more common choice. However, it has been shown that more than 80% of patients do not consistently maintain HbA1c control 2 years after initial monotherapy with metformin or sulphonylureas\textsuperscript{20}.

Among patients using a combination of oral antidiabetic drugs, 20.4% achieved the target control. The combination of oral antidiabetic drugs has been shown to be effective because of their different modes of action and minimal adverse effects\textsuperscript{21}. A combination of oral antidiabetic drugs is recommended if patients do not achieve a HbA1c level lower than 6.5% with monotherapy\textsuperscript{4,22}. Although a combination of metformin and sulphonylurea was widely used in the present study, just 11.8% of the patients receiving this combination achieved glycemic control. Other studies have shown that the addition of metformin to a sulphonylurea therapy increased the proportion of patients who achieved a HbA1c level lower than 7%\textsuperscript{23}.

The patients receiving insulin treatment had the highest mean HbA1c level (9.30%) compared with those receiving monotherapy (7.12%) or a combination of oral antidiabetic drugs (8.11%). A significant difference was observed in the three types of drug treatment patterns, and similar results have been observed in other studies\textsuperscript{8}. The poor control among patients receiving a combination of insulin and oral antidiabetic drugs shows that multitherapy might not provide satisfactory glycemic control. Interestingly, however, studies have shown that intensive insulin therapy alone in type 2 diabetic patients results in excellent glycemic control\textsuperscript{24}. Another cross-sectional study carried out found that the use of insulin or a combination of oral antidiabetic drugs was associated with improved glycemic control\textsuperscript{25}. Thus, patients treated with a combination of insulin and oral antidiabetic drugs required more aggressive treatment and monitoring, both in terms of adequate dosing and improved adherence, to achieve better outcomes. Reasons for failure to achieve adequate glycemic control in this present group of patients should be further examined.

Effectiveness of drug treatment depends primarily on the efficacy of the prescribed treatment and adherence of the patient to the treatment\textsuperscript{26}. It has previously been shown that diabetic patients at Malaysian public health clinics had poor adherence\textsuperscript{27}. It is also not surprising that diabetic patients who fail to comply with the prescribed clinical regimen show very poor outcomes\textsuperscript{28}. An increase in adherence by 10% can decrease the HbA1c value by 0.16%\textsuperscript{29}. This is also supported by other previous studies in diabetics, which showed that an increase in patient education and adherence has been associated with good glycemic control. In Hong Kong, a pharmacist-managed clinic for diabetic patients improved adherence and glycemic control without any change in medication or dosage\textsuperscript{30}. It has been suggested that greater effort should be placed in counseling and improving adherence rather than changing medication or altering the dose\textsuperscript{31}. Another study where health personnel were specifically dedicated to the care of diabetic patients also showed better glycemic control\textsuperscript{32}. This current work showed that improvement of adherence among patients results in better glycemic control, and that achievement of glycemic control was higher among adherent patients than among non-adherent patients. However, tackling non-adherence is not a simple matter, as it is multifactorial and might include cost, health belief, dosing frequency, personality disorders and patient–provider relationship\textsuperscript{28}. Thus, poor glycemic control amongst patients receiving multitherapy might need to be reviewed if satisfactory adherence is not achieved. Patients that are adherent on monotherapy would probably be better served than those who are non-adherent on multitherapy. If adherence could be resolved, it is possible that the outcome of treatment would be much more satisfactory. As for the duration with which patients live with diabetes increases, they should frequently be reminded to not become complacent, but to continue to maintain good glycemic control, through adherence to medications, dietary controls, exercise, and regular monitoring and review, in order to possibly delay the development of the complications of diabetes.

The study had some limitations. One of the limitations was that confounding factors, such as diet and the quantification of sugar intake, were not carried out. It would have been extremely difficult to obtain accurate data. The other limitation was that the time between the first estimation of HbA1c and the second HbA1c was not the same for all patients. Some patients had their first HbA1c reading taken 2 months before the study.

In summary, factors such as age, shorter duration of diabetes mellitus, monotherapy and good adherence were found to impact the achievement of good glycemic control. As diabetes is a progressive chronic disease, complications increase and drug therapy becomes much more complex with time\textsuperscript{19,33}. However, current findings show the lack of control in patients using combinations of oral antidiabetics, and insulin and multiple oral antidiabetics compared with those treated with monotherapy. This is an issue of concern, as there was less benefit to patients prescribed multiple therapy. To that end, it is vital that
healthcare professionals pay special attention to specific groups, such as younger diabetics, those with a longer duration of diabetes and those who are not adherent, to ensure good glycemic control among diabetic patients. One way is to examine all aspects of the patient, and accordingly individualize the choice of glycemic goals, lifestyle changes and the medications required to achieve those goals. Balancing the potential for lowering HbA1c should be carried out by taking into account patient characteristics, such as age, duration of diabetes mellitus, type of drug and adherence, to ensure long-term glycemic control.

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