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Factors Associated with $\text{HbA}_{1c}$ Levels in Poorly Controlled Type 2 Diabetic Patients in North-East Malaysia

Nor Azlina A. Rahman$^1$, Aziz Al-Safi Ismail$^1$, Nor Azwany Yaacob$^1$, Lin Naing$^2$
Factors Associated with HbA1c Levels in Poorly Controlled Type 2 Diabetic Patients in North-East Malaysia

Nor Azlina A. Rahman¹, Aziz Al-Safi Ismail¹, Nor Azwany Yaacob¹, Lin Naing²

ABSTRACT

Objective: A study was conducted at all the health centres in Kelantan in North-East Malaysia to determine the common factors associated with poor controlled of type 2 diabetic patients.

Design: A cross-sectional study

Materials and Methods: A total of 208 patients with type diabetic control (HbA1c levels of more than 6.5%) were selected by stratified random sampling from all health centres in Kelantan. Socio-demographic data, physical examination, and fasting blood were taken from the patients to determine the related associated factors using multiple linear regression.

Results: The levels of HbA1c in the poorly controlled diabetic patients were significantly associated with fasting blood glucose (b=0.236, 95% CI=0.189, 0.283), educational level (primary education: b=-0.965, 95% CI=-1.550, -0.380; secondary and tertiary education: b=-0.625, 95% CI=-1.228, -0.021), marital status (b=0.933, 95% CI=0.426, 1.440) and patients receiving their care in health centres with Family Medicine Specialist (b=-0.495, 95% CI=-0.913, -0.076).

Conclusion: Fasting blood glucose and being married were associated with higher levels of HbA1c, while having had formal education and receiving diabetic care in health centres with Family Medicine Specialist were associated with lower levels of HbA1c in poorly controlled type 2 diabetic patients in Kelantan.

KEY WORDS

type 2 diabetes, poor glycaemic control, associated factors, HbA1c levels

INTRODUCTION

Diabetes mellitus is one of the commonest chronic non-communicable diseases globally, causing high morbidity and mortality. Worldwide prevalence of type 2 diabetes is increasing, and in Malaysia it raised from 0.6% in 1960, to 2.1% in 1982, 6.3% in 1986, and 8.3% in 1996 (Ismail and Gill, 1999, Rugayah et al., 1999, Zaini, 2000).

Majority of diabetic patients in Malaysia had poor glycaemic control, with 88% of them had HbA1c levels of more than 6.5% and 86% had fasting blood glucose (FBG) levels of above 6.1% (DCDCP, 1997). In Kelantan, 73% of diabetic patients in Hospital Universiti Sains Malaysia (HUSM) had HbA1c levels of more than 7%, and 60% had FBG levels of above 7.2 mmol/L (Eid et al., 2003). Another study done in Kelantan reported that 85.7% of the patients had HbA1c levels of more than 7.5%, with the mean HbA1c levels of 9.9% (Suhaiza et al., 2004). As a result, many patients end-up with chronic and serious complications. A study done in poorly controlled diabetics in Kelantan showed that 20.6% of them had nephropathy, 9.8% had neuropathy, 8.2% had retinopathy, 2.8% had foot ulcer and 2.4% had coronary heart disease (CHD) (Fauziah and Suhaiza, 2004). Earlier study done for Malaysia however showing higher prevalence of complications with 58% of the diabetic patients had neuropathy, 53% had retinopathy, 12% had foot ulcer and 9% had CHD (DCDCP, 1997).

Good glycaemic control can prevent or delay diabetic complications and reduce the cost of managing patients. The United Kingdom Prospective Diabetic Study (UKPDS) showed that each 1% reduction in HbA1c levels was assoc-
ated with reduction in the risk of 21% deaths related to diabe-
tes, 14% myocardial infarction and 37% microvascular
complications (Stratton et al., 2000). A study showed sig-
nificant increase in medical care charges for every 1% in-
crease in HbA1c levels above 7% (Gilmer et al., 1997).
Studies done on factors associated with glycaemic control
reported conflicting results (Ferrannini et al., 1992, Blaun
et al., 1997, Nichols et al., 2000, Schectman et al., 2002,
Eid et al., 2003, Rekeneire et al., 2003, Suhaiiz et al.,
2004). This could be due to the difference in the source
population and methodology used, categorisation of the
patients’ characteristics, and the difference in the classifi-
cation of poor and good glycaemic control. Our study how-
ever was trying to determine the factors associated with
HbA1c levels in only poorly controlled diabetic patients.

MATERIALS AND METHOD

Study population

This study was conducted at all health centres (HC) in
Kelantan in North-East Malaysia from August till October
2005. Only poorly controlled type 2 diabetic patients regis-
tered in the related HC aged 18 to 75 years old were select-
ed for this study, except those who were having acute ill-
ness which need hospitalization three months before and
during the study period and those on haemodialysis. HbA1c
levels of more than 6.5% were taken as poor glycaemic
control (Asian-Pacific Type 2 Diabetes Policy Group,

Methods

This is a cross-sectional study to determine the factors
associated with HbA1c levels in poorly controlled type 2
diabetic patients in Kelantan. Selection of subjects was by
proportionate stratified random sampling by the HC.
Patients who were chosen to participate in this study gave
their written consent. Socio-demographic data and diabetic
history were obtained from subjects using interviewed
questionnaire. The education level was classified into no
formal education ever received, having had primary educa-
tion (primary school), and having had secondary (sec-
ondary school) and tertiary education (university or other
higher institution). Marital status was divided into married
(currently married) and others (either single, divorced, or
widowed). Current smokers were those who were still
smoke currently, ex-smokers were those who previously
smoked but had stopped at least one month prior to the
study and non-smokers were those who never smoke
before. Diabetic history included duration of diabetes and
family history of diabetes.

Physical measurements were taken from subjects for
blood pressure and body mass index (BMI). BMI was cal-
culated as weight in kilograms divided by height in meter
squared (kg/m²). The weight of the subjects was measured
using Seca™ weighing machine to the nearest 0.5 kilogram
with subjects wearing light clothing and without shoes on.
The blood pressure was measured in millimeter mercury
(mmHg) using Omron™ automatic blood pressure monitor
which used oscillometric method and validated to ± 3

mmHg. Three measurements were taken from each subjec-
t’s right arm with the intervals of at least one minute.
Average from the last two measurements was taken as the
subjects’ blood pressure. Other conditions which can affect
the subjects’ blood pressure were also observed. The sub-
jects were asked to sit comfortably and the arms were sup-
ported at the heart level. The subjects were made sure to be
rested at least five minutes before first measurement. No
venepuncture was done immediately before taking the
blood pressure measurement (PAHI, 2003).

The subjects were asked to fast overnight about 8-14
hours (WHO, 1999) the night before the data collection to
get fasting blood from each subjects. The blood were ana-
lized in a commercial laboratory for HbA1c, levels, FBG and
fasting lipid profile including total cholesterol (TC),
triglycerides (TG), high density lipoprotein cholesterol
(HDL) and low density lipoprotein cholesterol (LDL). The
blood taken was kept in the ice-box for preservation before
reaching the laboratory in view of the distance of the HC
from the laboratory which was situated in the town of Kota
Bharu, the capital city of Kelantan.

About two milliliters (ml) of the blood was put into tube
containing EDTA to prevent it from clotting. This is for the
analysis of HbA1c, using ion-exchange high-performance
liquid chromatography by the D-10™ Haemoglobin A1c
Program. For the measurement of blood glucose, 1.5 ml of
the blood was put into tube containing fluoride (WHO,
1999). The fluoride would preserve the glucose before it
was analysed using enzymatic oxidation in the presence of
glucose oxidase by ADVIA™ Chemistry Systems. The
remaining 3.5 ml of blood was put into plain tube to let it
clot. The serum was then analysed by the ADVIA™
Chemistry Systems using enzymatic method to measure TC
and TG level. The cholesterol from non-HDL particles was
released and eliminated for the measurement of HDL level.
LDL levels was calculated by the Friedwald equation
(Friedwald et al., 1972).

Statistical analysis

Data were analysed using Stata version 8.0. Data were
checked for data-entry error, explored and cleaned before
analysis was done to check for completeness and accuracy
of the data. Data were presented as mean and standard
deviation or median and interquartile range depending on
the data distribution. Categorical data were expressed as
frequency and percentage. Small cells of categorical vari-
ables were combined as clinically meaningful if needed.

Simple linear regression was used to find the factors
associated with HbA1c levels in poorly controlled type 2
diabetic patients, followed by multiple linear regression.
The model was fit with linearity, normality and equal vari-
ance assumptions were satisfied, but in view of influential
effect of a few outliers, iteratively reweighted least square
(IRLS) robust regression was used, from which the inter-
pretation for regression coefficients with its 95% confidence
interval (CI) and p-value were made. Level of significant
was set at 0.05 with two-tailed fashion.

RESULTS

A total of 219 type 2 diabetic patients were recruited in this
study. Eleven subjects were excluded because their
HbA1c levels turned out to be less than 6.5% and their characteristics did not differ from the rest of the group. The total number of subjects available for analysis was 208. The mean age of these subjects was 55.6 years old (SD=8.55) and the median duration of diabetes was 6 years (IQR=7). Their median monthly household income was RM500 (IQR = 485). Majority of the subjects were females (59.6%), married (84.1%) and had positive family history of diabetes (55.3%). All of our subjects were Malays. Other sociodemographic variables were shown in Table 1.

Table 2 showed the clinical characteristics of the subjects. Majority of them had poor FBG levels of more than 6.1 mmol/L (93.7%). The percentage of subjects with TC levels of more than 5.2 mmol/L was 75.0%, LDL levels of more than 2.6 mmol/L was 91.3%, HDL levels of less than 1.1 mmol/L was 31.3% and TG levels of more than 1.7 mmol/L was 49.0%. Seventy five percent of the subjects were obese with BMI of more than 23 and 67.8% of them had systolic and/or diastolic hypertension. Those with SBP of more than 130 were 58.7% and DBP of more than 80 were 38.9%.

Simple linear regression found significant association between HbA1c levels and FBG, educational level, marital status and whether patients receiving their care in HC with FMS or not (data is not shown). The same factors were found to have significant association with HbA1c levels in multiple linear regression. IRLS robust regression was used to remedy the influential effects of a few outliers found during model assessment (Table 3). High HbA1c levels were associated with high FBG, having had no formal education, being married and receiving diabetic care in HC with Family Medicine Specialist (FMS).

With every one mmol/L increase in FBG levels, there was an increase of 0.236 unit (95% CI=0.189, 0.283) in HbA1c levels. Those who had had primary education had 0.965 unit (95% CI=1.550, -0.380) lower HbA1c levels as compared to those with no formal education, and those who had had secondary or tertiary education had 0.625 unit (95% CI=1.228, -0.021) lower HbA1c levels as compared to those with no formal education. Being married was associated with 0.933 unit (95% CI=0.426, 1.440) higher HbA1c levels as compared to others who were either widowed, divorced or single. Subjects receiving their diabetic care in HC with FMS had better HbA1c levels as compared to those who received their diabetic care in HC without FMS with the difference in HbA1c levels of 0.495 unit (95% CI=0.913, -0.076).

**DISCUSSION**

The socio-demographic characteristics of the 208 subjects in this study were almost similar with the findings of two other studies done in Kelantan, even though the studies recruited all type 2 diabetic patients, regardless of their glycaemic control (Eid et al., 2003, Suhaida et al., 2004). High HbA1c levels were found to be significantly associated with

<table>
<thead>
<tr>
<th>Table 1. Socio-demographic characteristics of 208 subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics</td>
</tr>
<tr>
<td>-----------------------------------------------------------</td>
</tr>
<tr>
<td>Occupation</td>
</tr>
<tr>
<td>Government</td>
</tr>
<tr>
<td>Private sector</td>
</tr>
<tr>
<td>Self-employed</td>
</tr>
<tr>
<td>Pensioner</td>
</tr>
<tr>
<td>Housewife</td>
</tr>
<tr>
<td>Others⁴</td>
</tr>
<tr>
<td>Educational level</td>
</tr>
<tr>
<td>No formal education</td>
</tr>
<tr>
<td>Primary education</td>
</tr>
<tr>
<td>Secondary and tertiary education</td>
</tr>
<tr>
<td>Smoking status</td>
</tr>
<tr>
<td>Non-smoker</td>
</tr>
<tr>
<td>Current smoker</td>
</tr>
<tr>
<td>Ex-smoker</td>
</tr>
<tr>
<td>Marital status</td>
</tr>
<tr>
<td>Married</td>
</tr>
<tr>
<td>Others⁴</td>
</tr>
<tr>
<td>Family history of diabetes</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>HC² with FMS⁵</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
</tbody>
</table>

⁴ Self-employed but currently not working anymore
² HC = Health Clinic
⁵ FMS = Family Medicine Specialist
Table 2. Clinical characteristics of 208 subjects

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%)</td>
<td>10.21 (1.712)</td>
<td>10.14 (1.683)</td>
<td>10.17 (1.691)</td>
</tr>
<tr>
<td>Fasting blood glucose (mmol/L)</td>
<td>11.83 (3.662)</td>
<td>12.03 (4.159)</td>
<td>11.95 (3.958)</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.78 (0.952)</td>
<td>6.35 (1.248)</td>
<td>6.12 (1.170)</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.8 (1.1)</td>
<td>1.7 (1.1)</td>
<td>1.7 (1.0)</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>1.126 (0.2027)</td>
<td>1.324 (0.2724)</td>
<td>1.244 (0.2646)</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/L)</td>
<td>3.72 (0.860)</td>
<td>4.07 (1.099)</td>
<td>3.93 (1.021)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.90 (3.511)</td>
<td>26.39 (4.000)</td>
<td>25.83 (3.919)</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>138.1 (20.13)</td>
<td>134.4 (20.11)</td>
<td>135.9 (20.15)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>77.7 (10.42)</td>
<td>78.9 (9.82)</td>
<td>78.4 (10.06)</td>
</tr>
</tbody>
</table>

* Median (Interquartile range)  
* SD = standard deviation  
* LDL = low-density lipoprotein  
* HDL = high-density lipoprotein

Table 3. Factors associated with HbA1c levels by Multiple Linear Regression

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>b coefficient (95% CI of β)</th>
<th>t statistic (df)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting blood glucose (mmol/L)</td>
<td>0.236 (0.189, 0.283)</td>
<td>9.94 (200)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Educational level</td>
<td>0.000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No formal education</td>
<td>-0.965 (-1.550, -0.380)</td>
<td>-3.25 (200)</td>
<td>0.001</td>
</tr>
<tr>
<td>Primary education</td>
<td>-0.625 (-1.228, -0.021)</td>
<td>-2.04 (200)</td>
<td>0.042</td>
</tr>
<tr>
<td>Secondary and tertiary education</td>
<td>-0.625 (-1.228, -0.021)</td>
<td>-2.04 (200)</td>
<td>0.042</td>
</tr>
<tr>
<td>Marital status</td>
<td>0.000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>0.933 (0.426, 1.440)</td>
<td>3.63 (200)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Married</td>
<td>0.000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HC with FMS</td>
<td>-0.495 (-0.913, -0.076)</td>
<td>-2.33 (200)</td>
<td>0.021</td>
</tr>
</tbody>
</table>

* IRLS robust regression (n=208), R² = 0.353  
* CI = confidence interval  
* df = degree of freedom

High FBG, having had no formal education, being married and receiving diabetic care in HC with Family Medicine Specialist (FMS) in this study.

Even though FBG is not exactly an associated factor for HbA1c levels, but it was found to have highly significant association with the HbA1c levels. This finding is similar with a few other studies which found highly significant correlation between FBG and HbA1c levels (Schmitt et al., 2000; Bonora et al., 2002). HbA1c levels is currently accepted as the recommended tools to monitor the glycaemic control in diabetic patients because it can measure the average control during the preceding two to three months (Goldstein et al., 2004). However, the result of this study and supported by the few other studies gave a justification for the usage of FBG levels to monitor the glycaemic control in diabetic patients during clinic follow-up, especially in remote or rural areas where the HbA1c testing might not be easily available.

Formal education was found to be significantly associated with better HbA1c levels in this study. A study done in Pakistani Moslems with type 2 diabetes showed that illiterate women were more likely to have poorer glycaemic control and less likely to understand about the management of diabetes, thus they might find it more difficult to learn how to apply their knowledge to daily life (Hawthorne and Tomlinson, 1999). There is still unclear relationship between literacy and health, however, people with low literacy are more likely to report having poor health, using the emergency room and being admitted as inpatients. Patients illiteracy could be the underlying cause of non-compliance to medication, simply because they cannot read their drug prescription (Marcus, 2006).

Health literacy, defined as the skills needed to perform basic reading and numerical tasks required to function in the health care environment, might also play a role in the outcome of diabetes. It is more common among patients with low educational level, elderly and ethnic minorities (Ad Hoc Committee on Health Literacy, 1999). Patients with poor health literacy levels would have difficulty in doing simple and more difficult tasks, such as reading a simple prescription label, or more difficult instructions such as complex dosing schedules, physician recommendations, educational brochures, etc. (Schillinger et al., 2002, Rothman et al., 2004). A study found that diabetic patients with low health-literacy had significantly poorer knowledge about the treatment of diabetes (Rothman et al., 2002). Another study found that inadequate health literacy was independently associated with worse glycaemic control (Schillinger et al., 2002). Unfortunately, physicians rarely think about patients' health literacy. With current practice
Factors Associated with HbA1c, Levels in Poorly Controlled Type 2 Diabetic Patients in North-East Malaysia

Epidemiology of Diabetes Complication Study found that patients who received specialist care were significantly associated with lower HbA1c levels (Zgibor et al., 2000).

The benefits of subspecialty care in management of diabetic patients include better information, dedication, commitment, focus and attention to the spectrum and complexities of life for these patients. Specialists may also have more experience and comfort with OHA and thus be more aggressive with their use when glycaemic control is inadequate (Cobin, 2002; Shah et al., 2005). Specialists were also thought to demonstrate less "clinical inertia", defined as the recognition of a problem with a patient's management but fail to act (Shah et al., 2005). Clinical inertia could be the cause of inadequate glycaemic control in diabetic patients because their health care providers failed to intensify their management accordingly. Specialists were found to be more aggressive with insulin initiation than primary care physicians, which reflects specialists' greater familiarity with starting insulin treatment and this may contribute to the lower HbA1c levels seen with specialist care. However, clinical inertia observed in diabetes care practice could also be due to valid clinical or social circumstances, such as significant or frequent hypoglycaemia despite high levels of HbA1c, comorbidities or other patients’ factors (Shah et al., 2005).

R² value for multiple linear regression in this study is 0.353, meaning that only 35.3% of the variance in HbA1c levels in the sample was explained by the four significant variables observed. There were many other factors which could be associated with HbA1c levels in poorly controlled type 2 diabetics which were not studied here, and health care providers’ factor may also play a significant role, which is out of the scope of this study. The cross-sectional nature of this study however prevent any causal relationship to be made from any significantly associated variables found.

In conclusion, higher FBG levels and being married were significantly associated with higher HbA1c levels, while formal education and receiving diabetes care in HC with FMS were associated with better HbA1c levels in poorly controlled type 2 diabetics in Kelantan, North-East Malaysia.

ACKNOWLEDGEMENT

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