The Prevalence of Diabetic Retinopathy in Trang Province Determined by Retinal Photography and Comprehensive Eye Examination

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Objective: *To determine the prevalence of diabetic retinopathy (DR) in Trang province using retinal photography and comprehensive eye examination.*
Method: *Seven hundred fourteen patients with diabetes (7% of the total number of diabetes in the province) were examined by single-field digital retinal photography interpreted by a retinal specialist and a stereoscopic method using indirect ophthalmolscopy and slit lamp biomicroscopy with wide field contact lens. The latter method was performed by an experienced ophthalmologist assisted by the same retinal specialist.*
Results: *There was 19.2% nonproliferative diabetic retinopathy (NPDR), and 1.1% proliferative diabetic retinopathy (PDR), identified by the comprehensive examination for the right eyes. This modality also identified 18.5% NPDR, and 1.3% PDR, for the left eyes. There was 23.8% nonproliferative diabetic retinopathy (NPDR), and 1.4% proliferative diabetic retinopathy (PDR) identified by retinal photography for the right eyes. This modality also identified 22.6% NPDR, and 1.3% PDR for the left eyes. The sight-threatening cases were identified by both modalities with approximately 3% for both eyes. The photography had moderate agreement (K = 0.5, both eyes) with the comprehensive examination for the identification of diabetic macular edema with 78.6% and 68.8% sensitivity for the right and left eyes. For the identification of moderate NPDR, severe NPDR, and PDR, the photography had substantial agreement (K = 0.7, both eyes) with 88.2% and 83.3 sensitivity for the right and left eyes.*
Conclusions: *Trang province may have approximately 300 sight-threatening DR patients. This may project to 180,000 patients nationwide. Retinal photography may determine more cases than clinical examination. Combination of both modalities for DR identification may yield a closer estimate to the real prevalence.*

Keywords: *diabetic retinopathy screening, digital retinal photography, prevalence of diabetic retinopathy*

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The population of patients with diabetes worldwide is expected to increase dramatically in the coming decades. It was predicted that the global prevalence of diabetes would increase from 4.5% to 6.2% by the year 2030[1]. Data from the International Collaborative Study of Cardiovascular Disease in Asia indicated that there was an estimated 9.6% prevalence of diabetes among Thai adults[2]. Therefore, approximately six million Thai adults are expected to have diabetes. Furthermore, it was found in the Thailand Diabetes Registry Project[3] that, among the 9,419 registrants, 43.9% had nephropathy, 30.7% had retinopathy, 8.1% had ischemic heart disease, and 4.4% had cerebrovascular disease. In implementing these estimations to the six million patients with diabetes, Thailand might have more than 1.5 million patients who are suffering from diabetic retinopathy.

The evaluation of retinopathy in the Thailand Diabetes Registry Project was conducted in the

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participated tertiary care centers, and performed by general ophthalmologists in each center using direct ophthalmoscopes[3]. Prior to the present project, there were many studies concerning the prevalence of diabetic retinopathy in Thailand. Although these studies were based on different care centers, the retinopathy was also evaluated by general ophthalmologists using indirect ophthalmoscopes. In Trang province, the authors conducted a study in 1997 to evaluate the prevalence of diabetic retinopathy (DR) in the eye clinic of Trang provincial hospital. Nine hundred eighty eight patients with diabetes were examined by a general ophthalmologist using indirect ophthalmoscopes, and 393 (20.62%) had retinopathy.

In this present study, the authors re-evaluate the prevalence of diabetic retinopathy in Trang province using two different diagnostic modalities, digital retinal photography[4-6] and comprehensive eye examination[7]. The former was interpreted by a retinal specialist, the latter was performed by an experienced ophthalmologist with an assistance of the same retinal specialist using indirect ophthalmoscopes and slit lamp biomicroscopy with wide field contact lens. Diagnostic accuracy of the digital photography was also evaluated using the comprehensive eye examination as standard.

Material and Method

Setting and subjects

The present study was conducted in Trang provincial hospital. Ten percent of patients with diabetes were randomly recruited from the existing database of each of the nine districts of Trang province. All patients signed written informed consent for giving permission of having two examinations in each of their eyes. They were excluded if they had any contraindication for using mydriatic eye drops, had retinal diseases that precluded the diagnosis of diabetic retinopathy, and had ocular media not clear enough to make a diagnosis by either diagnostic modality used in this study.

Method and measurements

All included patients were examined by two diagnostic modalities after their pupils were dilated by one drop of 1% tropicamide under surveillance of potential angle closure by a comprehensive ophthalmologist. Each patient was examined first in the right eye and then the left eye. The preceding examination for each eye was 45° single-field[8] digital image capture of the posterior pole, including the optic disc and macula, using a Kowa® non-mydriatic fundus camera (Kowa Optimed, Tokyo, Japan). The subsequent comprehensive examination was indirect ophthalmoscopy performed by a comprehensive ophthalmologist. If the examination revealed any obvious or suspected pathologic findings that suggested DR, the patients were then re-examined by a retina specialist using both indirect ophthalmoscopy and slit lamp biomicroscopy with wide field contact lens. The same retina specialist interpreted the 5-million pixel retinal image of each patient one month after the capture. The outcomes measured were the prevalence of DR and diabetic macular edema (DME) identified by each diagnostic modality and an accuracy of the retinal photography in identifying referral cases, compared with the comprehensive examination. The latter was used as standard.

International clinical disease severity scales and referral criteria

The DR severity level and the presence of DME were based on the International Clinical Diabetic Retinopathy and Diabetic Macular Edema Disease Severity Scales[9]. In short, DR was classified into five severity levels: no retinopathy, mild retinopathy, moderate retinopathy, severe non-proliferative diabetic retinopathy (NPDR), and proliferative diabetic retinopathy (PDR). Mild NPDR included cases with microaneurysms only. Severe NPDR included cases with more than 20 microaneurysms in each of four quadrants, venous beadings in two or more quadrants, or intraretinal microvascular abnormalities in at least one quadrant. Other cases with more than just microaneurysms alone, but less than severe NPDR, fell into the moderate NPDR category. PDR included cases with neovascularization, and vitreous or preretinal hemorrhage. DME was defined as apparent retinal thickening or hard exudates in the posterior pole, and was categorized into "presence" or "absence".

Based on these international clinical disease severity scales, two referral criteria, for applying the retinal photography in community hospitals to identify cases for referral to Trang Hospital, were established for the present study. In the first criterion, eyes were labeled for referral if they were diagnosed as moderate NPDR, severe NPDR, and PDR. The second criterion included eyes with severe NPDR and PDR.

Statistical analysis

Kappa coefficient (K), sensitivity, and specificity were used to compare the examination results between retinal photography interpretation and comprehensive eye examination.

Statistical analysis was performed using SPSS software version 8.2 (SPSS Inc., Chicago, IL, USA). K was interpreted as follows: < 0, no agreement; 0.0-0.19, poor; 0.20-0.39, fair; 0.40-0.59, moderate; 0.60-0.79, substantial; and 0.80-1.0, almost perfect agreement[10].

Results

Of all 10,212 patients with diabetes registered in the provincial database of nine districts, 1,021 patients (10%) were randomly recruited from each district for the present study. However, only 714 of these patients (7% of the total number of diabetes in the province) presented in the eye clinic. Of these 714 patients, on their right eye, 44 were judged as ungradable by the comprehensive examination and 96 had cloudy ocular media limiting the retinal photography interpretation; on their left eye, 50 and 103 were also judged for the same reason. The demographic characteristic of these patients is presented in Table 1. The prevalence of each DR severity level and DME identified by the comprehensive eye examination and retinal photography for both the right and left eyes are presented in Table 2. Moderate NPDR was the most prevalent level and the photography identified more prevalence of the retinopathy in almost all severity levels including the presence of DME.

There was 19.2% nonproliferative diabetic retinopathy (NPDR), and 1.1% proliferative diabetic retinopathy (PDR), identified by the comprehensive examination for the right eyes. This modality also identified 18.5% NPDR, and 1.3% PDR, for the left eyes. There was 23.8% nonproliferative diabetic retinopathy (NPDR), and 1.4% proliferative diabetic retinopathy (PDR) identified by retinal photography for the right eyes. This modality also identified 22.6% NPDR, and 1.3% PDR for the left eyes. The sight-threatening cases (severe NPDR and PDR) were found in 2.8% and 3.6% by the comprehensive examination and the retinal photography for the right eyes respectively, whereas 2.3% and 3.1% were found by the examination and the photography for the left eyes.

In an assessment of diagnostic accuracy, the patients with ungradable results of either eye by either diagnostic modality were excluded. Thus, 559 patients were included in this assessment for comparison of both eyes. The prevalence of DR and DME for this group of patients are presented in Table 3. The photography could have moderate agreement (K = 0.5, both eyes) with the comprehensive examination for the identification of DME with less than 80% sensitivity. For the identification of moderate NPDR, severe NPDR, and PDR (the first referral criterion), the photography could have substantial agreement (K = 0.7, both eyes) with 88.2% and 83.3% sensitivity for the right and left eyes. However, the K value and sensitivity became much lower (K = 0.3, fair agreement, 41.2% and 35.0% sensitivity for the right and left eyes) for the identification of severe NPDR and PDR.

Table 1. Demographic characteristic of the patients (n = 714)

Characteristics	Number (%)
Type I/II diabetes (n)	10/704
Male/female (n)	193/521
Age group: (n [%])	
16-30 years old	7 (1.0)
31-50 years old	179 (25.1)
51-70 years old	424 (59.4)
71-87 years old	104 (14.6)

Discussion

The previous studies concerning DR in Thailand were conducted between 1990 and 1999 in Chiang Mai, Chonburi, Nakornratchasima, Trang, and Lampang. It had been reported in these studies, published in local medical journals, that the prevalence of NPDR determined by indirect ophthalmoscopy performed by comprehensive ophthalmologists was varied between 12% and 25%; the prevalence of PDR was between 1.9% and 5.2%.

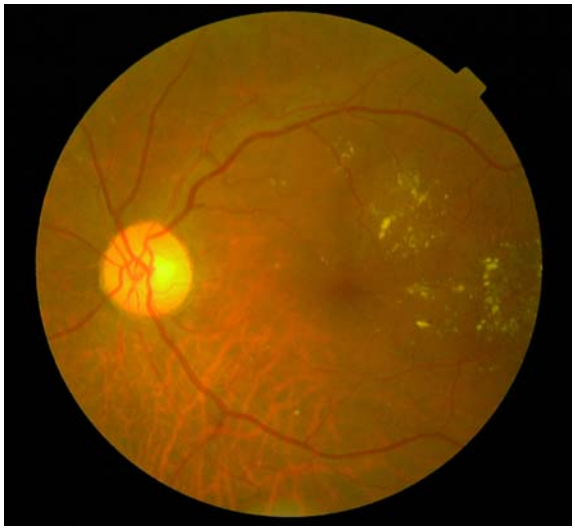

Fig. 1 A single-field retinal photography including the optic disc and macular for diabetic retinopathy screening

Table 2. The prevalence of diabetic retinopathy severity levels and the presence of diabetic macular edema (n = 714)

	Right eyes		Left eyes	
	Clinical exam	Photography	Clinical exam	Photography
No DR	525 (73.5)	438 (61.3)	523 (73.2)	440 (61.6)
Mild NPDR	42 (5.9)	47 (6.6)	40 (5.6)	46 (6.4)
Moderate NPDR	83 (11.6)	107 (15.0)	78 (10.9)	103 (14.4)
Severe NPDR	12 (1.7)	16 (2.2)	14 (2.0)	13 (1.8)
PDR	8 (1.1)	10 (1.4)	9 (1.3)	9 (1.3)
Ungradable	44 (6.2)	96 (13.4)	50 (7.0)	103 (14.4)
DME	14 (2.5)	30 (5.4)	16 (2.9)	26 (4.7)

DR = diabetic retinopathy, NPDR = nonproliferative diabetic retinopathy, PDR = proliferative diabetic retinopathy, DME = diabetic macular edema, Clinical exam = comprehensive examination by the retinal specialists, Photography = interpretation of digital retinal photography by the retinal specialist

Table 3. The prevalence of diabetic retinopathy severity levels and the presence of diabetic macular edema after excluding ungradble cases (n = 559)

	Right eyes		Left eyes	
	Clinical exam	Photography	Clinical exam	Photography
No DR	428 (76.6)	396 (70.8)	430 (76.9)	399 (71.4)
Mild NPDR	38 (6.8)	45 (8.1)	33 (5.9)	43 (7.7)
Moderate NPDR	76 (13.6)	96 (17.2)	76 (13.6)	96 (17.2)
Severe NPDR	11 (2.0)	15 (2.7)	14 (2.5)	13 (2.3)
PDR	6 (1.1)	7 (1.3)	6 (1.1)	8 (1.4)
DME	14 (2.5)	30 (5.4)	16 (2.9)	26 (4.7)

DR = diabetic retinopathy, NPDR = nonproliferative diabetic retinopathy, PDR = proliferative diabetic retinopathy, DME = diabetic macular edema, Clinical exam = comprehensive examination by the retinal specialists, Photography = interpretation of digital retinal photography by the retinal specialist

Table 4. Kappa coefficient, sensitivity, and specificity for the identification of the diagnostic categories (n = 559)

	Right eyes			Left eyes		
	K	Se	Sp	K	Se	Sp
DME	0.48	78.6	96.5	0.51	68.8	97.2
Referral I	0.73	88.2	92.3	0.69	83.3	92.0
Referral II	0.34	41.2	97.2	0.31	35.0	97.4
All DR levels	0.55	n/a	n/a	0.56	n/a	n/a

K = kappa coefficient, se = sensitivity, sp = specificity, DME = diabetic macular edema, referral I = referring cases with moderate, severe nonproliferative, and proliferative diabetic retinopathy, referral II = referring cases with severe nonproliferative, and proliferative diabetic retinopathy, DR = diabetic retinopathy

Compared to these studies, the prevalence of NPDR and PDR determined by the comprehensive eye examination in the present study, 19.2% and 1.1% respectively, was approximated the same, whereas the prevalence of NPDR determined by retinal photography, 23.8%, was still in the higher range. These results may reflect that the prevalence of DR in Trang province did not significantly change over the past decade.

The standard method for diagnosis of DR is the interpretation of standard 7-field stereoscopic retinal photography described in the Early treatment Diabetic Retinopathy Study (ETDRS)[11]. This method is impractical and was not used in the majority of studies in the community. Although both diagnostic modalities in the present study are not standard, the prevalence of sight-threatening retinopathy including severe NPDR, PDR, (approximately 3%) and DME (approximately 4%), diagnosed by indirect ophthalmoscopy and slit lamp biomicroscopy with wide field contact lens by the retinal specialist in the present study, should not be much different from that determined by the ETDRS method.

There were previous studies comparing the ETDRS methods and digital retinal photography. In a study by Lin et al in 2002, there was highly significant agreement (K = 0.97) between the degree of retinopathy detected by single-field nonmydriatic monochromatic digital photograph and that was seen in seven standard 35-mm color stereoscopic mydriatic fields (the ETDRS method). The sensitivity of digital photography compared with color photography was 78%, with a specificity of 86%[12]. However, the study by Lin was not a population-based and had only 197 patients enrolled. In another study by Bursell et al in 2001, there was substantial agreement (K = 0.65) between the clinical level of diabetic retinopathy assessed from the undilated 3-field, stereoscopic, digital retinal images and the dilated ETDRS photos. Agreement was excellent (K = 0.87) for suggested referral to ophthalmology specialists for eye examinations[13]. The study by Bursell was neither a population-based and had only 54 patients enrolled. These studies suggested that the retinal photography would be used for diabetic retinopathy screening; however, the use of 3-field stereoscopic photography as in Bursell's study might not be practical in a community setting.

The present study has shown that both diagnostic modalities, although performed by the same retina specialist, could have only moderate agreement in determination of each DR level and DME. The agreement was much improved when the patients were grouped in a criterion that moderate NPDR, severe NPDR, and PDR cases were referred. However, if the referral criterion was changed to include only cases with severe NPDR and PDR, the agreement was much poorer. This means the cutoff between mild and moderate NPDR is easier to recognize by both modalities than the cutoff between moderate and severe NPDR. However, the drawback of including moderate NPDR in the referral criteria, for applying the retinal photography in community hospitals to identify cases for referral to Trang Hospital, is that 11-15% more cases may be referred. Cost-effectiveness analysis of referral based on this criterion should be conducted before implementing into the existing healthcare system.

The advantage of the comprehensive eye examination over the photography is its ability to examine peripheral lesions, which may be missed in the single-field photography[14]. Retinal photography, on the other hand, may have advantages in detecting subtle changes that can easily be missed during a live examination, especially when time was a constraint. In addition, the photography has an advantage in implementing as an alternative to clinical examination to identify cases for referral[15].

The patients in the present study were well informed regarding the two diagnostic modalities and their potential side effects. It had also been written in the consent that they might have a slight chance of having some side effects of the mydriatic medications including angle closure. However, all patients were examined to rule out anterior chamber shallowness, which is an important risk factor of angle closure, and this serious complication never occurred in the present study.

In summary, the prevalence of NPDR and PDR in Trang was approximately 20% and 1.3% respectively. The sight-threatening cases were approximately 3%, which may be projected into 300 patients in Trang and 180,000 cases nationwide. Retinal photography may determine more cases than clinical examination. Combination of both modalities in DR screening may yield a closer to ideal prevalence.

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การศึกษาความชุกของโรคเบาหวานที่จอประสาทตาในผู้ป่วยเบาหวานจังหวัดตรัง โดยการถ่ายภาพจอประสาทตาและการตรวจตาอย่างละเอียด

ศุภชัย ศุภพฤกษ์สกุล, ไพศาล ร่วมวิบูลย์สุข, วรรษา เชาวกุล

วัตถุประสงค์: *เพื่อค้นหาความชุกของโรคเบาหวานที่จอประสาทตาในจังหวัดตรัง ด้วยวิธีการอ่านภาพถ่ายจอประสาทตาและการตรวจตาอย่างละเอียด*

วัสดุและวิธีการ: *เป็นการวิจัยเชิงพรรณนา ณ จุดเวลาใดเวลาหนึ่ง (Cross-Sectional Descriptive Design) ในผู้ป่วยเบาหวานทุกอำเภอของจังหวัดตรังโดยสุ่มมาร้อยละ10 จำนวน 714 คน ผู้ป่วยจะได้รับถ่ายภาพจอประสาทตา หลังจากขยายม่านตาด้วย 1% tropicamide จากนั้นจะได้รับการตรวจจอประสาทตาอย่างละเอียดโดยจักษุแพทย์ทั่วไป ผู้ป่วยที่ตรวจพบพยาธิสภาพของโรคเบาหวานที่จอประสาทตาจะได้รับการตรวจซ้ำโดยจักษุแพทย์ทางจอประสาทตา หลังจากนั้น 1 เดือนภาพถ่ายภาพจอประสาทตาจะได้รับการแปลผลโดยจักษุแพทย์ทางจอประสาทตาคนเดิม เพื่อศึกษาความชุกของโรคเบาหวานที่จอประสาทตาจากการตรวจทั้ง 2 วิธี*

ผลการศึกษา: *ความชุกของโรคเบาหวานที่จอประสาทตาชนิด non-proliferative diabetic retinopathy (NPDR) และ proliferative diabetic retinopathy (PDR) จากการตรวจตาโดยละเอียดจากจักษุแพทย์พบ 19.2% และ 1.1% ตามลำดับ ในขณะที่ความชุกของโรคเบาหวานที่จอประสาทตาชนิด non-proliferative diabetic retinopathy (NPDR) จากการตรวจด้วยถ่ายภาพพบสูงกว่าถึง 23.8% การยอมรับของการตรวจ diabetic macular edema (DME)ทั้ง 2 วิธีอยู่ในช่วงปานกลางโดยมีความไวน้อยกว่า 80% การตรวจทั้ง 2 วิธีจะแยก mild และ moderate non-proliferative diabetic retinopathy (mild และ moderate NPDR) ง่ายกว่าการแยก moderate และ severe non-proliferative diabetic retinopathy (moderate และ severe NPDR)*

สรุป: *ความชุกของโรคเบาหวานที่จอประสาทตาชนิด non-proliferative diabetic retinopathy (NPDR) และ proliferative diabetic retinopathy (PDR) จังหวัดตรังพบประมาณร้อยละ 20 และ1.3 ตามลำดับ ส่วนผู้ป่วย sight-threatening พบ 3% การตรวจตาโดยการถ่ายภาพจอประสาทตาจะทำให้ตรวจโรคเบาหวานที่จอประสาทตาได้มากขึ้น ดังนั้นการตรวจคัดกรองโรคเบาหวานที่ จอประสาทตาร่วมกันระหว่างการถ่ายภาพจอประสาทตาและการตรวจตาอย่างละเอียดน่าจะได้ความชุกโรคเบาหวานที่จอประสาทตาที่เป็นจริง*