Thailand Diabetes Registry Project: Current Status of Dyslipidemia in Thai Diabetic Patients

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Objective: *To determine the prevalence of dyslipidemia in adult Thai type 2 diabetes who attended diabetes clinics in university and tertiary-care hospitals.*

Material and Method: *A cross-sectional, multi-center, hospital-based diabetes registry was conducted in 11 diabetic clinics in tertiary medical centers in Bangkok and major provinces between April and December, 2003. A group of 9,419 diabetic patients were registered. Individual Demographic data including education and socioeconomic status were collected. The results of the physical examination for complications, history screening and laboratory results were recorded. The prevalence of the various complications of diabetes was analyzed and the percentage achievement of metabolic control calculated.*

Results: *Of the 9,419 diabetic patients registered 8,769 had complete demographic and plasma lipid data. Mean age was 59.5 13.3 years. The percentage of male patients was 33.9%. In the present study, there were 8464 type 2 diabetes and 383 type 1 diabetes. History of coronary artery disease and cerebrovascular disease were present in 8.1 and 4.2 percent of the patients, respectively. More than 80% of the patients had dyslipidemia. The patients with CVD had higher proportion of achieving the LDL target (< 100 mg/dl, 43 vs 34%). More than half of the patients (55%) were taking lipid lowering medications, but one-third (30%) did not despite having fulfilled indications. The patients covered by government supported health plan were less likely to received lipid-lowering medication than the patients covered by private health plans(OR 0.65, 95%CI 0.57-0.75). The two most commonly used lipid-lowering agents were HMG CoA reductase inhibitors (76%) and fibrates (19%), both agents were used in combination in 5% of the patients. Only 40.1% of the patients on lipid-lowering medications reached the target LDL goal (<100 mg/dl).*

Conclusion: *Elevated LDL cholesterol was the most common lipid abnormality in the present study. Although 55% of the patients were taking lipid lowering agents, another 42% of the patients needed the medication. More than half of the patients treated needed more intensive lipid lowering in order to achieve the LDL goal. If the authors wish to follow the current(2005) American Diabetes Association recommendations, we would have to treat up to 97% of diabetic patients with lipid lowering agents.*

Keywords: *Diabetes registry, Diabetes, Dyslipidemia, Lipid lowering agents*

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CardioVascular Disease (CVD) is the most common cause of death in diabetic patients, three-quarters of diabetic patients die from CVD. The risk of CVD in diabetes is equivalent to that in patients who have history of coronary artery disease[1]. Patients who have both diabetes and coronary artery disease are at greatest risk. Lipid lowering is one of the important strategies for reducing CVD events[2]. The NCEP III categorized diabetics in the group with as high coronary risk as patients with established coronary artery disease, and their LDL cholesterol levels should be lowered to less than 100 mg/dl[3].

Recent studies suggest that a more aggressive target for lipid lowering may have added benefits[4,5]. The Heart Protection Study (HPS)[4] demonstrated that for diabetic patients over 40 years of age who also had total cholesterol levels of more than 135 mg/dl, the reduction of LDL levels by 30% from baseline resulted in a 25% reduction in the first event rate for major coronary artery events; independent of baseline LDL, pre-existing vascular disease, type or duration of diabetes, or adequacy of glycemic control.

In the Collaborative Atorvastatin Diabetes Study (CARDS)[5], patients with type 2 diabetes randomized to 10 mg atorvastatin daily had a similar significant reduction in cardiovascular events including stroke. Recent clinical trials, in high-risk patients such as those with acute coronary syndromes or previous cardiovascular events[6-8],have demonstrated that more aggressive therapy with high doses of HMG CoA reductase inhibitors-with the aim of achieving an LDL of less than 70 mg/dl-led to a significant reduction in further cardiovascular events.

From the above evidence, the American Diabetic Association (ADA) had recommended[9] that the serum lipid targets for diabetic patients should be: LDL-cholesterol less than 100 mg/dl, triglycerides less than 150 mg/dl and HDL-cholesterol more than 40 mg/dl for males and 50 mg/dl for females. According to the results of HPS, the ADA (2005) recommended more aggressive lipid lowering strategy. The diabetics over 40 years of age and having serum total cholesterol more than 135 mg/dl should receive a lipid lowering agent to decrease their serum cholesterol by 30-40% and to lower their LDL-cholesterol to less than 100 mg/dl and to less than 70 mg/dl for patients with a previous CVD history.

Understanding the current dyslipidemia status in diabetics is very important for health policy. Making the appropriate recommendations is, more complicated than finding effective treatments since the process involve an assessment of cost-effectiveness of each treatment. However, we first need to know the current lipid situation among Thai diabetic patients; therefore, the authors conducted a multi-center registry of diabetic patients in 11 tertiary care hospitals and medical schools across the country.

Material and Method

The Diabetic Registry Project is a cross-sectional, hospital-based study carried out between April and December, 2003. This multi-center registry was conducted in the diabetic clinics of eleven tertiary care centers in university and regional hospitals in Thailand. The present study was approved by the ethics committees at each participating hospital and signed informed consents were obtained from all the participants.

The diagnosis of diabetes mellitus was made according to the ADA criteria 1997[10]. The patients treated in the diabetes clinics who expected to come for follow-up for at least one year were registered. The registry data were recorded on a case record form. The authors included: demographic data; pertinent parts of physical examinations; laboratory examinations performed within 12 months prior to registration; specific medications (including insulin, oral hypoglycemic agents, antihypertensive agents, lipid lowering agents and aspirin); and, diabetic complications verified by physician's reports.

Fasting plasma glucose, serum total cholesterol, HDL cholesterol (HDL-C) and triglyceride levels were determined by the enzymatic methods. LDL cholesterol (LDL-C) was calculated using the Friedewald's formula (LDL-C = total cholesterol – HDL-C – TG/5). Glycosylated hemoglobin (HbA1c), plasma creatinine, and urine microalbumin levels were determined by the central laboratory of each hospital using standard methods with local quality control. Urine analysis was performed using a urine specimen taken in the morning.

Blood pressure was measured on the right arm after resting 5 minutes (twice, 30 seconds apart) using an automated blood pressure machine (OMRON T4). Hypertension was defined as systolic blood pressure > 140 mmHg and/or diastolic blood pressure > 90 mmHg, or was considered present if the patient was being treated with antihypertensive drugs. Height and weight were measured in light clothing and were used for Body Mass Index (BMI) calculation. Information on alcohol consumption, cigarette smoking, medication and history of diabetes were obtained through an interview.

The authors categorized smoking status as: 1) current smokers were still smoking on the day of examination or quitted smoking for less than one year; 2) ex-smokers had stopped smoking for at least one year; and, 3) non-smokers-had never smoked.

The authors defined drinking status as: 1) current drinkers-continued to drink up to the day of the examination; 2) abstainers-had not drunk for at least one year before the examination; and, 3) non-drinkers-had never drunk or had drunk < 2 times per month.

The authors categorized healthcare coverage into government supported health plan (including universal health coverage and social security welfare) or privately paid health insurance.

The patients with dyslipidemia were defined as all patients who had been taking lipid lowering agents and patients without lipid lowering agents whose lipid levels were over the target (i.e. LDL < 100 mg/dl). In 2005, the ADA recommended a more aggressive lipid strategy. Diabetic patients over 40 years old with serum total cholesterol > 135 mg/dl should receive a lipid lowering agent in order to decrease serum cholesterol by 30-40% and the LDL-cholesterol to < 100 mg/dl (for patients without any previous CVD history or 70 mg/dl for patients with a previous CVD history).

Statistical analysis

Category data of studied variables were compared with Chi-square test and Fisher's exact tests. Differences in mean values of studied variables were compared using t- test and Mann-Whitney U test with 0.05 levels of significance.

The crude odds ratio was calculated to define each factor that influenced the use of lipid lowering agents. Confounding factors were then adjusted by applied multiple logistic regression and this was calculated to define the factors that influenced the use of lipid lowering agents. Whenever two variables were very similar and had multi-co-linearity, only one of them was included in the model.

Statistical analyses were performed using STATA version 8.0 (STATA Corporation, College Station TX, US).

Results

Complete demographic and plasma lipid concentration were available for 8,769 of the 9,419 registered diabetic patients, comprising 8,464 patients with type 2 diabetes and 383 with type 1 diabetes. In this population, 9.2% had a history of CVD (8.0 and 4.3% for coronary artery disease and cerebrovascular disease, respectively) (Table 1).

The diabetic patients with a history of CVD were older and had a longer duration of diabetes. Glycemic control in these patients was at the same level as those without history of CVD. The patients with CVD (vs those without CVD) had a higher proportion of achieving the LDL target (i.e. LDL < 100 mg/dl, 43 vs 34%). More than 80% of the study patients had dyslipidemia (*i.e.* an LDL > 100, triglycerides > 150 or HDL < 40, 50 mg/dl).

Half of the study patients (55%) were taking lipid-lowering medications, however, another one-third (30%) did not take any lipid-lowering medication even though they should. The lipid-lowering medications most used were HMG CoA reductase inhibitors (76%) and fibrates (19%). They were used in combination

Table 1. Patient characteristics divided by history of cardiovascular disease

	DM without CVD (n = 7728)		DM with CVD (n = 1041)		p-value
Age (year)	59.2	(12.5)	66.0	(9.2)	<0.05
Female sex (%)	67.2%		58.9%		<0.05
Duration of DM (year)	10.1	(7.4)	13.6	(8.5)	<0.05
BMI (Kg/m^2)	25.6	(4.3)	25.7	(4.3)	NS
HbA1c (%)	8.2%	(1.9)	8.2%	(1.9)	NS
Lipid lowering medication	53.1%		57.2%		<0.05
LDL < 100 mg/dl	34.2%		43.1%		<0.05
LDL < 70 mg/dl	7.4%		11.1%		<0.05
HDL > 40 (male), 50 (female) mg/dl	68.4%		63.6%		<0.05
Triglyceride < 150 mg/dl	63.5%		58.4%		<0.05
Any dyslipidemia	83.0%		80.1%		<0.05

about 5% of the time. Only about 40.1% of the medication-taking patients reached the LDL goal < 100 mg/dl (Table 2).

After a multiple logistic regression was performed by adjusting for age, sex, history of CVD, history of hypertension, health plan, obesity, retinopathy and smoking status, the authors found that patients with a history of cardiovascular disease had twice changed to taking lipid lowering agents (OR 2.1, 95%CI 1.8-2.6). The patients who were covered by a government health plan had less chance of getting lipid-lowering medication (OR 0.61, 95%CI 0.53-0.70) than those who were covered by private health plans (Fig. 1).

Although the patients on the government plan had less chance of getting lipid-lowering agents, the difference in serum lipid levels in each plan was not significant (i.e. 114.7 ± 35.1 vs 116.7 ± 33.0 mg/dl, NS). They also had a similar proportion of optimum plasma lipid levels (LDL < 100 mg/dl) (35.8 vs 32.9%).

If the authors agreed that the first priority of pharmacological therapy is to lower LDL cholesterol to a target goal of 100 mg/dl, about 87% of diabetic patients would need lipid-lowering agents. If the authors used current ADA recommendation, almost all diabetic patients, especially those over 40 years old, would need lipid-lowering medication (Table 3).

Discussion

The authors demonstrated that dyslipidemia is very common among diabetics. More than 80% of the presented diabetic patients were diagnosed with dyslipidemia. The present study showed a higher rate of dyslipidemia than a previous report[11]. This finding may be explained by changes in the diet and life-style of diabetic patients.

About 55% of our diabetic patients had been taking lipid-lowering agents and HMG CoA reductase inhibitor is the most commonly used. Although more than half of the presented patients were taking lipid-lowering agents, only 35.3% of our patients achieved a plasma LDL < 100 mg/dl and only 40.1% of medication-taking patients achieved a reduction in LDL to < 100 mg/dl.

The patients who had a history of CVD got better lipid care than to those without history of CVD. The diabetic patients with a history of CVD had a higher proportion of patients whose plasma LDL was either less than 100 or less than 70 mg/dl and, they also had higher chance of taking lipid-lowering agents (OR 2.1, 95%CI 1.8 -2.6). The present finding may reflect the physician's concern in the importance of lipid lowering treatment in diabetic patients with established cardiovascular disease.

The difference in health plans may influence access to lipid-lowering agents. Patients on the government supported health plans had less chance of getting lipid-lowering agents; notwithstanding, the data showed no evidence of a compromise in their lipid care, as indicated by the non-significant difference in the plasma LDL and the number of patients who achieved a plasma LDL < 100 mg/dl between patients using government supported vs other health plans.

Table 2. Percentage of diabetic patients whose plasma was LDL < 100 mg/dL^{-1} (n = 8769)

Patient*	No lipid lowering agents	Taking lipid lowering agents	All
LDL < 100 mg/dl	1137 (29.3)	1962 (40.1)	3099 (35.3)
LDL > 100 mg/dl	2743 (70.7)	2927 (59.9)	5670 (64.7)
Total	3880 (100)	4889 (100)	8769 (100)

*The parameter values are presented with number of patients (%)

Table 3. Percentage of diabetic patients who may need lipid lowering agents

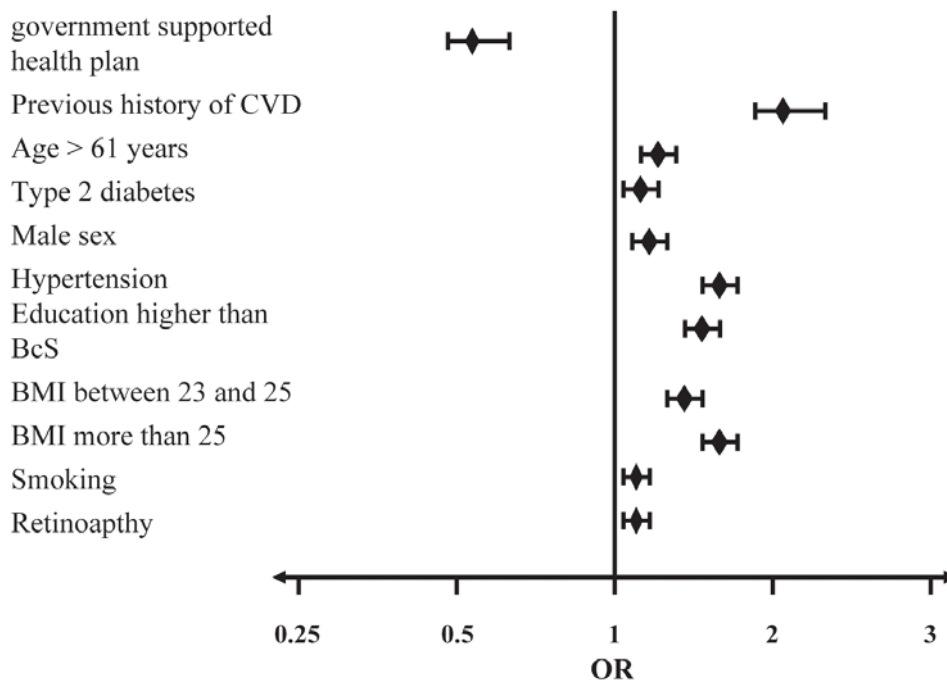| Patient*	NCEP III target	New 2005 ADA lipid target	
		All	Age > 40
No need for lipid lowering agents	13	2.7	1.4
Need for lipid lowering agents	87	97.3	98.6

Fig. 1 Multiple logistic regressions of factors that influenced the need for using lipid-lowering agents

Conclusion

Elevated LDL cholesterol was the common type of dyslipidemia found in the present registry of diabetics. Although more than half of the patients (55%) were taking lipid-lowering medications, an additional 30% needed to be taking lipid-lowering agents if the authors wished to follow the intensive lipid-lowering strategy according to the 2005 ADA recommendation[9]. Thus, the authors may recommend all patients take lipid-lowering agents together with aspirin for prevention of CVD and especially in diabetic patients age more than 40. A cost-effectiveness study of the new recommendation is necessary.

Acknowledgments

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โครงการลงทะเบียนผู้ป่วยเบาหวานในประเทศไทย: สถานการณ์เกี่ยวกับโรคไขมันในเลือดสูงในผู้ป่วยโรคเบาหวานในประเทศไทย

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วัตถุประสงค์: เพื่อศึกษาถึงความชุกของโรคไขมันในเลือดสูง, และการควบคุมระดับไขมันในผู้ป่วยเบาหวานชนิดที่ 2 ที่เป็นผู้ใหญ่ที่มารับการรักษาที่คลินิกโรคเบาหวานของโรงพยาบาลมหาวิทยาลัยและโรงพยาบาลศูนย์

วัสดุและวิธีการ: การศึกษานี้เป็นการลงทะเบียนผู้ป่วยเบาหวานที่มารับการรักษาที่คลินิกเบาหวานของโรงพยาบาลระดับตติยภูมิทั้งหมด 11 แห่ง มีการเก็บข้อมูลด้านประวัติ, การตรวจร่างกายและการตรวจเลือดเพื่อนำมาวิเคราะห์หาความชุกของโรคไขมันในเลือดสูง, ปัจจัยที่เกี่ยวข้อง, การใช้ยาลดไขมันและการควบคุมระดับไขมันในผู้ป่วยเหล่านี้

ผลการศึกษา: ความชุกของไขมันในเลือดสูงในผู้ป่วยเบาหวานชนิดที่ 2 ที่เป็นผู้ใหญ่คิดเป็นร้อยละ 80 ประมาณร้อยละ 55 ของผู้ป่วยเบาหวานได้รับการรักษาด้วยยาลดไขมัน เพียงร้อยละ 42 ของผู้ป่วยที่ได้รับการรักษาด้วยยาลดไขมันสามารถลดระดับ LDL ให้น้อยกว่า 100 มก. ต่อ ดล. นอกจากนี้ ร้อยละ30 ของผู้ป่วยไม่ได้รับยาลดไขมัน แม้มีความจำเป็นต้องได้รับ โดยผู้ป่วยที่ได้รับการสนับสนุนค่าใช้จ่ายในการรักษาพยาบาลจากรัฐบาล จะมีโอกาสที่ได้รับยาลดไขมันน้อยกว่ากลุ่มอื่น ยา HMG CoA reductase inhibitor และFibrate เป็นยาที่นิยม ใช้มากที่สุด 76% และ 19% ถ้าจะรักษาผู้ป่วยตามข้อแนะนำใหม่ปี พ.ศ. 2548 ของสมาคมโรคเบาหวาน แห่งสหรัฐอเมริกา ประมาณร้อยละ 97 ของผู้ป่วยโรคเบาหวานอาจจำเป็นต้องได้รับยาลดไขมัน

สรุป: การควบคุมระดับไขมันในผู้ป่วยเบาหวานในประเทศไทย ยังทำได้น้อยกว่าเกณฑ์เป้าหมายมาก โดยเฉพาะถ้าจะปฏิบัติตามข้อแนะนำใหม่ปี พ.ศ. 2548 ของสมาคมโรคเบาหวานแห่งสหรัฐอเมริกา ดังนั้นจึงควรมีมาตรการที่ช่วยส่งเสริมให้มีการตระหนักถึงความสำคัญของโรคไขมันสูงในผู้ป่วยโรคเบาหวาน โดยตั้งเป้าไปที่ทั้งผู้ป่วยและแพทย์ผู้รักษา