TITLE PAGE

Title: Effect of Hypertension and Dyslipidemia on glycemic control among Type 2 Diabetes patients

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Abstract

Background: Type 2 diabetes is a common and serious condition associated with reduced life expectancy and considerable morbidity. Hypertension and dyslipidaemia are common co-morbidities in patients with type 2 diabetes which can lead to micro-vascular and macro-vascular complication. Strict control of blood glucose, blood pressure and cholesterol could minimize the complications of DM. Good glycemic control is essential in preventing the complication of diabetes. Little is known about the effect of co-morbidities of hypertension and dyslipidemia on glycemic control in Thailand.

Objective: To determine effect of hypertension and dyslipidemia on glycemic control in Type 2 Diabetes patients in Thailand.

Methods: This study was a hospital based cross-sectional study and also part of the an assessment on quality of care among patients diagnosed with Type 2 Diabetes and Hypertension visiting Hospitals in care of Ministry of Public Health and Bangkok Metropolitan Administration in Thailand, 2010-2012. The data were collected from the medical records of 79,543 type 2 diabetes patients. Hba1c level was the main outcome of the study and the patients were diagnosed as controlled by HbA1c level less than 7%. The type 2 diabetes patients were also categorized into 4 groups according to presence of co-morbidities; diabetes alone, diabetes with hypertension, diabetes with dyslipidemia and diabetes with both co-morbidities in order to assess the glycemic control in each group. Data analysis was done by using multiple logistic regression.

Results: In this study, 34.4% (95% CI: 34.0 -34.8) of DM patients were found to have Hba1c <7% (controlled). Among them, 42.2% (95% CI: 40.5-43.9) of patients from DM alone group, 43.2% (95% CI: 41.8-44.6) of patients from DM with hypertension group, 32.5% (95% CI: 32.8 -33.8) of patients from DM with dyslipidemia group and 33.3% (95% CI: 32.8 -33.8) of patients from DM with both co-morbidities group were getting control of HbA1c level. Bivariate logistic regression revealed that patients with dyslipidemia had 1.5 times the odds of getting uncontrolled of Hba1c level compared to patients with DM alone (OR=1.5, 95% CI:1.4-1.6). Elevated Triglyceride is significantly associated with poor glycemic control (OR=1.4, 95% CI:1.43-1.54). However hypertension was not significantly associated with HbA1c level in this study. In multiple logistic regression, DM patients with both comorbidities of hypertension and dyslipidemia had 1.5 times the odds of getting uncontrolled HbA1c level compared to DM alone patients (OR: 1.47, 95% CI:1.36-1.59).

Conclusion: According to the results, dyslipidemia was the strong predictor of determining glycemic control by Hba1c level in type 2 diabetes patients.

Key words: Type 2 diabetes mellitus, hypertension, dyslipidemia**.** HbA1c

INTRODUCTION

Diabetes is a lifelong chronic disease characterized by elevated blood sugar level. There are two main types of diabetes, referred to as type 1 and type 2. Type 2 diabetes results from insulin resistance i.e the body's cells don't respond to insulin or the body doesn't produce enough insulin from the pancreas(1).Diabetes is a global endemic with rapidly increasing prevalence in both developing and developed countries. It is projected that the number of individuals with diabetes will rise from an estimated 385 million in 2010 to 439 million in 2030(2). Majority of them are from developing world (3).In Thailand NCDs are estimated account for 71% of all deaths in which diabetes was contributed 6%. According to 2010 WHO data base, about 7.3% of the individuals had diabetes in Thailand(4). Hypertension, overweight and dyslipidemia are often accompanied with Type 2 diabetes that affect morbidity and mortality (5)(6).

Good glycemic control is essential in preventing diabetic complications such as cardiovascular diseases, diabetic nephropathy and retinopathy etc.(6). The level of glycosylated hemoglobin (HbA1c) provides a useful measure of the glycemic control of diabetes patients (7)(8). Studies in other countries revealed that there was a positive correlation between Triglyceride level and HbA1c (9)(10). HbA1c was also associated with body mass index and hypertension(11).

Diabetes has been considered as a global concern to reduce morbidity and mortality. Although many studies on DM have undertaken worldwide, little is known about the effect of Hypertension and Dyslipidaemia on HbA1c level in Thai population with Nationally representative sample. The aim of this study was to determine effect of hypertension and dyslipidemia on glycemic control in Type 2 Diabetes patients by HbA1c level.

MATERIALS AND METHODS

Study design

This study was a hospital based cross-sectional study and utilized the data that is part of the study: "An assessment on quality of care among patients diagnosed with Type 2 Diabetes and Hypertension visiting Ministry of Public Health and Bangkok Metropolitan Administration Hospitals in Thailand (Thailand DM/HT)" which was conducted from 2010 to 2012. Nationally representative sample of 174,578 patients with diabetes and/or hypertension were randomly selected from 600 hospitals across Thailand. The sample was selected based on the probability proportional to size of the patients for each hospital. Data collection involved medical record review conducted by well trained research nurses.

Study outcome The primary outcome of this study was the proportion of DM patients who were getting control of diabetes by HbA1c level less than 7% according to absence or presence of comorbidities and the effect of co-morbidities (hypertension and dyslipidemia) on the HbA1C level was the secondary outcome. The patients were considered to have dyslipidemia if there was at least one abnormal level in the lipid profile (LDL >100 mg/dl, HDL <40 mg/dl, and triglycerides >150 mg/dl) and have hypertension if the blood pressure was more than 130/80 mmHg(12).

Statistical analysis

- *Methods for describing baseline characteristics of the sample:* Demographic characteristics of the participants were described using frequency and percentage for categorical data and mean and standard deviation for continuous data.
- *Methods for answering the research question(s):* The proportion of the patients with HbA1c level<7% was calculated among four different category groups; diabetes alone, diabetes with hypertension, diabetes with dyslipidemia and diabetes with both hypertension and dyslipidaemia. The 95% confidence interval (CI) was also computed based on normal approximation to binomial distribution. To determine the effect of hypertension and dyslipidemia on HbA1c level, odds ratios (ORs) and their 95% confidence intervals (95%CIs) were estimated using multiple logistic regression and adjusted for demographic characteristics and those showing the univariate relationship with the outcome variable such as age, gender, BMI and duration of diabetes etc.

- *Software, level of significant, and ethics*: the data were analyzed by Stata software version 12.0 (Stata Corp, College Station, TX). All test statistics were two-sided and a p-value of less than 0.05 was considered statistical significant. This project was approved by ethical board of Khon Kaen University.

RESULTS

A total of 3.373,089 type 2 DM and/or hypertension patients were visited the hospitals in care of Ministry of Public Health and Bangkok Metropolitan Administration in Thailand during 2010 to 2012. From 174,578 randomly selected patients, 95,035 were excluded for being having hypertension alone, hence 79,543 type 2 DM patients were included in the analysis (Fig.1)

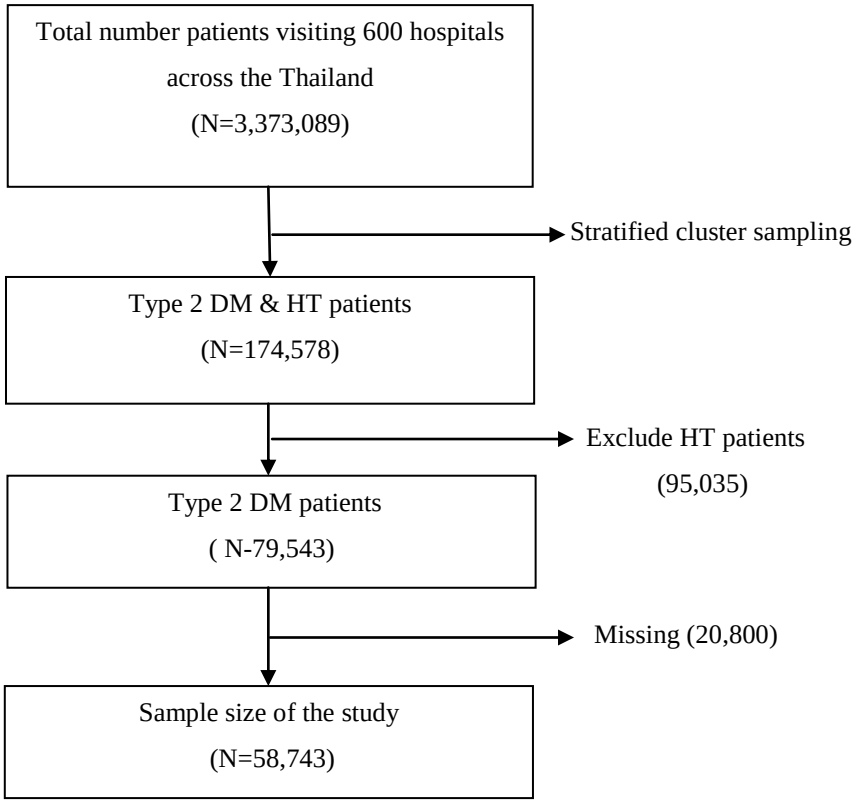

Fig. 1. The inclusion flow chart

Characteristics of patients

Among 79,543 Type 2 DM patients, majority of them (89.9%) were female, with mean age of (59.3±10.7) years ranged from 20 to 98 years. They were mainly agricultural workers (42,8%) followed by housekeeper (23.3%). Mean duration of diabetes was (7.17±4.64) and only one third, 34.46% of the patients had good glycemic control. More than half (61.47%) of the patients had hypertension and majority of the patients (85.69%) had comorbidity of dyslipidaemia.

Table 1. Characteristics of type 2 diabetic patients.

Characteristics	No.	Percentage
Age		
Mean ± standard deviation		59.3±10.7
Median (Min:Max)		60(20,98)
Gender		
Male	17,529	29.95
Female	41,145	70.05
Total	58,737	100.0
Occupation		
Farmer or farm worker	24,074	41.85
Government employee	2,554	4.42
Trader or Merchant	4,435	7.71
State Enterprise Employee	237	0.41
Private corporation officer	443	0.77
Laborer (include day labors)	9,975	17.34
Student	17	0.03
Housekeeper/ unemployed person	13,617	23.67
Self-Employed/Own Business	180	0.31
Monk/nun/priest	223	0.39
Other	1,774	3.09
Total	57,519	100.0
BMI(Kg/m2)		
< 25	26,666	49.16
25 to 30	19,925	36.74
>30	7,647	14.10
Total	54,238	100.0
Mean ± standard deviation		25.5± 4.44
Median (Min:Max)		25.1(8,98,91.96)
Duration of diabetes		
< 7 years	24,744	61.66
≥ 7 years	15,370	36.32
Total	40,114	100.0
Mean ± standard deviation		7.17±4.64
Median (Min:Max)		6(0,55)
HbA1c level		
< 7%	20,242	34.46
≥ 7%	38,501	65.54
Total	587,43	100.00
Mean ± standard deviation		8±1.9
Median (Min:Max)		1.6(1,17)
Hypertension		
Yes	36,028	61.47
No	22,585	38.53
Total	58,613	100.0
Dyslipidaemia		
Yes	47,169	85.69
No	7,874	14.31
Total	55,043	100.0

TG level	26,544	52.31
< 150mg/dl	24,197	47.69
≥ 150mg/dl	50,741	100.0
Total		161.81±73.5
Mean ± standard deviation		146(40,400)
Median (Min:Max)		
LDL level	22,598	43.29
< 100mg/dl	29,607	56.71
≥ 100mg/dl	52,205	100.0
Total		110.69±36.9
Mean ± standard deviation		106(40,400)
Median (Min:Max)		
HDL level	16,730	34.61
< 40mg/dl	31,611	65.39
≥ 40mg/dl	48,341	100.0
Total		45.29±12.2
Mean ± standard deviation		44(20,100)
Median (Min:Max)		

Proportion of patients who are getting control with HbA1c level less than 7%

Out of 58,743 patients, 34.4% (95% CI: 34.0 -34.8) were getting control of HbA1c level. Among them 42.2% (95% CI: 40.5-43.9) of patients from patients with diabetes alone group, 43.2% (95% CI: 41.8-44.6) of patients from DM with hypertension group, 32.5% (95% CI: 32.8 -33.8) of patients from DM with dyslipidemia group and 33.3% (95% CI: 32.8 -33.8) of patients from DM with hypertension and dyslipidemia group were getting glycemic control (i.e HbA1c level less than 7%)**.**

Factors associated with Hba1c level

In type 2 diabetes patients, dyslipidemia is significantly associated with HbA1c level, DM patients with dyslipidemia were 1.5 times the odds of getting uncontrolled HbA1c level compared to those patients without dyslipidemia (OR=1.47, 95% CI:1.36-1.59). High level of triglyceride was a strong risk factor for poor glycemic control (OR=1.46, 95% CI: 1.40-1.51).

Table. 2. Crude odds ratios (OR) and 95% CI for getting poor glycemic control by using logistic regression analysis

Variable	Total	% Hba1c>7%	Crude OR	95%CI	p-value
Comorbities					<0.001
DM alone	1,843	57.76	1		
DM with HT	2,652	56.81	0.96	0.89-1.05	
DM with Dyslipidaemia	12,159	67.46	1.52	1.40-1.63	
DM with both	19,380	66.70	1.46	1.36-1.58	
Gender					<0.001
Male	10,885	61,87	1		
Female	27,614	67.11	1.25	1.21-1.30	

Age					<0.001
< 60 years	20,427	71.64	1		
≥ 60 years	18,009	59.75	0.59	0.57-0.61.	
Triglyceride					<0.001
<150 mg/dl	16,160	60.88	1		
≥150 mg/dl	16,888	69.79	1.40	1.43-1.54	
HDL					<0.001
≥40 mg/dl	20,540	64,98	1		
<40 mg/dl	11.309	67.60	1.12	1.08-1.17	
LDL					<0.001
<100 mg/dl	14,077	62.29	1		
≥100mg/dl	20,192	68.20	1.29	1.25-1.35	
BMI(Kg/m2)					<0.001
< 25	17,158	64.34	1		
25 to 30	13,401	67.26	1.14	1.09-1.18	
>30	5,252	68.68	1.22	1.15-1.28	
Duration of DM					<0.001
< 7 years	15,521	62.73	1		
≥ 7 years	10,973	71.39	1.48	1.42-1.55	

Table. 3. Odds ratios (ORs) for getting poor glycemic control and their 95% confidence intervals for each factor adjusted for all other factors presented in the table using multiple logistic regression.

Variable	Total	% Hba1c >7%	Crude OR	Adjusted OR	95%CI	p-value
Comorbities						<0.001
DM alone	1,843	57.76	1	1		
DM with HT	2,652	56.81	0.96	1.00	0.92-1.10	
DM with Dyslipidaemia	12,159	67.46	1.52	1.47	1.36-1.59	
DM with both	19,380	66.70	1.46	1.47	1.36-1.59	
Age						<0.001
<60 years	20,427	71.64	1	1		
≥60 years	18,009	59.75	0.59	0.57	0.55-0.59	
Duration of Diabetes						.<0.001
<7 years	15,521	62.73	1	1		
≥7 years	10,973	71.39	1.48	1.61	1.54-1.69	
Triglyceride						<0.001
<150 mgdl	16,160	60.88	1	1		
≥150 mgdl	16,888	69.79	1.40	1.46	1.40-1.51	

The effect of hypertension and dyslipidemia on determining HbA1c level of type 2 diabetes patients

The dyslipidemia, comorbidity of diabetes, was the strong predictor of determining the HbA1C level, i.e. DM patients with dyslipidemia comorbidity were 1.5 times the odds of getting poor glycemic control than those with diabetes alone (OR = 1.47; 95% CI: 1.36-1.59; $p < 0.001$). However hypertension is not associated with glycemic control in this study (OR = 1.00; 95% CI: 0.92-1.10; $p < 0.001$).

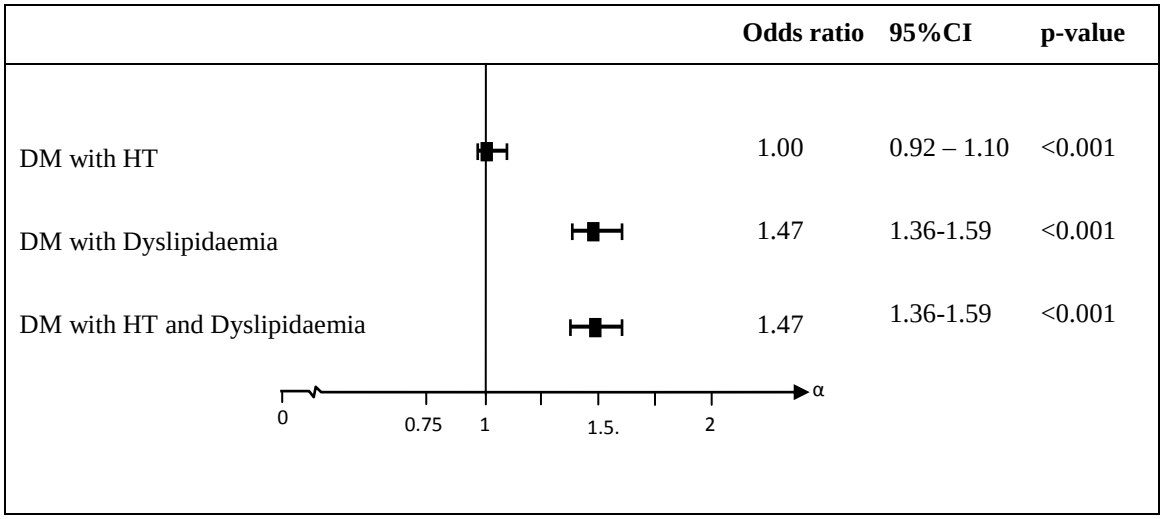

Fig. 2 The effect of hypertension and dyslipidaemia on determining Hba1C level, presented as odds ratio adjusted for age, gender, duration of diabetes using multiple logistic regression

DISCUSSIONS

According to the results, out of total 58,743 patients, only 34.46 % of the type 2 DM patients had good glycemic control, however majority of them did not achieve the target goal of HbA1c level <7%. Based on the data from Thai Diabetes Registry Project in 2006, only 37.7% of their participants were getting control of HbA1c <7%(13). Hence it is essential to pay greater attention on achieving good glycemic control of Type 2 DM patients in Thailand. The majority of the patients achieving the targeted goal of HbA1c level were old age group of more than 60 years which was not different from the study conducted in Malaysia(14) . This was because the mature patients perceived themselves to have better glycaemic control over their lives. Poor glycaemic control was associated with longer duration of diabetes which was not different from the study undertaken in Jodern(15).

The overall prevalence of hypertension, dyslipidemia and the obesity (BMI>30) of this population were 61.5%, 85.7% and 14.1 % respectively. Only 33% of the patients from DM with both comorbidities had good glycemic control. Poor glycemic control could be due to the presence of comorbities of hypertension and dyslipidemia . Both hypertension and dyslipidemia in diabetes patient can predispose to cardiovascular disease (CVD). Achieveing target goal of HbA1c level less than 7% is essential for preventing diabetic complications (5). This study revealed that there was no association between hypertension and HbA1c level which was not consistent with other studies (10). This could be the limitation of this study not being considered by antihypertensive use. Elevated TG level (47.75%) and raised LDL level (56.7%) were the prevalent pattern of dyslipidaemia in this study. Dyslipidemia, due to elevated TG and LDL, was significantly associated with poor glycaemic control in this study population. It was consistent with the studies conducted in other countries (8)(9).

In conclusion, majority of the type 2 DM patients in Thailand had poor glyeacmic control. More than half of the patients have hypertension and almost all the patients were coexisting with dyslipidaemia. Of particular interest there was no association between hypertension and HbA1c level. However DM patients with dyslipidaemia had 50% chance of getting poor glycemic control than patients with DM alone. Therefore dyslipidaemia was the strong predictor of determining glycemic control by HbA1c level.

Strength of the study

This study consisted of Nationally representative samp[le of larger sample size.

Limitation of the study

This cross- sectional study was limited to data available in hospital and not obtained prospectively. Comparisons cannot be made with community-based studies. Insufficient data and missing values were unavoidable because of the secondary data.

The design of study was cross-sectional study that showed the association of each factor might not be able to determine the cause and effect of each associated factor.

Conclusions

According to the results, dyslipidaemia was the strong predictor of determining glycaemic control by Hba1c level. Reduction of the modifiable risk factors such as BMI, hypertension and dyslipidaemia and good glycemic control through public health efforts may help to reduce the risk of DM and its chronic complications.

Recommendations

- Emphasize more on health education about risk factors, complications , treatment and glycaemic control of diabetes to the public.
- Population based and prospective study should be conducted in the future.

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