นิพนธ์ต้นฉบับ Original Article

# Diabetic Management Status of Type 2 Diabetic Outpatients at Maharat Nakhon Ratchasima Hospital: Diabetic Registry Project

Rittha Lertkoonalak, M.D.\*, Thanya Chetthakul, M.D.\*, Puntip Tantiwong, M.D.\*, Linjong Kantisophon, M.D.\*

#### **Abstract**

**Objective:** The aim of this study is to demonstrate a current status of diabetic management, microvascular and macrovascular complications of the patients with type 2 diabetes mellitus at Maharat Nakhon Ratchasima hospital. **Materials & Methods:** A cross-sectional, hospital-based diabetes registry was carried out from the data obtained between April to December 2003 during diabetic care of diabetic patients in diabetic clinic at Maharat Nakhon Ratchasima Hospital. Results: A total of 1,066 diagnosed diabetic patients, there were 1,000 patients with type 2 diabetes mellitus registered in this study, which consisted of 273 males and 727 females. The mean age was 59.4±10.9 years and the mean duration of diabetes mellitus was 8.2±6.8 years. We found only 37.6% of these patients achieved glycemic control of fasting plasma glucose under 130 mg/dL and 31.9% had an HbA1c level less than 7%. The overall prevalence of dyslipidemia, hypertension, and obesity (body mass index, BMI >25 kg/m<sup>2</sup>) found in this population were 47.7%, 60.7%, and 47.4% respectively. Our analysis also found that diabetic nephropathy is the most common complication, accounting for 33.6% of the patients followed by retinopathy 17.1%, ischemic heart disease 6.1% and cerebrovascular disease 3.4% respectively. **Conclusion:** The higher mean age of 59 years and longer duration 8.2 years of diabetes contributed to a high prevalence of diabetic complications, especially microvascular complication. Less than half of patients had good glycemic control combined with other metabolic control of blood pressure and lipid profile. Getting an annual check up is an important strategy for early identification and management of diabetic complication.

Division of Endocrinology, Department of Medicine, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima, 30000

## บทคัอย่อ: การดูแลผู้ป่วยเบาหวานชนิดที่ 2 ที่มารับการรักษาที่โรงพยาบาลมหาราชนครราชสีมาแบบผู้ป่วยนอก: โครงการลงทะเบียนผู้ป่วยเบาหวาน

ฤทธิ์ทา เลิศคุณลักษณ์, พ.บ., ชัญญา เชฏฐากุล, พ.บ., พรรณทิพย์ ตันติวงษ์, พ.บ., ลินจง ขันติโสภณ, พ.บ. หน่วยต่อมไร้ท่อ กลุ่มงานอายุรกรรม โรงพยาบาลมหาราชนครราชสีมา นครราชสีมา 30000 เวชสาร โรงพยาบาลมหาราชนครราชสีมา 2551; 32 (ฉบับผนวก): S87-94.

วัตถุประสงค์: เพื่อแสดงถึงสถานการณ์การดูแลผู้ป่วยเบาหวานชนิดที่ 2 และภาวะแทรกซ้อนของผู้ป่วยเบาหวาน ที่เข้ารับการรักษาที่โรงพยาบาลมหาราชนกรราชสีมา วัสดุและวิธีการ: การศึกษานี้เป็นการลงทะเบียนผู้ป่วยเบาหวานที่มารับการรักษาที่กลินิกเบาหวานของโรงพยาบาลมหาราชนกรราชสีมา ช่วงเดือนเมษายน ถึง ธันวากม 2546 มีการเก็บข้อมูลด้านประวัติและการตรวจร่างกาย และตรวจเลือดเพื่อหาความชุกของโรคแทรกซ้อน การบรรลุเป้าหมาย ในการรักษาโรคแบาหวาน และกวามผิดปกติที่พบร่วม ผลการศึกษา: มีผู้ป่วยทั้งสิ้น 1,066 กน เป็นเบาหวาน ชนิดที่ 2 จำนวน 1,000 กน เป็นชาย 273 กน และหญิง 727 กน อายุเฉลี่ย 59.4±10.9 ปี และเป็นเบาหวานนานเฉลี่ย 8.2±6.8 ปี ผู้ป่วยสามารถกวบกุมระดับน้ำตาลในเลือดได้ตามเป้าหมาย ร้อยละ 37.6 และระดับ HbA1c ถึงเป้าหมายร้อยละ 31.9 นอกจากนี้ยังพบว่ามีโรคกวามดันโลหิตสูงและ ใขมันผิดปกติสูงร้อยละ 60.7 และ 47.7 ตามลำดับ โรกแทรกซ้อนส่วน ใหญ่ที่พบเป็นโรคหลอดเลือดขนาดเล็กที่ตาร้อยละ 17.1 ที่ไตร้อยละ 33.6 และพบโรคแทรกซ้อนในหัวใจและสมอง ร้อยละ 6.1 และ 3.4 ตามลำดับ สรุป: ผู้ป่วยกลุ่มนี้มีอายุเฉลี่ยสูงและเป็นโรคเบาหวานมานาน ทำให้พบความผิดปกติอื่น ร่วมด้วยมาก ยังพบว่าการควบกุมระดับน้ำตาลในเลือดและเมตาบอลิก ยังทำได้ไม่ถึงเป้าหมาย จึงทำให้เกิดภาวะแทรกซ้อนได้มาก การตรวจเพื่อกันหาภาวะแทรกซ้อนตั้งแต่ระยะแรก เช่น การตรวจจอประสาทตา และการควบคุมปัจจัย ทางเมตาบอลิกอย่างเข้มงวด อาจสามารถลดความชุกของภาวะแทรกซ้อนของเบาหวานได้

Background: The health and economic burden of diabetes mellitus (DM) and its complications are well recognized globally. The worldwide prevalence of diabetes is projected to increase by 5.4 percent by the year 2025 with 170 percent increase in developing countries, particularly in Asia (including Thailand) and Africa. In Thailand the prevalence of diabetes has risen from 5.7 percent in 1991 to 9.6 percent in 2000. Chronic diabetic complications usually develop in any patient who lives a long life with the disease. Vascular complications are the main cause of morbidity and mortality in diabetic patients. Managment of diabetes comprises not only glucose control but also control of hypertension and dyslipidemia.

The objective of this study is to demonstrate a current status of diabetic management, microvascular and macrovascular complications of patients with type 2 diabetes mellitus at Maharat Nakhon Ratchasima Hospital.

### Patients and Methods Setting and Subjects

This is a part of the Diabetic Registry Project at 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 one of tertiary care centers in Thailand. The subjects of this study were diabetic

patients being treated in our diabetic clinic at Maharat Nakhon Ratchasima Hospital. The diagnosis of diabetes mellitus was made according to the American Diabetes Association (ADA) criteria 1997. (6) A total numbers of diabetic patients in this study who were registered at Maharat Nakhon Ratchasima Hospital were 1,066. From those patients, only 1,000 patients were type 2 diabetes and 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 consisted of demographic data, pertinent parts of physical examinations, laboratory tests 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 after resting for 5 minutes on the right arm twice for 30 seconds apart by using an automated blood pressure machines (OMRON T4 , Omron Corporation, Japan). 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 (BMI) was calculated as weight (kg)/height (m)². Information on alcohol consumption, smoking, medication and history of diabetes were obtained by interview.

Results of eye examinations within one year after registry date were recorded; including the results of retinal examinations, visual acuity, and cataract findings by the ophthalmologists with direct ophthalmoscope after full dilatation of pupils. Level of retinopathy was classified into non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) categories. (7) 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 occurring on or within the retina including its complications such as vitreous hemorrhage or pre-retinal hemorrhage. Level 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 evaluated and defined as the followings; positive microalbuminuria within one year which was confirmed for elevated urine microalbumin levels done at least two of three collections, overt proteinuria which was defined as a positive urine dipstick test at least 1+ level, and renal insufficiency which was defined when serum creatinine was more than 2 mg/dL.

We defined a history of ischemic heart disease (IHD) into two categories according to a clinical diagnosis; definite IHD and possible IHD. Definite IHD was one who had a positive result from cardiac catheterization or cardiac stress test, or who had a history of myocardial infarction. Possible IHD was one who had a history of angina or of using medications for treatment of IHD but had no history of definite IHD. We defined a history of stroke into three categories; ischemic stroke, hemorrhagic stroke and unknown.

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

We defined alcoholic drinking status into three categories as the following, current drinking was one who continued drinking until the day of examination, abstinence was one who quitted alcoholic drinking at least one year from 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, high density lipoprotein cholesterol (HDL-C) and triglyceride levels were determined by the enzymatic methods. Low density lipoprotein-cholesterol (LDL-C) was calculated using the Friedewald's formula (LDL = total cholesterol - HDL - TG/5). Glycosylated hemoglobin (HbA1c), plasma creatinine, and urine microalbumin were determined their levels by the central laboratory of Maharat Nakhon Ratchasima Hospital with standard methods including local quality control. Urine analysis was performed by using a urine specimen in the morning.

The study was approved by the ethics committee of the Endocrine Society of Thailand and by the Institutional Review Board of Maharat Nakhon Ratchasima Hospital. Informed consent for the study was obtained from each participant.

#### Statistical methods

Descriptive statistics was used to describe the studied subjects in mean  $\pm$  SD for continuous variables and percentage for categorical variables.

#### Results

A total of 1,000 patients with type 2 diabetes mellitus were registered in this study which consisted

of 273 males and 727 females. The mean age was 59.4±10.9 years and the mean duration of diabetes mellitus was  $8.2\pm6.8$  years. There were 46.7% of patients having a history of DM in their first-degree relatives, 60.7% having hypertension and 47.7% having of dyslipidemia. For the payment of diabetic treatment, 47.9% of patients had paid their payment as government officers, and 35.1% paid through the thirty-baht universal coverage. The proportion of diabetes mellitus according to age of patients and that according to the duration of diabetes are shown in Figure 1 and Figure 2, respectively. Proportion of type 2 diabetes peaked at age of 60-69.9 years and most of the patients had duration of diabetes of 1-5 years. The demographic and baseline characteristics of type 2 diabetic patients are demonstrated in Table 1. Proportion of diabetic patients with overweight (BMI 25-29.9 kg/m<sup>2</sup>) was 35.8% and those with obese (BMI>30 kg/m<sup>2</sup>) was 11.6%.

The percentages of type 2 diabetic patients who reached the target of diabetic management according to ADA recommendations<sup>(8)</sup> are demonstrated in **Table 2**. Only about one-third of patients could reach the goal of glycemic control which was FBS <130 mg/dL or HbA1c <7%. Nearly half of patients had diastolic blood pressure

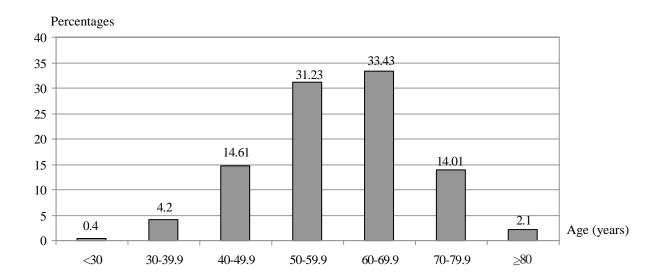


Figure 1. Percentage of type 2 diabetes mellitus by age of patients

**Figure 2.** Percentage of type 2 diabetes mellitus by duration of diabetes

**Table 1.** Demographics and baseline characteristics of type 2 diabetic patients

Parameters					
Age (years) (mean±SD)				59.4±10.9	
Sex (number) (%)					
male				273 (27.3)	
fe	male			ı	727 (72.7)
Smoking		(number			
N	on-si	3			824 (82.4)
Ex	x-sm				1.13711.2)
C	urrei	cers			4)
Alco	oholi	ing (num		5)	
N.	on-d	<u>;</u>			2)
A	bstir				5.1)
——————————————————————————————————————	urrer	ærs			- <del>2.9)</del>
	y ma	x (kg/m²)		per) (%)	
<18.5				-	47 (4.7)
18.5-24.9					479 (47.9)
25.0-29.9				358 (35.8)	
>30				116(11.6)	
Body mass index (kg/m²) (mean±SD)			25.1 <u>+</u> 4.5		
Systolic BP (mmHg) (mean±SD)				141.7 <u>+</u> 24.1	
Diastolic BP (mmHg) (mean <u>+</u> SD)				77.8 <u>+</u> 12.1	
$FBS (mg/dL) (mean \pm SD)$				151.9 <u>+</u> 54.2	
HbA1c (%)(mean <u>+</u> SD)				7.9 <u>+</u> 2.1	
Serum creatinine (mg/dL) (mean±SD)				1.5 <u>+</u> 1.1	
Total cholesterol (mg/dL) (mean±SD)				203.8 <u>+</u> 47.2	
Triglyceride (mg/dL) (mean±SD)				164.7 <u>+</u> 106.7	
HDL cholesterol (mg/dL) (mean±SD)				55.9 <u>+</u> 16.0	
LDL cholesterol (mg/dL) (mean <u>+</u> SD)			115.2 <u>+</u> 38.7		
Non-HDL cholesterol (mg/dL)			177.5 <u>+</u> 52.2		
(mean + SD) (n = 242)					

<80 mmHg; however, only one-third had systolic pressure <130 mmHg. About the status of lipid control, there were 50.2% with total cholesterol of <200 mg/dL, 56.9% with triglyceride <150 mmHg, 66.2% with HDL cholesterol >40 mg/dl in male and >50 mg/dL in female, and 35.8% with LDL cholesterol <100 mg/dL.

The complications of type 2 diabetic patients are demonstrated in Table 3. From 633 diabetic patients who were under the retinal examinations, the prevalence of diabetic retinopathy (DR) was 17.1% which consisted of non-proliferative DR (PDR) of 7.6% and proliferative DR (PDR) of 5%. One hof patients had overt proteinuria

**Table 2.** Percentage of type 2 diabetic patients who reached the ADA recommendation

Parameters	Number (%)
Systolic BP < 130 mmHg	333 (33.3)
Diastolic BP < 80 mmHg	565 (56.6)
FBS < 130 mg/dL	376 (37.6)
HbA1c < 7%	319 (31.9)
Total cholesterol < 200 mg/dL	502 (50.2)
Triglyceride <150 mg/dL	569 (56.9)
HDL cholesterol	
>40 mg/dL in male	
>50 mg/dL in female	662 (66.2)
LDL cholesterol < 100 mg/dL	358 (35.8)

and 8.0% had serum creatinine of more than 2 mg/dL. Nevertheless, the result of microalbuminuria was limited in this study. About macrovascular complications of diabetes, 6.1% of patients had a history of ischemic heart disease and 3.4% had a history of cerebrovascular disease.

Hypoglycemic agents used by type 2 diabetic patients are shown in **Table 4**. Sulfonylurea was the agent which was used by most of diabetic patients (80.4%), and metformin was the second common agent used (66.1%). Most of patients who controlled their glycemic levels with oral hypoglycemic drugs received a combination of two agents (60%). Insulin was used by 12.7%, i.e.: 46.5% received insulin in combination with single oral agent and 30.1% received insulin alone.

**Table 3.** Percentage of diabetic complications of type 2 diabetic patients

Parameters	Number (%)		
Diabetic Retinopathy (DR) (n = 633)			
Non-proliferative DR	48 (7.6)		
Proliferative DR	60 (9.5)		
Cataracts $(n = 814)$	338 (41.5)		
Legal blindness related with	9 (0.9)		
diabetes mellitus ( $n = 965$ )			
Diabetic nephropathy $(n = 962)$			
Overt proteinuria	246 (25.6)		
Serum creatinine >2 mg/dL	77 (8.0)		
History of foot ulcer $(n = 1000)$	66 (6.6)		
History of leg amputation (n=1000)			
Above knee amputation (AK)	2(0.2)		
Below knee amputation (BK)	4 (0.4)		
Toe amputation	8 (0.8)		
Absence of peripheral pulse ( $n = 1000$ )	48 (4.8)		
History of ischemic heart disease (n = 994)			
Possible	30 (3.0)		
Definite	31 (3.1)		
History of revascularization in patients			
with IHD $(n = 61)$			
Coronary bypass graft (CABG)	5 (8.2)		
Percutaneous coronary angioplasty	5 (8.2)		
(PTCA)			
History of cerebrovascular disease			
(CVD)(n=1000)			
Ischemic stroke	28 (2.8)		
Hemorrhagic stroke	3 (0.3)		
Stroke, unidentify	3 (0.3)		

**Table 4.** Percentage of type 2 diabetic patients treated with different hypoglycemic agents

Medication	Number (%)
Insulin	127 (12.7)
Sulfonylurea	804 (80.4)
Non-sulfonylurea insulin	23 (2.3)
secretagogues (glinide)	
Metformin	661 (66.1)
Thiazolidinediones (TZD)	12(1.2)
Alpha-glucosidase inhibitors (AGI)	17(1.7)
Diet control alone	71 (7.1)
Combination of oral hypoglycemic dru	ıgs
(OHD) in 873 patients without insulin	
Single drug	300 (34.4)
Two drugs	529 (60.6)
Three drugs	42 (4.8)
Four drugs	2(0.2)
Combination of insulin and OHD	
in 127 patients with insulin	
Insulin alone	38 (30.1)
Insulin with single OHD	59 (46.5)
Insulin with two OHD	29 (22.6)
Insulin with three OHD	1 (0.8)

Moreover, there were 7.1% of patients controlled their glycemic levels with only diet control.

#### **Discussion**

Diabetes mellitus is epidemic worldwide among increasing number of aging population and globalization. The WHO predicted a doubling number of diabetic patients in the next twenty years especially in developing countries in Asia. (2)

Diabetes is a chronic disease causing both micro-and macrovascular complications. (9) Hyperglycemia has been proved to cause diabetic retinopathy and nephropathy while the microvascular complication is the leading cause of blindness and chronic renal failure. Diabetic patients also bring other component of the so-called metabolic syndrome, i.e., hypertension, dyslipidemia, abdominal obesity and the consequent cardiovascular diseases. (10)

This study enrolled 1,000 patients with diabetes type 2 which were large enough to assess, determine and evaluate the diabetic care, diabetic management and diabetes-related complication in

tertiary care level medical center at Maharat Nakhon Ratchasima Hospital.

More than 90 percent of patients had type 2 DM and male to female ratio was 1:2.6 that is not different from previous studies in Thailand, which was about 1:3. The mean age of patients was 59.4±10.9 years, similar to other studies in Thailand, which the range of age was 55.1-64.6 years. (11) The duration of DM was 8.2 years, equivalent to other study in Thailand, which fell in the range of 8.4-10 years. The patients with BMI  $\geq$ 25 kg/m<sup>2</sup> were 47.4%, which is consistent with earlier studies in Thailand Diabetes Registry Project. (11) The prevalence of hypertension was 60.7%, dyslipidemia was 47.7%. The most common diabetic complication was nephropathy 33.6% followed by diabetic retinopathy 17.1%. Our study cannot determine the accurate prevalence of diabetic nephropathy because the limitation in examining microalbuminuria so we could determine only patients who had overt proteinuria. The prevalence of patients who had overt proteinuria was 25.6%. The prevalence of diabetic nephropathy in our study was high because patients had long duration of diabetes mellitus, poor glycemic control and poor blood pressure control. Mean duration of diabetes mellitus from our data was 8.2 years. Our patients could for reach the target of diabetic management according to ADA recommendation for glycemic control 37.6%, for hypertensive control 33.3% and for LDL control 35.8%. This achievement was similar to those studied by the DiabCare Asia that was between 20-30%. (12) To improve standard of care of diabetic patients we set up laboratory to examine microalbuminuria for early detection and early management of diabetic patients before they turned to be overt diabetic nephropathy and tried to bring the patients to reach the target of ADA recom-mendation.

In this study we found diabetic retinopathy 17.1%. This was lower than 30.7% from Thailand diabetes Registry project. The patients whose eyes were taken eye examined by ophthalmologist were only 63.3%, compared to 75.6% from Thailand Diabetes Registry Project. Hence, our study could

underestimate the real prevalence of diabetic retinopathy. Retinal examination by ophthalmologists annually in asymptomatic patients is an important issue in taking care of diabetic patients for early detection and intervention for diabetic retinopathy in combination while aggressive glycemic and blood pressure control would reduce the prevalence of diabetic retinopathy therefore reduce the numbers of patients who developed legal blindness.

Previous, large studies have shown that diabetic complication can be prevented by good glycemic control combined with other metabolic control of blood pressure and lipid profile. Getting an annual check up is an important strategy for early identification and management of diabetic complication. (13,14)

Type 2 diabetes mellitus is an important health problem in Maharat Nakhon Ratchasima Hospital. Both long term follow up and long term management are very important issues in taking care of patients with diabetes mellitus in order to decrease burden of diabetic complication both microvascular and macrovascular.

#### Acknowledgements

This study was supported by the Health Systems Research Institute, Thailand and the Endocrine Society of Thailand. The authors wish to thank many staff and nurses in diabetic center at Maharat Nakhon Ratchasima Hospital for their contributions and especially Dr. Somchai Insiripong for English revision. We would also like to thank Dr. Sanong Suksaweang from the Institute of Medicine of the Suranaree University of technology for his advice and correction regarding English.

#### References

- 1. Amos AF, McCarty DJ, Zimmet P. The rising global burden of diabetes and its complication: estimates and projection to the year 2010. Diabet Med 1997; 14 (Suppl 5): S1-85.
- 2. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projection. Diabetes Care 1998; 21: 1414-31.
- 3. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000

- and projections for 2030. Diabetes Care 2004; 27: 1047-53.
- 4. Aekplakorn W, Stolk RP, Neal B, Suriyawongpaisal P, Chongsuvivatwong V, Cheepudomwit S, et al. The prevalence and management of diabetes in Thai adults: the international collaborative study of cardiovascular disease in Asia. Diabetes Care 2003; 26: 2758-63.
- Williams R, Van Gaal L, Lucioni C; CODE-2 Advisory Board. Assessing the impact of complications on the cost of Type II diabetes. Diabetologia. 2002; 45: S13-7.
- Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 2003; 26: S5-20.
- Wilkinson CP, Ferris FL 3rd, Klein RE, Lee PP, Agardh CD, Davis M, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology 2003; 110: 1677-82.
- American Diabetes Association. Standards of medical care in diabetes. Diabetes Care 2005; 28 (Supp 1): S4-36.

- Gilmer TP, O'Connor PJ, Manning WG, Rush WA. The cost to health plans of poor glycemic control. Diabetes Care 1997; 20: 1847-53.
- 10. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005; 365: 1415-28.
- 11. Rawdaree P, Ngarmukos C, Deerochanawong C, Suwanwalaikorn S, Chetthakul T, Krittiyawong S, et al. Thailand diabetes registry (TDR) project: clinical status and long term vascular complications in diabetic patients. J Med Assoc Thai 2006; 89 (Suppl 1): S1-9.
- 12. Chuang LM, Tsai ST, Huang BY, Tai TY; Diabcare-Asia 1998 Study Group. The status of diabetes control in Asia: a cross-sectional survey of 24,317 patients with diabetes mellitus in 1998. Diabet Med 2002; 19: 978-85
- 13. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complication in patients with type 2 diabetes (UKPDS 33). Lancet 1998; 352: 837-53.
- Reichard P, Britz A, Cars I, Nilsson BY, Sobocinsky-Olsson B, Rosenqvist U. The Stockholm Diabetes Intervention Study (SDIS): 18 months' results. Acta Med Scand 1988; 224: 115-22.