

Factors Related to Poor Glycemic Control in Type 2 Diabetic Outpatients in a Medical Center

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Purpose. Educating patients with type 2 diabetes mellitus (DM) is an important part of successful treatment. Identifying disease-related characteristics of DM will enable health-care providers to better select patients for compensatory intervention. The purpose of this study was to investigate the clinical characteristics related to glycemic control in patients with type 2 DM.

Methods. Data were collected from questionnaires administered at our out-patient clinic from April to May 2001. Patients included in this study had to be over 30 years of age and were required to undergo a minimum follow-up period of 6 months at our out-patient clinic. The glycosylated hemoglobin (HbA_{1c}) value obtained from 2 months preceding the study visit to 1 month afterward was used as measurement of short-term glycemic control (HbA_{1c}-S). The mean HbA_{1c} value and at least one other HbA_{1c} value obtained 3 months from the HbA_{1c}-S in the year preceding the visit was used as measurement of long-term glycemic control (HbA_{1c}-L).

Results. Of the 1081 questionnaires collected, 136 were eliminated because of incomplete data, resulting in a final study population of 945. Long duration of DM, illiteracy, either insulin therapy alone or in combination with oral hypoglycemic agents, and self-monitoring of blood glucose were significant factors ($p < 0.05$) related to inferior short-term glycemic control ($R^2 = 12.96\%$). Significant factors related to poor long-term glycemic control included the duration of DM, illiteracy, either insulin therapy alone or in combination with oral hypoglycemic agents, self-monitoring of blood glucose, and lack of exercise ($R^2 = 15.51\%$).

Conclusions. Type 2 diabetic patients with a long duration of DM and who are illiterate need more intensive intervention. Oral hypoglycemic agents are more appropriate than insulin. (Mid Taiwan J Med 2005;10:90-8)

Key words

clinical characteristic, factor, glycemic control, questionnaire, type 2 DM

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INTRODUCTION

Diabetes mellitus (DM) is an important public health problem worldwide and is reported to be among the five leading causes of death in most countries [1]. DM is reaching epidemic

status; it is estimated that the number of cases will approach 300 million by 2025 [2]. DM presents a substantial socioeconomic and quality-of-life burden, mainly as a result of its chronic complications. The Diabetes Control and Complications Trial [3] and the U.K. Prospective Diabetes Study (UKPDS) [4] demonstrated that microvascular complications in type 1 and type 2 DM can be reduced by improving glycemic control. Diet control, weight reduction, and adequate self-management remain the cornerstones of diabetic treatment. Because DM is a disease that requires a high level of self-management, successful patient education is an important component of glycemic control. Overall, 90% to 95% of diabetic patients have type 2 DM. However, previous evaluations of factors related to glycemic control have mainly been conducted in individuals with type 1 DM [5-9]. To our knowledge, only one group has investigated the influential factors on glycemic control among insulin-using adults with type 2 DM [10]. Thus, little is known about the characteristics related to poor glycemic control in patients with type 2 DM. We believe that knowledge of the demographic, socioeconomic and diabetes-related characteristics will enable health-care providers to better select patients for compensatory intervention. The purpose of this study was to explore the clinical characteristics related to glycemic control in patients with type 2 DM.

PATIENTS AND METHODS

Patients with type 2 DM needed to be over 30 years of age and were required to undergo a minimum follow-up period of 6 months at our out-patient clinic. Type 2 DM was diagnosed based on the criteria proposed in the 1997 Report of the Expert Committee of the American Diabetes Association [11]. The questionnaire was given to consecutive patients at the out-patient

clinic. An out-patient clinic nurse read and explained the meaning of the questions in Taiwanese to help illiterate patients complete the questionnaire. Data were collected from self-reported questionnaires administered from April to May 2001. Items in the questionnaire explored basic data, duration of DM, education level, monthly household income, therapeutic modality, status of exercise, self-monitoring of blood glucose, and diabetic education. Exercise was defined as a minimum of 30 minutes of aerobic exercise (e.g. walking, jogging, bicycling) performed long enough to sweat at least twice a week. Self-monitoring of blood glucose was defined as monitoring blood glucose at least once per week; alternative self-monitoring methods such as urinalysis were excluded. Diabetic education was defined as attending at least one individual diabetic education meeting with a diabetic educator or dietitian. The HbA_{1c} level was used as an index of glycemic control. A single HbA_{1c} value obtained from 2 months preceding the study visit to 1 month after was used as measurement of short-term glycemic control (HbA_{1c}-S) for the past 2 to 3 months. The mean HbA_{1c} value, and at least one other HbA_{1c} value obtained 3 months from the HbA_{1c}-S in the year preceding the visit, was used as measurement of long-term glycemic control (HbA_{1c}-L) for the past 6 to 12 months. HbA_{1c} level was measured by ion-exchange high-performance liquid chromatography (HPLC) (HLC-723 GHbV; Tosoh, Tokyo, Japan).

Statistical analysis

All data are presented as mean \pm standard deviation (SD). The differences between sexes were compared by either the Student *t* test or the χ^2 test. The associations between continuous variables, HbA_{1c}-S and HbA_{1c}-L, were assessed by Pearson's correlation. The within-characteristic differences of HbA_{1c}-S or HbA_{1c}-L were

Table 1. Clinical characteristics of the patients

	All (n = 945)	Men (n = 403)	Women (n = 542)	<i>p</i>
Age (yr)	61.03 ± 10.50	60.21 ± 10.83	61.63 ± 10.21	0.390
BMI (kg/m ²)	25.12 ± 3.59	24.82 ± 3.07	25.35 ± 3.93	0.020
DM duration (yr)	9.27 ± 6.61	9.00 ± 6.62	9.47 ± 6.60	0.278
Education level, No. (%)				0.001
Illiterate/uneducated	209 (22.1)	32 (7.9)	177 (32.7)	
Primary school	380 (40.2)	147 (36.5)	233 (43.0)	
Junior high school	111 (11.7)	59 (14.6)	52 (9.6)	
Senior high school	141 (14.9)	86 (21.3)	55 (10.1)	
Junior college or higher	104 (11.0)	79 (19.6)	25 (4.6)	
Monthly household income, No. (%)				0.001
< 1470 USD	716 (75.8)	274 (68)	442 (81.5)	
1470–2940 USD	145 (15.3)	82 (20.3)	63 (11.6)	
> 2940 USD	84 (8.9)	47 (11.7)	37 (6.8)	
Therapeutic modality, No. (%)				0.126
Diet control	16 (1.7)	11 (2.7)	5 (0.9)	
OHA	724 (76.6)	308 (76.4)	416 (76.8)	
OHA and insulin	154 (16.3)	60 (14.9)	94 (17.3)	
Insulin alone	51 (5.4)	24 (6.0)	27 (5.0)	
Exercise, No. (%)				0.035
No	261 (27.6)	97 (24.1)	164 (30.3)	
Yes	684 (28.9)	306 (75.9)	378 (69.7)	
SMBG, No. (%)				0.004
No	672 (71.1)	267 (66.3)	405 (74.7)	
Yes	273 (28.9)	136 (33.7)	137 (25.3)	
Diabetic education, No. (%)				0.703
No	290 (30.7)	121 (30.0)	169 (31.2)	
Yes	655 (69.3)	282 (70.0)	373 (68.8)	
HbA _{1c} -S	7.75 ± 1.55	7.66 ± 1.58	7.82 ± 1.53	0.120
HbA _{1c} -L	7.53 ± 1.42	7.48 ± 1.45	7.56 ± 1.40	0.417

Values are presented as mean ± SD. BMI = body mass index; DM = diabetes mellitus; OHA = oral hypoglycemic agent; SMBG = self-monitoring of blood glucose.

evaluated by an analysis of variance (ANOVA) and the Scheffe's test. The significant factors related to poor glycemic control were identified by multiple linear regression analysis. A *p* value of less than 0.05 was considered statistically significant.

RESULTS

In total, 1081 questionnaires were collected. Of these, 136 were eliminated because of incomplete data, resulting in a final study population of 945. Table 1 shows the clinical characteristics of the patients. The mean age was 61.03 ± 10.50 years. There was no significant difference in age between the men and women

(*p* = 0.390). The mean body mass index (BMI) was 25.12 ± 3.59 kg/m², and the mean duration of DM was 9.27 ± 6.61 years. Female patients had a higher BMI than male patients (*p* = 0.020); however, DM duration was similar between men and women (*p* = 0.278). Education level, monthly household income, exercise and self-monitoring of blood glucose status were significantly different between men and women; however, the therapeutic modality and diabetic education status were not significantly different. Of the 945 patients, 1.7% were treated with diet alone, 76.6% were treated with oral hypoglycemic agents (OHAs), 16.3% were treated with insulin and OHAs, and 5.4% were treated with insulin alone.

Table 2. Association between clinical characteristics and HbA_{1c}-S and the within-characteristic difference of HbA_{1c}-S

Characteristic	HbA _{1c} -S	<i>p</i>	Scheffe's test
Age (yr)	$\gamma = 0.055$	0.093	
BMI (kg/m ²)	$\gamma = -0.055$	0.872	
DM duration (yr)	$\gamma = 0.202$	< 0.001	
Education level		0.004	(0) > (4)
(0) Illiterate	7.99 ± 1.67		
(1) Primary school	7.73 ± 1.51		
(2) Junior high school	7.91 ± 1.62		
(3) Senior high school	7.64 ± 1.50		
(4) Junior college or higher	7.31 ± 1.35		
Monthly household income		0.396	
< 1470 USD	7.76 ± 1.53		
1470–2940 USD	7.61 ± 1.44		
> 2940 USD	7.89 ± 1.91		
Therapeutic modality		< 0.001	
(1) Diet control	6.96 ± 1.65		(3) > (1)
(2) OHA	7.52 ± 1.46		(3) > (2)
(3) OHA and insulin	8.66 ± 1.52		(4) > (1)
(4) Insulin alone	8.50 ± 1.50		(4) > (2)
Exercise		0.332	
No	7.83 ± 1.58		
Yes	7.72 ± 1.54		
SMBG		0.004	
No	7.65 ± 1.46		
Yes	8.00 ± 1.74		
Diabetic education		0.477	
No	7.70 ± 1.48		
Yes	7.78 ± 1.58		

Values are presented as mean ± SD. BMI = body mass index; DM = diabetes mellitus; OHA = oral hypoglycemic agent; SMBG = self-monitoring of blood glucose.

The mean HbA_{1c}-S and HbA_{1c}-L values were 7.75 ± 1.55% and 7.53 ± 1.42%, respectively; values were not significantly different between men and women (HbA_{1c}-S, *p* = 0.120; HbA_{1c}-L, *p* = 0.417).

Tables 2 and 3 show that age and BMI were not associated with HbA_{1c}-S and HbA_{1c}-L. DM duration positively correlated with HbA_{1c}-S and HbA_{1c}-L ($\gamma = 0.202$, *p* < 0.001; $\gamma = 0.227$, *p* < 0.001). Education level had a significant influence on glycemic control (HbA_{1c}-S, *p* = 0.004; HbA_{1c}-L, *p* = 0.003). The glycemic control of illiterate patients was worse than that of patients with at least a junior-college level of education. Monthly household income was not a significant factor related to poor glycemic control

Table 3. Association between clinical characteristics and HbA_{1c}-L and the within-characteristic difference of HbA_{1c}-L

Characteristic	HbA _{1c} -L	<i>p</i>	Scheffe's test
Age (yr)	$\gamma = 0.049$	0.139	
BMI (kg/m ²)	$\gamma = 0.012$	0.720	
DM duration (yr)	$\gamma = 0.227$	< 0.001	
Education level		0.003	(0) > (4)
(1) Illiterate	7.76 ± 1.15		
(2) Primary school	7.51 ± 1.39		
(3) Junior high school	7.59 ± 1.31		
(4) Senior high school	7.50 ± 1.50		
(5) Junior college or higher	7.07 ± 1.28		
Monthly household income		0.598	
< 1470 USD	7.55 ± 1.42		
1470–2940 USD	7.43 ± 1.35		
> 2940 USD	7.48 ± 1.56		
Therapeutic modality		< 0.001	
(1) Diet control	6.77 ± 1.01		(3) > (1)
(2) OHA	7.29 ± 1.32		(3) > (2)
(3) OHA and insulin	8.43 ± 1.38		(4) > (1)
(4) Insulin alone	8.40 ± 1.52		(4) > (2)
Exercise		0.064	
No	7.67 ± 1.45		
Yes	7.47 ± 1.41		
SMBG		0.007	
No	7.44 ± 1.35		
Yes	7.74 ± 1.56		
Diabetic education		0.219	
No	7.44 ± 1.31		
Yes	7.57 ± 1.46		

Values are the mean ± SD. BMI = body mass index; DM = diabetes mellitus; OHA = oral hypoglycemic agent; SMBG = self-monitoring of blood glucose.

(HbA_{1c}-S, *p* = 0.396; HbA_{1c}-L, *p* = 0.598). The therapeutic modality was a significant factor (HbA_{1c}-S, *p* < 0.001; HbA_{1c}-L, *p* < 0.001). Therapy consisting of insulin, alone or in combination with OHAs, indicated worse glycemic control than diet control or OHAs alone. Exercise and diabetic education status were not significant factors, but exercise was marginally significant in long-term glycemic control (*p* = 0.064) (Table 3). Patients who self monitored their blood glucose had poorer glycemic control than those who never monitored their blood glucose (HbA_{1c}-S 7.65 ± 1.46% vs 8.00 ± 1.74%, *p* = 0.004; HbA_{1c}-L 7.44 ± 1.35% vs 7.74 ± 1.5%, *p* = 0.007).

Table 4. Multiple linear regression analysis of the predictors of glycemic control

Variable	HbA _{1c} -S		HbA _{1c} -L	
	β (SE)	<i>p</i>	β (SE)	<i>p</i>
Age	0.011 (0.008)	0.178	0.007 (0.007)	0.318
Female	0.024 (0.104)	0.821	-0.055 (0.096)	0.567
Age \times duration	-0.002 (0.001)	0.032	-0.001 (0.001)	0.025
DM duration	0.126 (0.046)	0.007	0.124 (0.042)	0.004
Education 1	-0.298 (0.131)	0.023	-0.319 (0.120)	0.008
Education 2	-0.136 (0.182)	0.454	-0.222 (0.166)	0.182
Education 3	-0.409 (0.180)	0.023	-0.275 (0.162)	0.091
Education 4	-0.833 (0.213)	0.000	-0.701 (0.187)	0.000
Income 2	0.162 (0.148)	0.273	—	—
Income 3	0.436 (0.184)	0.182	—	—
DM Rx 2	0.351 (0.373)	0.348	0.355 (0.373)	0.341
DM Rx 3	1.327 (0.391)	0.001	1.326 (0.387)	0.001
DM Rx 4	1.036 (0.429)	0.016	1.186 (0.419)	0.005
SMBG	0.237 (0.109)	0.030	0.211 (0.101)	0.037
Exercise	—	—	-0.200 (0.100)	0.045
	F = 9.888, total R^2 = 12.96%		F = 12.638, total R^2 = 15.51%	

EC = estimated coefficient; SE = standard error; Education 1 = primary school; Education 2 = junior high school; Education 3 = senior high school; Education 4 = junior college or higher; Income 2 = household income 1470–2940 USD; Income 3 = household income > 2940 USD; DM Rx 2 = OHA; DM Rx 3 = OHA and insulin; DM Rx 4 = insulin alone; SMBG = self-monitoring of blood glucose.

Multiple linear regression analysis revealed that a long duration of DM, illiteracy, therapy consisting of insulin, alone or in combination with OHAs, and self-monitoring of blood glucose were significant factors related to poor short-term glycemic control (Table 4). These four predictors accounted for 12.96% of the variance ($R^2 = 0.1296$) (Table 4). The highest regression coefficients were for the therapeutic modality of OHAs combined with insulin ($\beta = 1.327$), followed by the therapeutic modality of insulin alone ($\beta = 1.036$), an education level of junior college or higher ($\beta = -0.823$), self-monitoring of blood glucose ($\beta = 0.237$), and duration of DM ($\beta = 0.126$). In addition to these four predictors, a lack of exercise was also a significant factor related to poor long-term glycemic control. The estimated coefficient for exercise was -0.200 ($p = 0.045$). These five predictors accounted for 15.51% of the variance ($R^2 = 0.1551$) (Table 4).

DISCUSSION

Type 2 DM is a progressive disease in

which β cells deteriorate with DM duration; most patients require a multi-pharmaceutical approach to control their plasma glucose level. The UKPDS revealed that the HbA_{1c} level in both conventional and intensive groups decreased in the first study year and then subsequently increased with each following year. The median HbA_{1c} level in the intensive group was 6.6% in the first 5-year follow-up period but progressively increased to 8.1% in the third 5-year follow-up period [4]. Our result was consistent with the UKPDS which reported that the longer a patient has DM the poorer glycemic control will be. However, Nichols and co-workers demonstrated that a shorter duration of DM was a factor related to poor glycemic control [10]. This discrepancy may have been due to the different inclusion criteria. In our study, we excluded patients in whom DM had recently been diagnosed and those with a follow-up period of less than 6 months because the initial HbA_{1c} levels do not reflect real short-term glycemic control. In addition, glycemic control in those individuals was unstable during

the first few months.

Considering the benefits and risks of intensive glycemic control and the lifespan of patients, controlling blood glucose levels is less important in elderly patients than in young patients. Thus, we would expect that age is a factor related to poor glycemic control, as shown by Nichols and co-workers [10]. However, age was not a factor related to glycemic control in our study. They also found that lower BMI was the strongest and most consistent factor related to poor glycemic control. Their explanation was that improved glycemic control causes weight gain, a finding consistent with the UKPDS in which the intensive group gained 2- to 5-kg compared with the conventional group. Individuals in the intensive group gained weight, but their glycemic control worsened over time. In our study, BMI was not a significant factor related to glycemic control. Harris and co-workers also found that BMI was not related to glycemic control [12].

Socioeconomic status is often an important factor in morbidity among nondiabetic patients. One study [7] revealed that education level and income were related to glycemic control in patients with type 1 DM; a low education level, a low monthly income, and a low socioeconomic status indicated poor glycemic control. However, Harris and co-workers [12] showed that education level and income were not factors related to glycemic control in patients with type 2 DM. In our study, we found that illiteracy but not income was a factor related to poor glycemic control. The finding that illiteracy is related to poor glycemic control may be explained by the fact that a lack of understanding of DM, OHAs and insulin, leads to poorer compliance and more patients switching to alternative medications.

Most patients with type 2 DM achieve good glycemic control when they are initially treated with OHAs, but only approximately 50% continue to have satisfactory glycemic control

after 10 years [13]. This clinical phenomenon is referred to as secondary failure of OHAs. The annual rate of secondary failure is about 0.7% to 2.7% per year [14]. These individuals are then often treated with insulin alone or OHAs combined with insulin. Our study revealed that therapy consisting of insulin, alone or in combination with OHAs, was a factor related to poor glycemic control. This finding was consistent with that reported by Harris and co-workers [12,15]. Poor glycemic control is most common among insulin-treated patients because the majority of them are patients with secondary failure of OHAs or patients presenting with chronic complications of DM. In fact, glycemic control is more difficult to achieve in those individuals than in individuals in whom DM responds to OHAs alone. This study was performed before the introduction of thiazolidinedions; therefore, whether glycemic control with three OHAs (sulfonylurea plus biguanide plus thiazolidinedions) in patients with secondary failure (maximal dose of sulfonylurea plus biguanide) is better than control with two OHAs (maximal dose of sulfonylurea plus biguanide) combined with bedtime insulin or insulin alone needs further investigation.

Education about diabetes, including knowledge about the disease and nutritional restrictions, remains one of the cornerstones of diabetic management. A model education program for patients with type 2 DM revealed that the HbA_{1c} level improved from $9.0 \pm 2.0\%$ to $7.8 \pm 1.6\%$ after 1 year of participation in a structured education program [16]. Our study showed that the HbA_{1c} level did not differ significantly between patients who were educated by a diabetic educator or dietitian and patients who were not; therefore, one education session seems to be insufficient to make a difference.

In our study, self-monitoring of blood glucose was a factor related to poor glycemic

control. This finding was consistent with that of Harris et al [12,15] but inconsistent with that of Nichols and et al [10]. We found that individuals who monitored their blood glucose had higher HbA_{1c}-S values; this observation indicates that patients with poor control are more motivated to monitor their blood glucose and that self-monitoring of blood glucose does not contribute to poor glycemic control. Our observation may also indicate that medical personnel are to blame for failing to educate patients to adjust their dosage based on the results of self-monitoring blood glucose levels.

Regular exercise is another cornerstone of diabetic management because it produces beneficial effects on this metabolic syndrome. A meta-analysis of the effects of exercise on glycemic control in patients with type 2 DM who were not being treated with drug co-interventions revealed that exercise reduced HbA_{1c} by an amount (0.66%) that should decrease the risk of diabetic complications [17]. Our study showed that exercise has a beneficial effect on long-term glycemic control. This finding supports our practice of advising our patients to exercise regularly.

In summary, the significant factors related to poor glycemic control in patients with type 2 DM were longer DM duration, illiteracy, therapeutic modality consisting of insulin, self-monitoring of blood glucose, and lack of exercise. We recommend that health-care providers pay more attention to type 2 diabetic patients with longer duration and/or who are uneducated. If there is no contraindication, OHAs should have priority over insulin. Whether glycemic control with triple oral therapy (sulfonylurea plus biguanide plus thiazolidinedions) is better than the maximal dose of sulfonylurea plus biguanide combined with bedtime insulin or insulin alone in secondary failure patients needs to be investigated further.

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某醫學中心第2型糖尿病門診病人血糖控制不良的相關因素

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目的 第2型糖尿病病人的衛教是成功治療的重要部分之一，確認病人及疾病的相關特徵，可以讓醫療照顧提供者，有較好的病人篩選依據，以提供所需的介入性衛教，本篇研究目的在探討第2型糖尿病病人血糖控制相關的臨床特徵。

方法 本研究以問卷方式收集2001年4月到5月門診病人資料作分析，納入的條件包括年齡大於30歲，及至少在門診追蹤6個月以上。進入研究前2個月內，或進入研究後1個月內的糖化血色素值，為短期血糖控制的指標(HbA_{1c}-S)。在HbA_{1c}-S之前的1年內，與HbA_{1c}-S間隔至少3個月以上的另一次糖化血色素值和HbA_{1c}-S的平均值，為長期血糖控制的指標(HbA_{1c}-L)。

結果 本研究共收集1081份問卷，剔除資料不全的136份問卷，最後共得到945份有效問卷。糖尿病罹病時間較久、文盲者、使用胰島素治療(單獨或與口服降血糖藥物併用)、自行監測血糖者，都是與短期血糖控制比較差的相關因素($p < 0.05$ ， $R^2 = 12.96\%$)。除了這些相關因素之外，缺乏運動也與長期血糖控制不佳相關($R^2 = 15.51\%$)。

結論 第2型糖尿病病人罹病時間較久、文盲者，需要更積極的介入性衛教。藥物的選擇，口服降血糖藥物優先於胰島素注射。(中台灣醫誌 2005;10:90-8)

關鍵詞

臨床特徵，因素，血糖控制，問卷，第2型糖尿病

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