Current Status of Dyslipidemia in Type 2 Diabetes Mellitus, Its Associated Factors, Its Association with Vascular Complications and Patterns of Lipid Lowering Therapy in Maharat Nakhon Ratchasima Hospital

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Abstract

Cardiovascular disease (CVD) is the major cause of death in diabetic patient. In order to decrease CVD, management of dyslipidemia is very important. American diabetes association (ADA) recommended that plasma LDL cholesterol should be <100 mg/dL. Currently (2005), ADA recommended more aggressive LDL target. Diabetic patients with plasma cholesterol >135 mg/dL must be treated except for the patients <40 years old. Plasma cholesterol must be lower by 30-40% with LDL <100 mg/dL for primary and 70 mg/dL for secondary CVD prevention. Understanding about current dyslipidemia status in people with diabetes is very important milestone for CVD Prevention diabetics. **Objectives**: To demonstrate a current status of dyslipidemia in type 2 diabetes mellitus, to demonstrate the associated factors of good lipid control, to demonstrate the association of lipid levels and the vascular complications and to demonstrate the patterns of lipid lowering therapy in Maharat Nakhon Ratchasima hospital. **Material and Methods**: One thousand type 2 diabetic patients who attended at least one year at diabetic clinics in Maharat Nakhon Ratchasima hospital from April to December 2003 were recruited. Individual demographic data including education, socioeconomic status, diabetic complications and plasma lipid concentration and other metabolic parameters within six months were recorded based on the ADA guideline. **Results**: There were 1,000 type 2 diabetes (Age 59.4±6.8 years, M: F 27.3%: 72.7%) from 1,066 diabetic patients. In this group, mean fasting plasma glucose was 151.9±54.2 mg/dL while HbA1c was 7.9±2.1 mg/dL. Seventy-five percent had hypertension, 6.1% had a history of coronary artery disease and 3.6% had a history of cerebrovascular disease. Plasma lipid profiles were mean total cholesterol of 203.8±47.2 mg/dL, mean LDL-C of 115.2±38.7 mg/dL, mean triglyceride of 164.7±106.7 mg/dL and mean HDL-C of 55.9±16.0

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mg/dL. Only 34.4% took lipid lowering agents, 27.3% with statin only, 5.9% with fibrate only and 1.4% with a combination. More than half of diabetic patients (65.6%) did not take lipid lowering agents, even ones who had LDL-C >100 mg/dL. **Conclusion:** Elevated LDL cholesterol was the most important dyslipidemia in diabetes. But only about 35% took lipid-lowering agents. The association between vascular complication and level of lipid control was demonstrated however correlation between cardiovascular disease and lipid level control was not identified.

บทคัดย่อ: ภาวะไขมันผิดปกติในเลือด ภาวะแทรกซ้อนทางหลอดเลือดและ การใช้ยาลดระดับไขมันในเลือด ในผู้ป่วยเบาหวานชนิดที่ 2 ในโรงพยาบาลมหาราชนครราชสีมา

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ภูมิหลัง: เป็นที่ทราบกันดีว่าโรคหัวใจและหลอดเลือดเป็นสาเหตุการเสียชีวิตที่พบได้บ่อยในผู้ป่วยเบาหวาน หนึ่งในปัจจัยเสี่ยงที่สำคัญคือภาวะไขมันผิดปกติในเลือด ซึ่งพบร่วมกับผู้ป่วยเบาหวาน การรักษาภาวะไขมันผิดปกติดังกล่าวจึงนับว่ามีความสำคัญเป็นอย่างยิ่ง สมาคมแพทย์โรคเบาหวานแห่งสหรัฐอเมริกาได้แนะนำให้ลดระดับไขมัน LDL-C ให้น้อยกว่า 100 มิลลิกรัมต่อเดซิลิตร และในปี พ.ศ. 2548 ได้แนะนำให้ลดระดับไขมัน LDL-C ต่ำลงยิ่งขึ้น โดยผู้ป่วยเบาหวานที่มีอายุมากกว่า 40 ปี (และมีระดับไขมัน LDL-C มากกว่า 135 มิลลิกรัมต่อเดซิลิตร) ควรลดระดับไขมันให้น้อยกว่า 100 มิลลิกรัมต่อเดซิลิตรในกรณีที่ยังไม่มีโรคหัวใจและหลอดเลือด และลดให้น้อยกว่า 75 มิลลิกรัมต่อเดซิลิตรในกรณีที่เป็นโรคหัวใจและหลอดเลือดแล้ว การศึกษาภาวะไขมันผิดปกติในเลือด ในผู้ป่วยเบาหวาน จึงมีความสำคัญ **วัตถุประสงค์:** เพื่อแสดงความผิดปกติของระดับไขมันในเลือดในผู้ป่วยเบาหวานชนิดที่ 2 ปัจจัยที่อาจจะมีผลต่อความผิดปกติดังกล่าว แสดงความสัมพันธ์ระหว่างความผิดปกติของไขมันในเลือดกับภาวะแทรกซ้อนทางหลอดเลือด นอกจากนี้ยังแสดงถึงการรักษาความผิดปกติของไขมันโดยการใช้ยาลดระดับไขมันในเลือด **ผู้ป่วยและวิธีการ:** ศึกษาผู้ป่วยเบาหวานชนิดที่ 2 ระหว่าง เดือนเมษายน-ธันวาคม 2546 จำนวน 1,000 ราย ที่คาดว่าจะมาติดตามการรักษาที่คลินิกผู้ป่วยเบาหวาน โรงพยาบาลมหาราชนครราชสีมาเป็นเวลาอย่างน้อย 1 ปี เก็บข้อมูลเกี่ยวกับระดับการศึกษาและเศรษฐฐานะ ผู้ป่วยได้รับการตรวจร่างกายเพื่อค้นหาภาวะแทรกซ้อนของเบาหวาน ตรวจเลือดเพื่อวัดระดับไขมันในระยะ 6 เดือนแรกของการติดตามการรักษา บันทึกผลของการควบคุมเบาหวาน ระดับไขมันในเลือดและความชุกของภาวะแทรกซ้อนจากเบาหวาน โดยอาศัยเกณฑ์จากแนวทางการรักษาผู้ป่วยเบาหวานโดยสมาคมแพทย์เบาหวานแห่งสหรัฐอเมริกา **ผลการศึกษา:** ผู้ป่วยเบาหวานชนิดที่ 2 จำนวน 1,000 ราย อายุเฉลี่ย 59.4±6.8 ปี สัดส่วนเพศชายและเพศหญิงร้อยละ 27.3 และ 72.7 ตามลำดับ ค่าเฉลี่ยของระดับน้ำตาลในเลือดขณะอดอาหารเท่ากับ 151.9±54.2 มิลลิกรัมต่อเดซิลิตร ค่าเฉลี่ยของ HbA1c เท่ากับ 7.9±2.1 มิลลิกรัมต่อเดซิลิตร พบภาวะความดันโลหิตสูงร่วมด้วยร้อยละ 70.5 เคยมีโรคหลอดเลือดหัวใจตีบร้อยละ 6.1 เคยมีโรคหลอดเลือดสมองร้อยละ 3.6 ค่าเฉลี่ยระดับไขมันคอเลสเตอรอลในเลือดเท่ากับ 203.8±47.2 มิลลิกรัม ต่อเดซิลิตร ค่าเฉลี่ยระดับไขมัน LDL-C เท่ากับ 115.2±38.7 มิลลิกรัมต่อเดซิลิตร ค่าเฉลี่ยระดับ

ไขมันไตรกลีเซอไรด์เท่ากับ 164.7±106.7 มิลลิกรัมต่อเดซิลิตร ค่าเฉลี่ยระดับไขมัน HDL-C เท่ากับ 55.9±16.0 มิลลิกรัมต่อเดซิลิตร จากการศึกษานี้พบว่าผู้ป่วยเบาหวานชนิดที่ 2 ร้อยละ 34.6 เท่านั้น ที่ได้รับยาลดระดับไขมันในเลือด โดยได้รับยาในกลุ่ม statin ร้อยละ 27.3 ได้รับยาในกลุ่ม fibrate ร้อยละ 5.9 และร้อยละ 1.4 ได้รับยาทั้ง 2 ชนิด มากกว่าครึ่งหนึ่งของผู้ป่วยกลุ่มนี้ยังไม่ได้รับยาลดระดับไขมันในเลือด โดยเฉพาะกลุ่มผู้ป่วยที่มีระดับไขมัน LDL-C เท่ากับหรือมากกว่า 100 มิลลิกรัมต่อเดซิลิตร มีจำนวนร้อยละ 65.7 ที่ยังไม่ได้รับยาลดระดับไขมันในเลือด **สรุป:** ภาวะไขมันในเลือดสูง โดยเฉพาะระดับไขมัน LDL-C สูง เป็นความผิดปกติของไขมันที่มีความสำคัญที่พบได้บ่อยในผู้ป่วยเบาหวานชนิดที่ 2 แต่พบว่ามีผู้ป่วยเพียงแค่ร้อยละ 35 เท่านั้นที่ได้รับการรักษาโดยได้รับยาลดระดับไขมันในเลือด นอกจากนี้ จากการศึกษายังแสดงถึงความสัมพันธ์ของความผิดปกติของไขมันในเลือดกับการเกิดภาวะแทรกซ้อนทางหลอดเลือด แต่อย่างไรก็ตามการศึกษานี้ไม่สามารถแสดงความสัมพันธ์การเกิดโรคหลอดเลือดหัวใจกับความผิดปกติของไขมันในเลือด

Introduction

Cardiovascular disease (CVD) is the most common cause of death in diabetic subjects. Three-fourths of diabetic patients dies of CVD. Coronary artery disease is the most common CVD in diabetic subjects. Diabetic subjects have risk of CVD equivalent to the subjects with history of coronary artery disease[1]. The subjects who have both diabetes and history of coronary artery disease have much worse fate. Lipid lowering is one of the important strategies in reducing CVD[2]. As coronary risk categorized by NCEP III the target of LDL-c level in diabetic subjects must be low as in subjects with history of coronary artery disease[3]. Recent studies showed more aggressive target of lipid lowering might add more benefits[4,5]. The Heart Protection Study (HPS) demonstrated that diabetic patients over the age of 40 years with a total cholesterol >135 mg/dL, LDL reduction about 30% from baseline with simvastatin was associated with 25% reduction in the first episode of major coronary artery events independent of baseline LDL, preexisting vascular disease, type or duration of diabetes or adequacy of glycemic control. Similarly in the Collaborative Atorvastatin Diabetes Study (CARDS), patients with type 2 diabetes randomized to atorvastatin 10 mg daily had a 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 statins to achieve an LDL less than 70 mg/dL led to a significant reduction in further events. Thus, American Diabetic Association recommended[9] that serum lipid target for diabetic subjects are LDL-cholesterol less than 100 mg/dL, triglyceride less than 150 mg/dL and HDL-cholesterol more than 40 (male), 50 (female) mg/dL. According to HPS information, ADA recommended more aggressive lipid strategy. The diabetic subjects who are more than 40 years old with serum total cholesterol more than 135 mg/dL should receive lipid lowering agent in order to decrease serum cholesterol by 30-40% and LDL-cholesterol to less than 100 (for the subjects without previous CVD history), 70 (for the subjects with previous CVD history) mg/dL.

Understanding about current dyslipidemia status in people with diabetes is very important for making appropriate recommendation in management of coronary risk in diabetic population. Objectives of this study are to demonstrate a current status of dyslipidemia in patients with type 2 diabetes mellitus, to demonstrate the associated factors of good lipid control, to demonstrate the association of lipid levels and the vascular complications, and to demonstrate the patterns of lipid lowering therapy in Maharat Nakhon Ratchasima Hospital.

Research Design and Methods

Setting and Subjects

This is a part of the Diabetic Registry Project in Maharat Nakhon Ratchasima Hospital, a cross-sectional study, which was carried out from April to December 2003. It was conducted in the diabetic clinic of Maharat Nakhon Ratchasima Hospital which is a tertiary care centers in Thailand. The subjects of this study were diabetic patients treated in our diabetic clinic and needed to accept to be participants in this registry. The diagnosis of diabetes mellitus was made according to the American Diabetes Association criteria 1997[10]. The total number of diabetic patients who were registered at Maharat Nakhon Ratchasima hospital was 1,066. From those, 66 patients were type 1 diabetes and 1,000 patients were type 2 diabetes and only type 2 diabetic patients were included in the analysis.

Methods and Measurements

The registry data were recorded in the case record form by interviewing and examining the patients and reviewing their medical records which composed of demographic data, pertinent physical examination, laboratory examinations performed during the last 12 months of recruitment, specific medications including insulin, oral hypoglycemic agents, antihypertensive agents, lipid lowering agents and aspirin and diabetic complications. All of them were verified by physician's reports.

Blood pressure was measured at right arm, after 5-minute rest, twice for 30 seconds apart, by using an automated blood pressure machines (OMRON T4). Hypertension was defined as systolic blood pressure $\geq$ 140 mmHg and/or diastolic blood pressure $\geq$ 90 mmHg, or was considered to be present if the patient was being treated with antihypertensive drugs. Height and weight were measured in light clothing and body mass index was calculated as weight (kg) / height $(m)^2$. Information on alcohol consumption, smoking, medication and history of diabetes were obtained by interview.

Eye examinations within one year from registry day emphasizing on retinal examinations, visual acuity and cataract findings were performed. The retinal examinations were evaluated by the opthalmologists from each center with direct opthalmoscopy after full dilatation of pupils. Levels of retinopathy were classified into non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) categories[11]. NPDR was defined and characterized by an increase in vascular permeability or vascular closure; such as microaneurysms, dot and blot hemorrhage and exudates. PDR was defined if there was vasoproliferation of new vessels on or within the retina including its complications such as vitreous hemorrhage or pre-retinal hemorrhage. Severity of retinopathy was based on the

grading of the worse eye. Visual acuity was assessed by using the Snellen's chart. Legal blindness was defined as visual acuity of less than 6/60 in the better eye with best possible correction.

Nephropathy was and defined as the followings; positive microalbuminuria was defined if two of three tests were positive within one year, proteinuria was defined if urine dipstick test for protein was at least 1+ level, and renal insufficiency was defined when serum creatinine >2 mg/dL.

History of ischemic heart disease (IHD) was classified into two categories according to a clinical diagnosis; definite IHD in cases of positive and cardiac catheterization, cardiac stress test or history of myocardial infarction and possible IHD in cases of a history of angina or using medications for IHD without definite IHD. A history of stroke was classified into three categories; ischemic stroke, hemorrhagic stroke and unknown.

We defined smoking status into three categories; current smoking was one who continued smoking until the day of examination or who quitted smoking less than one year before the day of examination, ex-smoker was one who quitted smoking at least one year before the day of examination and non-smoking was one who had never smoked.

We defined alcoholic drinking status into three categories; current drinking was one who continued drinking until the day of examination, abstinence was one who quitted alcoholic drinking at least one year before the day of examination, and non-alcoholic drinking was one who had never drunk alcohol or drank less than 2 times per month.

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 = total cholesterol-HDL-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 by using a urine specimen in the morning.

The study was approved by the ethic committee of the Endocrine Society of Thailand and by the ethic committee of each hospital. Informed consent for the study was obtained from all participants.

Statistical methods

Descriptive statistics was used to describe the studied subjects. Proportions of studied variables were compared with Chi-square and Fisher's exact tests. Differences in mean values of studied variables were compared by using t-test and Mann-Whitney U test. The crude odds ratio was calculated to define a univariate association between a lipid profile level and an occurrence of each vascular complication. Statistical analyses were performed with STATA version 8.0 (Stata Coroperation, College Station TX, U.S.). If p- values were ≤ 0.05, they would be considered statistically significant.

Results

From 1,066 diabetic patients, 1,000 subjects who were diagnosed as type II diabetes were recruited for the analysis. There were 727 females and 273 males. Patients' age ranged from 33 to 83 years with a mean age of 59.4 ± 6.8 years and the duration of diabetes varied

from newly diagnosed to 30 years. Mean fasting plasma glucose was 151.9±54.2 mg/dL and mean HbA1c was 7.9±2.1 mg/dL. In this group, 70.5% had hypertension, 6.1% had a history of coronary artery disease and 3.6% had a history of cerebrovascular disease. Plasma lipid profiles were mean total cholesterol of 203.8±47.2 mg/dL, mean LDL-C of 115.2±38.7 mg/dL, mean triglyceride of 164.7±106.7 mg/dL and mean HDL-C of 55.9±16.0 mg/dL. The percentages of patients with type 2 diabetes mellitus according to the levels of lipid control were demonstrated in Table 1. According to the recommen-dations for adults with diabetes mellitus from the American Diabetes Association (ADA)[9], 35.8% of the patients had LDL-C less than 100 mg/dL, 56.9% had triglyceride less than 150 mg/dL and 66.2% had HDL-C level more than 40 mg/dL in male and more than 50 mg/dL in female.

Table 1 Percentage of patients with types 2 diabetes according to the levels of lipid control

Levels of lipid control	Percentage
LDL (mg/dL)	
< 100	35.8
100 - <130	31.6
130 - <160	21.0
≤ 160	11.6
Triglyceride (mg/dL)	
< 150	56.9
150- <400	39.4
≤ 400	3.7
HDL (mg/dL)	
male > 40 & female > 50	66.2
male ≤ 40 & female ≤ 50	33.8

Clinical characteristics associated with good LDL-C level (less than 100 mg/dL), according to the ADA recommendation[3], were demonstrated in Table 2, ie. systolic BP, diastolic BP, body mass index (BMI), gender (less female), smoking status and hypertension status. The group of patients with good LDL-C levels had lower means of systolic BP, diastolic BP and BMI, lower percentages of female gender and hypertension but a higher percentage of current smoking than those with higher LDL-C levels. Nevertheless, age of patients, duration of diabetes, fasting plasma glucose, HbA1c, serum creatinine, triglyceride, HDL-C and alcoholic drinking status were not significantly associated with a good LDL-C level.

Clinical characteristics associated with a good triglyceride level (less than 150 mg/dL), according to the ADA recommendation, were shown in Table 3, ie. diastolic BP, fasting plasma glucose, total cholesterol, LDL-C, BMI and hypertension status. The group of patients with a good triglyceride level had lower means of diastolic BP, fasting plasma glucose, HbA1c, total cholesterol, LDL-C, HDL-C level, BMI and a lower percentage of hypertension. The following factors were not significantly associated with a good triglyceride level ie. gender, age of patients, duration of diabetes, systolic BP, serum creatinine, smoking and alcoholic drinking status.

Clinical characteristics associated with good HDL-C level (>40 mg/dL in male and >50 mg/dL in female), according to the ADA recommendation, were demonstrated in Table 4, ie. total cholesterol, triglyceride, gender, status of smoking and alcoholic drinking. The group of patients with a good HDL-C level had a lower

Table 2 Clinical characteristics according to LDL-C levels in type 2 diabetes

Parameters*	LDL-C < 100 mg/dL	LDL-C ≤100 mg/dL	*P*-value
Age (years)	59.8±11.1	59.2±10.7	0.400
Duration of DM (years)	8.4±7.1	8.1±6.6	0.449
Systolic BP (mmHg)	138.0±24.0	143.7±23.9	<0.001
Diastolic BP (mmHg)	76.5±11.5	78.5±12.4	0.010
FBS (mg/dL)	151.1±57.7	152.3±52.3	0.754
HbA1c (%)	7.8±2.0	8.0±2.2	0.225
Creatinine (mg/dL)	1.5±1.2	1.4±1.0	0.669
Total cholesterol (mg/dL)	167.0±29.1	224.3±42.7	<0.001
Triglyceride (mg/dL)	166.1±115.8	163.9±101.3	0.764
HDL-C (mg/dL)	54.8±17.5	56.6±15.0	0.105
LDL-C (mg/dL)	77.5±16.9	136.3±30.6	<0.001
BMI (kg/m2)	24.4±4.4	25.5±4.6	<0.001
Female (%)	67.8	75.4	0.009
Smoking (%)			0.018
Non-smoking	77.9	84.9	
Ex-smokers	13.8	9.9	
Current smoking	8.4	5.3	
Alcohol (%)			0.764
Non-drinking	72.0	72.0	
Abstinence	14.3	15.6	
Current drinking	13.7	12.4	
Hypertension (%)	66.4	72.8	0.034

* Data are presented as mean ± standard deviation (SD) and percentages.

mean of triglyceride level and lower percentages of female patients and alcoholic drinking than a group with lower HDL-C levels. Nevertheless, the group of good HDL-C level had higher total cholesterol and LDL-C and also higher percentages of current smoking and current alcoholic drinking. Moreover, other factors which were not significantly associated with a good HDL-C level included age of patients, duration of diabetes, systolic BP and DBP, fasting plasma glucose, HbA1c, serum creatinine, BMI and hypertension status.

Table 5, 6 and 7 demonstrated the univariate associations between vascular complications of type 2 diabetic patients and the levels of LDL-C, triglyceride and HDL-C respectively. AS compared with a group of diabetic patients with LDL-C <100 mg/dL, a group with LDL-C of 130-<160 mg/dL had a significant association with an occurrence of hypertension with an odds ratio (OR) (95% confidential interval) of 1.14 (1.02-1.27). Whereas a group with LDL-C of >160 mg/dL had significant associations with an occurrence of hyper-

tension with OR of 1.18 (1.04-1.33), with DR (both NPDR and PDR) with OR of 1.86 (1.15-3.01) and also with PDR with OR of 2.16 (1.11-4.20).

AS compared with a group of diabetic patients with a triglyceride level <150 mg/dL, a group with triglyceride level 150-<400 mg/dL had significant associations with an occurrence of hypertension with OR of 1.09 (1.00-1.18) and with positive proteinuria with OR of 1.33 (1.06-1.65). Moreover, a group with triglyceride level >400 mg/dL had also significant associations with a history of peripheral vascular disease (PVD) with OR of 4.88 (2.23-10.69) and with positive proteinuria with OR of 1.87 (1.21-2.87), as compared with the group of triglyceride <150 mg/dL.

As compared with a group of diabetic patients with HDL-C ≥60 mg/dL, a group of HDL-C <40 mg/dL had significant associations with an occurrence of blindness (both DM-related and non-DM related) with OR of 3.28 (1.02-10.55), with a history of foot ulcer with OR of 2.06 (1.06-3.98), with positive proteinuria

Table 3 Clinical characteristics according to triglyceride (TG) levels in type 2 diabetes

Parameters*	**TG < 150 mg/dL**	**TG ≥ 150 mg/dL**	***P* - value**
Age (years)	59.7±11.0	59.1±10.7	0.343
Duration of DM (years)	8.4±7.1	8.0±6.2	0.386
Sytolic BP (mmHg)	141.2±24.1	142.2±24.2	0.505
Diastolic BP (mmHg)	76.9±12.4	78.9±11.6	0.011
FBS (mg/dL)	146.6±48.4	158.8±60.4	<0.001
HbA1c (%)	7.8±2.1	8.1±2.12	0.017
Creatinine (mg/dL)	1.43±1.07	1.5±1.1	0.785
Total cholesterol (mg/dL)	192.6±40.3	218.6±51.4	<0.001
Triglyceride (mg/dL)	102.0±27.6	247.4±115.6	<0.001
HDL-C (mg/dL)	59.3±16.2	51.6±14.6	<0.001
LDL-C (mg/dL)	112.8±35.9	118.3±40.7	0.029
BMI (kg/m2)	24.8±4.5	25.5±4.6	0.014
Female (%)	70.8	75.2	0.117
Smoking (%)			0.213
Non-smoking	81.3	83.8	
Ex-smokers	12.7	9.3	
Current smoking	6.0	6.9	
Alcohol (%)			0.258
Non-drinking	70.6	73.8	
Abstinence	16.7	13.0	
Current drinking	12.7	13.2	
Hypertension	67.8	74.1	0.031

* Data are presented as mean ± standard deviation (SD) and percentages.

with OR of 1.59 (1.17-2.18) and with renal insufficiency (Cr >2 mg/dL) with OR of 2.57 (1.51-4.35). Nevertheless, there was no significant association between the lipid levels and the vascular complications such as histories of amputation, ischemic heart disease (both definite and possible IHD) and cerebrovascular disease. Moreover, our study could not demonstrate an association between lipid level and a presentation of microalbuminuria due to adequate data.

About lipid lowering agents in our patients, 34.6% were taking them, 33.2% with single agent (27.3% with statin only and 5.9% with fibrate only) and 1.4% with both. More than half of the patients (65.4%) did not take lipid lowering agents. In a group of LDL-C >100 mg/dL, only 34.3% had lipid lowering agents (28.2% statin only, 4.7% fibrate only and 1.4% both). Therefore, according to the ADA recommendation, 65.7% of those with high LDL-C levels did not take lipid lowering agents

Table 4 Clinical characteristics according to HDL-C levels in type 2 diabetes

Parameters	HDL-C >40 mg/dL in male and >50 mg/dL in female	HDL-C ≤40 mg/dL in male and ≤50 mg/dL in female	*P* - value
Age (years)	59.1 ± 10.7	60.0±11.2	0.234
Duration of DM (years)	8.0 ± 6.6	8.7 ± 7.1	0.114
Systolic BP (mmHg)	142.0 ± 24.2	141.0 ± 24.0	0.537
Diastolic BP (mmHg)	78.0 ± 12.1	77.4 ± 12.2	0.472
FBS (mg/dL)	152.1 ± 51.7	151.5 ± 59.1	0.869
Hba1c (%)	8.0 ± 2.1	7.8 ± 2.1	0.172
Creatinine (mg/dL)	1.4 ± 1.1	1.5 ± 1.0	0.637
Total cholesterol (mg/dL)	209.4 ± 47.8	193.0 ± 44.2	<0.001
Triglyceride (mg/dL)	144.7 ± 79.6	204.2 ± 137.9	<0.001
HDL-C (mg/dL)	63.3 ± 14.3	41.6 ± 6.3	<0.001
LDL-C (mg/dL)	118.2 ± 39.2	109.3 ± 37.0	<0.001
BMI (kg/m2)	25.3 ± 4.6	24.8 ± 4.3	0.103
Female (%)	446 (67.3)	281 (83.4)	<0.001
Smoking (%)			<0.001
Non-smoking	79.0	89.0	
Ex-smokers	13.6	6.5	
Current smoking	7.4	4.5	
Alcohol (%)			0.002
Non-drinking	68.8	78.3	
Abstinence	15.8	13.7	
Current drinking	15.4	8.0	
Hypertension	69.4	72.7	0.277

* Data are presented as mean ± standard deviation (SD) and percentages.

Table 5 Univariate analysis between vascular complications and LDL-C levels in type 2 diabetes

Parameters	LDL 100-<130 mg/dL Odds Ratio (95%CI)*	LDL 130-<160 mg/dL Odds Ratio (95%CI)*	LDL >160 mg/dL Odds Ratio (95%CI)*
Hypertension	1.03 (0.93-1.15)	1.14 (1.02-1.27)	1.18 (1.04-1.33)
NPDR + PDR	0.91 (0.57-1.45)	1.20 (0.75-1.93)	1.86 (1.15-3.01)
Only NPDR	0.95 (0.47-1.91)	1.02 (0.46-2.23)	1.76 (0.72-4.33)
Only PDR	0.87 (0.45-1.68)	1.38 (0.73-2.62)	2.16 (1.11-4.20)
Blindness	1.87 (0.62-5.65)	1.03 (0.25-4.28)	1.94 (0.47-8.00)
History of Foot ulcer	0.96 (0.51-1.81)	1.62 (0.89-2.97)	1.55 (0.75-3.22)
History of Amputation	2.27 (0.42-12.29)	4.27 (0.84-21.82)	4.66 (0.79-27.52)
Absence of dorsalis pedis pulse	0.88 (0.45-1.74)	1.04 (0.50-2.17)	0.69 (0.24-2.00)
History of IHD †	1.00 (0.57-1.73)	0.61 (0.29-1.28)	0.62 (0.24-1.58)
History of Any Stroke	1.36 (0.60-3.10)	1.88 (0.81-4.35)	0.93 (0.26-3.31)
Only Ischemic Stroke	1.62 (0.62-4.19)	1.96 (0.72-5.34)	1.32 (0.35-5.02)
Only Hemorrhagic Stroke	1.14 (0.07-18.22)	1.75 (0.11-27.81)	0
Positive Proteinuria	0.86 (0.66-1.13)	0.88 (0.65-1.19)	1.23 (0.89-1.69)
Renal insufficiency (Cr > 2 mg/dL)	0.91 (0.55-1.51)	1.16 (0.68-1.96)	1.30 (0.71-2.40)

* Crude odd ratio with 95% confidential interval when compare with a group of LDL-C level of less than 100 mg/dL

† Ischemic heart disease which composes of definite IHD and possible IHD

Table 6 Univariate analysis between vascular complications and triglyceride levels in type 2 diabetes

Parameters	TG 150-399 mg/dL Odds Ratio (95%CI)*	TG >400 mg/dL Odds Ratio (95%CI)*
Hypertension	1.09 (1.004-1.18)	1.16 (0.97-1.38)
NPDR + PDR	0.98 (0.68-1.40)	1.04 (0.45-2.37)
Only NPDR	0.78 (0.43-1.38)	0.44 (0.06-3.10)
Only PDR	1.16 (0.71-1.92)	1.57 (0.60-4.12)
Blindness	1.46 (0.59-3.65)	1.70 (0.22-13.06)
History of Foot ulcer	1.44 (0.90-2.31)	0.96 (0.24-3.85)
History of Amputation	0.64 (1.99-2.07)	0
Absence of dorsalis pedis pulse	1.25 (0.68-2.27)	4.88 (2.23-10.69)
History of IHD †	0.91 (0.54-1.52)	1.75 (0.66-4.65)
History of Any Stroke	0.72 (0.36-1.42)	0
Positive Proteinuria	1.33 (1.06-1.65)	1.87 (1.21-2.87)
Renal insufficiency (Cr > 2 mg/dL)	1.15 (0.77-1.71)	0.94 (0.31-2.87)

* Crude odd ratio with 95% confidential interval when compare with a group of triglyceride level of less than 150 mg/dL

† Ischemic heart disease which composes of definite IHD and possible IHD

Table 7 Univariate analysis between vascular complications and HDL-C levels in type 2 diabetes

Parameters	HDL ≥ 40 - < 60 mg/dL Odds Ratio (95%CI)*	HDL < 40 mg/dL Odds Ratio (95%CI)*
Hypertension	1.03 (0.95-1.13)	1.06 (0.93-1.02)
NPDR + PDR	0.97 (0.65-1.43)	1.41 (0.86-2.32)
Only NPDR	1.33 (0.70-2.52)	1.70 (0.74-3.93)
Only PDR	0.76 (0.44-1.30)	1.33 (0.68-2.60)
Blindness	1.12 (0.37-3.39)	3.28 (1.02-10.55)
History of Foot ulcer	1.18 (0.68-2.04)	2.06 (1.06-3.98)
History of Amputation	1.39 (0.42-4.60)	1.39 (0.26-7.52)
Absence of dorsalis pedis pulse	1.38 (0.74-2.60)	1.67 (0.75-3.73)
History of IHD †	0.86 (0.50-1.48)	1.54 (0.79-3.02)
History of Any Stroke	1.60 (0.77-3.33)	0.56 (0.12-2.51)
Only Ischemic Stroke	2.20 (0.89-5.45)	0.92 (0.19-4.50)
Positive Proteinuria	1.81 (0.92-1.51)	1.59 (1.17-2.18)
Renal insufficiency (Cr > 2 mg/dL)	1.20 (0.75-1.93)	2.57 (1.51-4.35)

* Crude odd ratio with 95% confidential interval when compare with a group of HDL-C level of more or equal to 60 mg/dL

† Ischemic heart disease which composes of definite IHD and possible IHD

in spite of their need. The percentages of lipid lowering agents used in type 2 diabetic patients according to LDL-C, triglyceride and HDL-C levels were demonstrated in table 8.

Table 8 Lipid lowering agents (LLA) used in type 2 diabetes mellitus according to levels of lipid profiles

Levels of lipid control	Statin only (%)	Fibrate only (%)	Combination (%)	No LLA (%)	Total (%)
- LDL-C (mg/dL) (n=996)	27.3	5.8	1.3	65.4	100
< 100	25.8	7.8	1.1	65.3	100
100 - <130	18.7	3.8	0.3	77.1	100
130 - <160	29.7	4.8	1.9	63.6	100
≤ 160	51.3	7.0	3.5	38.3	100
- Triglyceride (mg/dL) (n=999)	27.3	5.9	1.4	65.4	100
< 150	26.4	2.8	1.1	69.7	100
150- <400	28.4	8.9	1.3	61.4	100
≥ 400	29.7	21.6	8.1	40.5	100
- HDL-C (mg/dl) (n=997)	27.3	5.9	1.4	65.4	100
male > 40 & female > 50	28.8	3.9	1.8	65.5	100
male ≤ 40 & female ≤ 50	24.3	9.8	0.6	65.3	100

Discussion

Type 2 diabetes is an important cardiovascular risk factor. A significant component of the risk in type 2 diabetes is thought to be its characteristic abnormal lipid profile ie. raised low-density lipoprotein, low high-density lipoprotein and elevated triglycerides. Lipid management aimed at lowering LDL-C, raising HDL-C and lowering triglycerides has been shown to reduce macrovascular disease and mortality in type 2 diabetes. Trials of statins and fibrates in numbers of patients with diabetes have indicated that such agents can reduce cardiovascular complications in these patients. We demonstrated the current status of dyslipidemia, its association with vascular complication and current usage of lipid lowering agents in type 2 diabetes. According to the ADA recommendation for adult with diabetes and dyslipidemia, about 36%, 57% and 66% of our diabetic patients had achieved the goal of LDL-C<100 mg/dL, triglyceride <150 mg/dL and HDL-C >40 mg/dL in male and >50 mg/dL in female respectively.

Cardiovascular disease is not only the major cause of mortality in diabetes but also a major contributor to morbidity. Type 2 diabetes and its common coexisting conditions, hypertension and dyslipidemia, are the major independent risk factors for vascular complication. We demonstrated a group of diabetes who achieved LDL-C <100 mg/dL had lower means of systolic and diastolic blood pressure, a group of diabetes who achieved triglyceride <150 mg/dL had a better diabetic control with mean FBS of 146.6 mg/dL and mean HbA1c of 7.8%. We also found that both groups of diabetes had a lower percentage of hypertension. With the univariate analysis, we could identify an association between vascular complication of type 2 diabetes and the lipid level including LDL-C, triglyceride and HDL-C, we could also demonstrate the correlation between dyslipidemia in type 2 diabetes and microvascular complications including diabetic retinopaty, blindness, positive proteinuria and renal insufficiency, and also the correlation between dyslipidemia and macrovascular complications in cases with a history of peripheral vascular disease (foot ulcer and amputation). Nevertheless, our study could not demonstrate an association of lipid level and cardiovascular complication.

Type 2 diabetes is associated with a substantially increased risk of cardiovascular disease, three-fourths of diabetes dies of cardiovascular disease and NCEP III had categorized diabetes as coronary risk, therefore its LDL-C must be lower to the same target as in coronary artery disease subjects. Many studies[2,4,5] had clearly showed the benefit of lipid lowering therapy with statin for both primary and secondary preventions of cardiovascular disease in diabetic patients. In our study, only 34.4% of our patients with type 2 diabetes took lipid lowering agents which composed of 27.3% with statin only, 5.9% with fibrate only and 1.4% with a combination. More than half of our diabetic patients (65.7%) did not take any lipid lowering agent, even in patients who had LDL-C >100 mg/dL. According to ADA recommendation, most of diabetic patients especially whose ages were >40 years old needed lipid lowering agents.

Limitation of this study

Because it is cross-sectional study, it can demonstrate only the association between the risk factors

and lipid levels without identifying any causation. Some vascular complications such as histories of IHD or CVA may be underestimated because sometimes we gathered data only by asking them without seeing any evidence, it can be a recall bias.

Conclusions

Elevated LDL cholesterol was the most important dyslipidemia in diabetes. But only about 35% of our patients took lipid lowering agents. More than half of the patients even who had LDL-C $\geq$100 mg/dL in spite of necessity, did not take lipid lowering drugs, according to ADA recommendation. We also demonstrated the association between vascular complication and level of lipid control but we could not identify correlation between cardiovascular disease and lipid level control.

Acknowledgements

This study was supported by the Health Systems Research Institute, Thailand and the Endocrine Society of Thailand. We are indebted to many staff and nurses in every center for their contribution.

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