Prevalence of Diabetic Retinopathy and Associated Factors in Type 2 Diabetes Mellitus in Maharat Nakhon Ratchasima Hospital

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Objective: To determine the prevalence of diabetic retinopathy (DR) and its associated factors in type 2 diabetes in Department of Medicine, Maharat Nakhon Ratchasima Hospital. **Patients and Methods:** A cross-sectional, hospital-based study was carried out between April and December 2003. Diabetic patients, type2 in diabetic clinics in Maharat Nakhon Ratchasima Hospital were registered. Their associated factors such as fasting blood glucose, glycosylated hemoglobin (hemoglobin A1c; HbA1c), blood pressure (BP), serum creatinine, urinary examination, etc was collected. Retinal examination of the participants was performed by ophthalmologists. **Results:** 633 of 1066 (59.4%) diabetic patients received retinal examination using direct ophthalmoscopy after full dilatation of pupils. The prevalence of DR was 17% (n=108) which consisted of non-proliferative DR (NPDR) 7.6% (n=48), proliferative DR (PDR) 9.5% (n=60). Patients with DR significantly had longer duration of diabetes, higher HbA1c, higher systolic BP levels, higher incidence of nephropathy (proteinuria or renal insufficiency) than those without DR. The factors associated with DR expressed as adjusted Odds ratio (95% confidence interval) were 1) duration of diabetes 1.2 (0.6-2.28) for duration of 5-9.9 years, 2.1 (1.13-4.04) for duration of 10-14.9 years, 1.9 (0.81-4.27) for duration of 15-19.9 years, 4.6 (2.09-10.18) for duration of ≥20 years when compared with duration of diabetes of less than 5 years, 2) latest HbA1c ≥7% 2 (1.13-3.59) when compared with HbA1c <7%, 3) systolic BP ≥ 130 mmHg 1.8 (1.14-2.92) when compared with systolic BP <130 mmHg, 4) nephropathy status i.e. positive proteinuria 1.8 (1.05-2.96) and renal insufficiency 2.4 (1.23-4.87) when compared with no nephropathy. **Conclusion:** Diabetic retinopathy is one of the common complications of diabetes. The authors found the factors associated with DR were longer duration of diabetes, high latest HbA1c level, high systolic BP and present diabetic nephropathy.

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บทคัดย่อ:　ความชุกและปัจจัยที่สัมพันธ์กับเบาหวานในจอประสาทตา ในผู้ป่วยเบาหวานชนิดที่ 2 ของ
โรงพยาบาลมหาราชนครราชสีมา

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หน่วยต่อมไร้ท่อ กลุ่มงานอายุรกรรม โรงพยาบาลมหาราชนครราชสีมา

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วัตถุประสงค์: เพื่อศึกษาความชุกและปัจจัยที่สัมพันธ์กับเบาหวานในจอประสาทตาในผู้ป่วยเบาหวานชนิดที่ 2 ของ
โรงพยาบาลมหาราชนครราชสีมา **ผู้ป่วยและวิธีการ:** ทำการศึกษาแบบภาพตัดขวางแบบ hospital-based ที่ โรงพยาบาล
มหาราชนครราชสีมา ตั้งแต่เมษายน พ.ศ. 2546 ถึง ธันวาคม พ.ศ. 2546 ในผู้ป่วยเบาหวานของโรงพยาบาลมหาราช
นครราชสีมาที่ลงทะเบียน โดยมีจักษุแพทย์เป็นผู้ตรวจจอประสาทตาของผู้ป่วยเบาหวาน **ผลการศึกษา:** ผู้ป่วยเบาหวาน
ชนิดที่ 2 จำนวน 633 คน จากผู้ป่วยทั้งหมด 1,066 คน ที่ลงทะเบียน (ร้อยละ 59.4) ได้รับการตรวจโดยจักษุแพทย์ พบความ
ชุกของเบาหวานในจอประสาทตาของเบาหวานชนิดที่ 2 ร้อยละ 17 (108 คน) ประกอบด้วย NPDR ร้อยละ 7.6 (48
คน) และ PDR ร้อยละ 9.5 (60 คน) พบว่าผู้ป่วยที่มีรอยโรคของเบาหวานในจอประสามตามีระยะเวลาเป็นโรคเบาหวาน
นานกว่าและความดันโลหิตค่าบนสูงกว่าและสถานะเบาหวานลงไตมากกว่าผู้ป่วยที่ไม่มีเบาหวานในจอประสาทตา
โดยแสดงค่าความเสี่ยงเป็น adjusted odds ratio (95% confidential interval) ดังนี้ ระยะเวลาเป็นเบาหวาน 5-9.9 ปี, 10-
14.9 ปี, 15-19.9 ปี และ ≥ 20 ปี เมื่อเทียบกับระยะเวลาเป็นเบาหวานน้อยกว่า 5 ปี เท่ากับ 1.2 (0.6-2.28), 2.1 (1.13-4.04),
1.9 (0.81-4.27), 4.6 (2.09-10.18) ตามลำดับ, ระดับน้ำตาลสะสมมากกว่าร้อยละ 7 เมื่อเทียบกับระดับน้ำตาลสะสมน้อย
กว่า 7 เท่ากับ 2 (1.13-3.59), ระดับความดันโลหิตค่าบนมากกว่าหรือเท่ากับ 130 มิลลิเมตรปรอทเมื่อเทียบกับระดับความ
ดันโลหิตค่าบนน้อยกว่านี้ เท่ากับ 1.8 (1.14-2.92) สถานะของเบาหวานลงไตเมื่อเทียบกับผู้ที่ไม่มีเบาหวานลงไต ได้แก่
positive proteinuria 1.8 (1.05-2.96) และไตเสื่อม 2.4 (1.23-4.87) **สรุป:** ภาวะแทรกซ้อนของเบาหวานในจอประสาท
ตาของผู้ป่วยเบาหวานชนิดที่ 2 ของโรงพยาบาลมหาราชนครราชสีมา พบได้ร้อยละ 17 ปัจจัยที่สัมพันธ์กับภาวะแทรก
ซ้อนของเบาหวานในจอประสาทตาได้แก่ ระยะเวลาที่เป็นเบาหวาน, ระดับน้ำตาลสะสม, ระดับความดันโลหิตค่า
บนและภาวะแทรกซ้อนของเบาหวานลงไต

Introduction

Diabetic Retinopathy (DR) is one of the common complications of diabetes. Unfortunately, in many cases the patients are not aware of any symptoms until it is too late for effective treatment. More than 60% of those with type 2 diabetes mellitus (T2DM) have some degrees of retinopathy twenty years after diagnosis[1]. DR is a common cause of visual loss in the world and it is a potentially blinding complication of diabetes that damages the retina. It was found that the diabetic patients

who were at risk of having the complication of diabetic retinopathy were patients who suffered from the diabetes for a long time. Moreover, these complications were found in older people, and patients with associated diseases (co-morbidity) such as higher systolic blood pressure, the presence of proteinuria and higher glycosylated hemoglobin levels (HbA1c level)[1-3]. Therefore, the purpose of the present study was to determine the prevalence and the factors associated with DR in T2DM patients recruited in Maharat Nakhon Ratchasima Hospital.

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 during 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 in the present registry were diabetic patients who were treated in these diabetic clinics and agreed to participate in this registry. The diagnosis of diabetes mellitus was made according to the American Diabetes Association (ADA) criteria 1997[4]. The total number of diabetic patients who were registered at Maharat Nakhon Ratchasima Hospital was 1,066 diabetic patients. From those patients, 633 patients with type 2 diabetes had received the retinal examination and were included for further analysis.

Methods and Measurements

The registry data were obtained by interviewing and examining the patients and reviewing their medical records, and recorded in the case record form. Data included demographic characteristics, pertinent parts of

physical examinations, laboratory findings performed during the last 12 months prior to recruitment, use of medications including insulin, oral hypoglycemic agents, antihypertensive agents, lipid lowering agents and aspirin, and diabetic complications. All of them were verified by physician's medical records.

Results of eye examination reported within one year prior to registry day were recorded, including the results of retinal examination, visual acuity, and the presence of cataracts. The retinal examination was evaluated by the ophthalmologists from each center with direct ophthalmoscopy after full dilatation of pupils. In the present study, DR was classified into only the non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) categories[5]. NPDR was defined if it was characterized by an increase in vascular permeability or vascular closure; such as micro-aneurysms, dot and blot hemorrhage, and exudates. PDR was defined if vasoproliferation of new vessels occurred on or within the retina including complications such as vitreous hemorrhage or pre-retinal hemorrhage. Level of retinopathy was based on the grading of the worst 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. Cataract findings were defined as positive or negative results. Nephropathy was defined when a patient had at least one of following condition, positive proteinuria, defined as a positive urine dipstick test at 1+ level or more in at least two of three urine collections, or renal insufficiency, defined when serum creatinine (Cr) was greater than 2 mg/dL.

The authors defined smoking status into three categories as following: current smokers were those who

had continued smoking until the day of the examination or who quitted smoking less than one year prior to the day of the examination, ex-smokers were those who had stopped smoking at least one year prior to the day of the examination, and non-smokers were those who had never smoked. The authors defined alcoholic drinking status into three categories as following: current drinkers were those who continued drinking until the day of the examination, abstinence were those who had abstained from alcoholic for at least one year prior to the day of the examination, and non-alcoholic drinkers were those who had never drunk alcohol or had drunk less twice a month

      Fasting plasma glucose (FPG), 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). HbA1c, serum Cr, 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.

      Blood pressure (BP) was measured over the right arm twice, 30 seconds apart, after resting for 5 minutes, by using automated BP machines (OMRON T4). Hypertension was defined as systolic blood pressure $\geq$140 mmHg and/or diastolic blood pressure $\geq$90 mmHg, or patients 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, cigarette smoking, medication and history of diabetes were obtained by interviews.

The study was approved by the ethic committee Maharat Nakhon Ratchasima Hospital. Signed consent for the study was obtained from all participants.

Statistical Analyses

      Descriptive statistics were applied to the study data. Categories of studied variables were compared with Chi-square test and Fisher's exact test. Differences in mean values of studied variables were compared through student t-test and Mann-Whitney U test with 0.05 level of significance. The crude Odds Ratio (OR) was calculated to define each associated factor with diabetic retinopathy. Then confounding factors were adjusted by multiple logistic regressions to determine the associated factors with diabetic retinopathy. Whenever two variable were very similar and had mulicolinearity, only one of them would be included in the model. Statistical analyses were performed using STATA version 8.0 (Stata Coroperation, College Station TX, U.S.).

Results

      There were 633 patients with T2DM who were received retinal examinations. The prevalence of DR in this study was 17% (n=108) which consisted of NPDR 7.6% (48 patients) and PDR 9.5% (60 patients). The authors found that the prevalence of cataracts was 41.5%. The prevalence of diabetes-related legal blindness was 0.9% (n=5) and that of non- diabetes-related legal blindness was 1% (n=7). As shown in Fig 1, the prevalence of DR demonstrated a peak at an age of 50-79 years-old. Moreover, the prevalence of DR in patients with T2DM increased with a longer duration of diabetes from less than 5 years to more than twenty years as shown in Fig 2.

Prevalence (%)

Age (years)

(…) = number of subjects
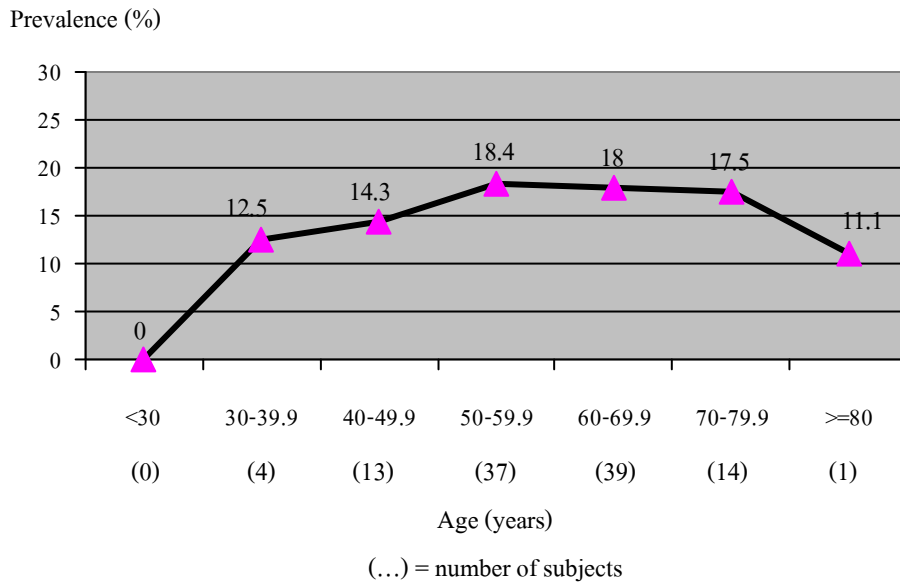
The clinical characteristics of patients according to DR status were demonstrated in Table 1. When the authors compared the clinical characteristics between diabetic patients with and without DR, those with DR had longer duration of diabetes, higher systolic BP, and higher serum Cr. Moreover, the percentages of patients with overt proteinuria and renal insufficiency were significantly higher in those with DR than those without.

The proportions of diabetic patients categorized by levels of metabolic control and BP control were demonstrated in Table 2. This was done using the cut points according to the recommendations for adults with diabetes from the ADA[6] Patients with DR had frequencies of HbA1c level more than or equal 7%, systolic BP level of more than or equal to 130 mmHg, serum Cr level more than 2 mg/dL significantly more
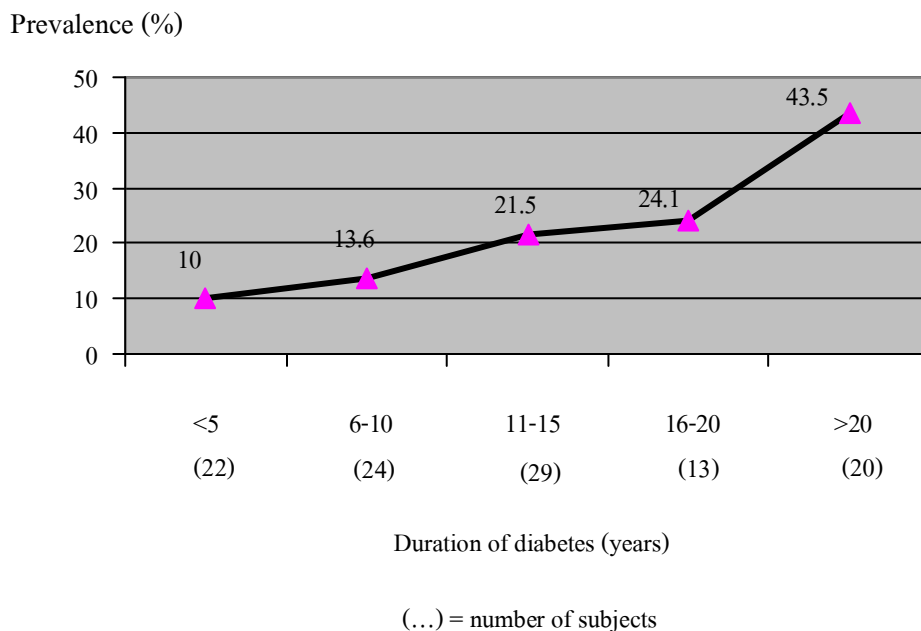
Prevalence (%)

Duration of diabetes (years)

(…) = number of subjects

Table 1 clinical characteristic of type 2 diabetic patients according to the retinopathy status

Parameters*	DR (N=108)	No DR (N=525)	P-value
Female (%)	80 (74.1)	379 (72.2)	0.626
Age (years)	59.5±9.2	58.6±11.1	0.385
Duration of DM (years)	11.9±7.9	8.1±6.5	<0.001
Body mass index (kg/m2)	25.2±4.6	25.6±5.5	0.478
Current smokers and ex-smokers (%)	14 (13.0)	84 (16.0)	0.427
Current drinkers and abstinence (%)	28 (25.9)	139 (26.5)	0.906
Systolic BP (mmHg)	139.2±22.7	149.5±24.1	<0.001
Diastolic BP (mmHg)	77.9±11.8	78.6±12.9	0.574
Fasting plasma glucose (mg/dl)	153.0±57.0	153.5±47.8	0.919
Hemoglobin A1c (%)	7.8±2.0	8.3±2.3	0.080
Serum creatinine (mg/dl)	1.7±1.2	1.4±1.0	0.017
Total cholesterol (mg/dl)	201.2±43.9	212.2±67.6	0.108
Triglyceride (mg/dl)	163.5±103.9	173.8±147.3	0.489
LDL cholesterol (mg/dl)	113.9±38.3	119.2±42.7	0.203
HDL cholesterol (mg/dl)	55.6±14.6	54.6±14.9	0.536
Overt proteinuria (%) (n=608)	42.3	20.6	<0.001
Renal insufficiency (%)	22 (20.6)	35 (6.7)	<0.001

*The parameter values are presented with mean ±SD and percentages.

than those without DR.

The factors associated with the occurrence of DR are demonstrated in Table 3. By multiple logistic regressions, factors associated with DR were duration of diabetes, HbA1c level, systolic BP level, proteinuria status, and serum Cr level. When compared with patients with duration of diabetes of less than five years, the duration of diabetes of 10-14.9 years and more or equal to 20 years or more were the risk factors associated with the occurrence of DR in T2DM, with adjusted odd ratio (95% confidence interval) were 2.1 (1.13-4.04) and 4.6 (2.09-10.18) respectively. Other risk factors associated with the occurrence of DR, odd ratio were latest HbA1c ≥7% 2.0 (1.13-3.59) when compared with HbA1c <7%, systolic BP≥130 mmHg 1.8 (1.14-2.92) when compared with systolic BP<130 mmHg, positive proteinuria 1.8 (1.05-2.96) when compared with those without proteinuria, and serum Cr more than 2 mg/dL 2.4 (1.23-4.87), when compared with those of less than 2 mg/dL.

Medications used among our diabetic patients are shown in Table 4. Patients with DR more frequently used insulin, antihypertensive agents, and oral hypoglycemic agents than those without DR.

Discussion

The prevalence of diabetic retinopathy in outpatients with T2DM was 17.1% (NPDR 7.6% and PDR 9.5%). The prevalence of diabetic retinopathy in the present study was lower than the prevalence of Thailand diabetic registry project[7], which found the

Table 2 Metabolic and blood pressure control in type 2 diabetic patients according to the retinopathy status (N=633)

Parameters (%)	DR (N=108)	No DR (N=525)	P-value
Systolic BP ≥130 mmHg	78.7	63.1	0.002
Diastolic BP ≥80 mmHg	49.1	42.9	0.236
Fasting plasma glucose > 130 mg/dl	70.4	63.1	0.148
Hemoglobin A1c ≥ 7 %	82.4	63.4	0.004
Total cholesterol ≥ 200 mg/dl	50.0	49.0	0.843
Triglyceride ≥150 mg/dl	42.6	43.2	0.902
LDL cholesterol ≥100 mg/dl	67.6	62.7	0.333
HDL cholesterol ≤40 mg/dl in male and ≤ 50 mg/dl in female	37.0	33.5	0.483

prevalence of diabetic retinopathy 31.4% (NPDR 22% and PDR 9.4%) In this study the patients whose eyes were examined by ophthalmologist were only 59.4%, compared to 75.6% from Thailand Diabetes Registry Project. Hence, our study could underestimate the real prevalence of diabetic retinopathy

The prevalence of cataracts in the present study was 41.5% since about half of the presented patients were 60 years-old, thus they were more likely to develop age-related cataract. It was difficult to determine whether a patient had senile cataract or cataract associated with diabetes.

The risk factors associated with retinopathy were longer duration of diabetes, HbA1c level more than 7%, Systolic BP level of more than 130 mmHg and presence of diabetic nephropathy.

A well-established linear relation exists between duration of diabetes and the presence and severity of DR. The most effective treatment to slow the progression of DR is good glycemic control. The United Kingdom Prospective Diabetes Study (UKPDS) in T2DM showed the efficacy of good glycemic control prevented DR, intensive glycemic control therapy reduced microvascular complications including DR by 25% and decrease the risk of retinal photocoagulation by 29%, compared with conventional therapy[8]. Furthermore, the UKPDS also showed a continuous relationship

Table 3 Factors associated with the occurrence of diabetic retinopathy in type 2 diabetes

Risk Factors	Adjusted Odd Ratio* (95% CI)	P-value
Duration of diabetes (years)		
< 5	1	
5-9.9	1.2 (0.62-2.28)	0.595
10-14.9	2.1 (1.13-4.04)	0.019
15-19.9	1.9 (0.81-4.27)	0.146
≥20	4.6 (2.09-10.18)	<0.001
Glycosylated hemoglobin (%)		
<7	1	
≥7	2.0 (1.13-3.59)	0.017
Systolic blood pressure (mmHg)		
<130	1	
≥130	1.8 (1.14-2.92)	0.012
Overt proteinuria	1.8 (1.05-2.96)	0.031
Serum creatinine (mg/dl)		
≤ 2	1	
> 2	2.4 (1.23-4.87)	0.011

*Adjusted for the duration of diabetes, glycosylated hemoglobin level, systolic blood pressure level, presence of proteinuria and serum creatinine level

Table 4 Medication used for type 2 diabetic patients according to the retinopathy status (N=633)

Medication (%)	DR (N=108)	No DR (N=525)	P-value
Insulin	26.9	11.6	<0.001
Oral hypoglycemic agents	88.0	93.5	0.045
Antihypertensive agents	77.8	67.2	0.031
Lipid lowering agents	42.6	34.5	0.109
Aspirin	44.4	36.6	0.125

between the risk of microvascular complications and the degree of glycemic control. Every percentage point decrease in HbA1c was associated with 35% risk reduction[9]. The effort to achieve good glycemic control in diabetics should be a priority from the time of diagnosis because the benefit of glycemic control declines substantially in patients with advanced DR. Moreover, the UKPDS demonstrated the influence of tight blood pressure control and found that a 10/5 mmHg reduction in BP levels was associated with a 34% reduction in progression of retinopathy. Hypertension impairs the autoregulation of retinal blood flow in diabetics compared with nondiabetics. It also enhances the endothelial damage and expression of vascular endothelial growth factor (VEGF) and its receptors in poorly controlled diabetics. Another risk factor associated with DR in the present study was the presence of nephropathy. Renal disease, as evidenced by proteinuria or elevated serum Cr level was demonstrated to be a factor associated with DR in previous studies[1,10]. Type 1 diabetes patients with diabetic nephropathy almost always have DR; even patients who have microalbuminuria are at increased risk of DR. The relationship between diabetic nephropathy and DR is not as strong in T2DM. In one study of T2DM with significant proteinuria, 77% had diabetic nephropathy while only 56% of those patients had DR[11].

Though the treatment of DR is for blindness prevention, it could not improve the visual acuity of the patients. In terms of vision protection, it would be more effective to prevent the development of DR (before the history of blurred vision) than to save the rest of the visual acuity. 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 BP control would reduce the prevalence of DR therefore reduce the numbers of patients who developed legal blindness.

Acknowledgements

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