

CHAPTER IV

THE RESULTS

4.1 The population

4.1.1 Participation data

Consecutive patients were recruited from Khon Kaen Regional hospital Ophthalmologic department from August to November 2006. Of 388 patients approached, informed consents were taken in all patients, fundus photographs were not taken in 7 patients because of the misunderstanding in research process. 8 patients were IDDM, 3 were IDDM with laser photocoagulation, 11 patients received posterior segment surgery or laser photocoagulation and 2 had bilateral mature cataract obscured the retinal findings which were met exclusion criteria. 363 type 2 diabetic patients with at least 1 eligible eye were enrolled in the study.

Table 4 Participation data of all recruited diabetic patients

Inclusion and exclusion	Number of participants
Participants with completed informed consent	388
Participants with fundus photographs	381
Participants with dilated indirect ophthalmoscopy	388
Participants with completed examinations	381
Participants with exclusion criteria	18
Final enrolled participants (one eye randomly selected)*	363

*One eye was randomly selected from each enrolled participants. In case with one eligible eye, there is no need for random selection. The eligible eye was recruited automatically.

4.1.2 The demographic data

Table 6 summarizes the demographic data for all enrolled study participants. The mean age of patients enrolled was 57.65 years (range 32-79 years) with predominantly female population (75.2%). Mean duration of diabetes was 8.2 years (range 0-32 years). Most of the participants were diagnosed as diabetes equal or less than 10 years (38.8 % within 0-5 years and 33.3 % within 6-10 years). Only 1.4 % of patients were diagnosed as diabetes more than 20 years. A best corrected visual acuity of 6/18 or better was measured in 69.1%, 70.5% of right and left eye respectively. A best corrected visual acuity of 6/24 or worse was measured in 30.9%, 29.5 % of right and left eye respectively.

Table 5 The demographic characteristics of the enrolled patients

Characteristics	Type II DM patients (n=363)
Mean age (yr)	57.7 (Range 32-79)
Sex	
- Male	90 (24.8%)
- Female	270 (75.2%)
Duration of diabetes (yr)	Range 0-32
- 0-5	141 (38.8 %)
- 6-10	121 (33.3 %)
- 11-15	62 (17.7 %)
- 16-20	34 (9.4 %)
- > 20	5 (1.4 %)
Mean duration (yr)	8.2 (SD 5.9)
Visual acuity	
- OD : 6/18 or better	251 (69.1 %)
: 6/24 or worse	112 (30.9 %)
- OS : 6/18 or better	256 (70.5 %)
: 6/24 or worse	107 (29.5 %)

4.1.3 The prevalence of diabetic retinopathy

The prevalence of diabetic retinopathy in this study was 42.1 % (a hospital-based program) and the prevalence of sight- threatening diabetic retinopathy was 17.7 %.(sight-threatening DR included severe NPDR, PDR and CSME)

4.2 Proportion of mydriatics need and poor quality images

Table 6 The proportion of mydriatics need and poor quality images

	Total (%)	The right eye (%)	The left eye (%)
Total enrolled images	363	177	186
Significant cataract	72 (19.8)	32 (18.1)	40 (21.5 %)
Mydriatics need	88 (24.2)	39 (22.0)	49(26.3)
Poor quality images*	19 (5.2)	8 (4.5)	11
Causes of poor quality images			
- significant cataract	13 (68.4)	5 (62.5)	8
- Technical problem	5 (26.3)	3 (37.5)	2
- Other**	1(5.3)	0	1

* Poor image quality: the presence of lesions not discernible determined by the ophthalmologist (can identify only disc and major vessels or the quality less than this)

**Other: pterygium (involve the visual axis)

Of the 363 enrolled photographs, 94.8 %(344 / 363) were assessed as acceptable quality and 5.2 %(19/363) were poor quality. There were 24.4 %(88 /363) of images needed mydriatics to achieve good image quality. For causes of poor image quality, significant cataract is the first rank (68.4%,13 /19), the second is technical problem (26.3%,5/19) and the third is pterygium (5.3%,1/19).

4.3 Grading of diabetic retinopathy by reference standard

Table 7 Distribution of retinopathy severity in all enrolled participants and randomly selected eyes based on dilated indirect ophthalmoscopy

DR classification*	Enrolled Participants' eyes			Randomly selected eyes		
	Total (%)	OD (%)	OS (%)	Total (%)	OD (%)	OS (%)
No DR	430(60.4)	214 (58.9)	216(59.5)	210(57.9)	108(61.0)	102(54.8)
Mild NPDR	65 (9.1)	33 (9.1)	32(8.8)	37(10.2)	14(7.9)	23(12.4)
Moderate NPDR	167(23.5)	84(23.1)	83(22.9)	91(25.1)	48(27.1)	43(23.1)
Severe NPDR	16(4.4)	6(1.7)	10(2.8)	8(2.2)	1(0.6)	7(3.8)
PDR	34(4.8)	17(4.7)	17(4.7)	17(4.7)	6(3.4)	11(5.9)
Ungradable**	14(1.9)	9(2.5)	5(1.4)	-	-	-

* Based on the Proposed International Clinical Diabetic Retinopathy Disease Severity Scales

** Ungradable fundus finding determined by the ophthalmologist using dilated indirect ophthalmoscopy

Of the Enrolled Participants' eyes, 712 eyes (98.03%) were able to be graded using dilated indirect ophthalmoscopy, 14 eyes (1.97%) were ungradable (corneal scar 1, pthisis bulbi 3, mature cataract 10). The distribution of eyes by disease severity is shown in table 8. The proportion of diabetic retinopathy severity in enrolled Participants' eyes and randomly selected eyes are comparable. Absent of retinopathy was detected in 61%, 54.8% of right and left randomly selected eyes. 7.9% and 12.4% of right and left randomly selected eyes were mild NPDR. 27.1% and 23.1% were moderate NPDR, 0.6% and 3.8% were severe NPDR and 3.4% and 5.9% were PDR.

4.4 Grading of diabetic retinopathy by reference standard and interpretation of the photographs by family physicians

Table 8 The distribution of diabetic retinopathy severity in 363 randomly selected eyes based on the dilated indirect ophthalmoscopy and interpretation of fundus photographs by family physicians

DR Classification*	Indirect ophthalmoscopy	The 1 st family physician	The 2 nd family physician	The 3 rd family physician	The 4 th family physician	The 5 th family physician
Total	363	363	363	363	363	363
No DR	210(57.9)	219(60.3)	176(48.5)	33(9.1)	37(10.2)	205(56.5)
Mild NPDR	37(10.2)	40(11.0)	46(12.7)	51(14.0)	70(19.3)	53(14.6)
Moderate NPDR	91(25.1)	49(13.5)	96(26.4)	91(25.1)	176(48.5)	52(14.3)
Severe NPDR	8(2.2)	14(3.9)	13(3.6)	127(35.0)	30(8.3)	20(5.5)
PDR	17(4.7)	8(2.2)	9(2.5)	46(12.7)	50(13.8)	7(1.9)
Ungradable**	-	33(9.1)	23(6.3)	15(4.1)	0	26(7.2)

* Based on the Proposed International Clinical Diabetic Retinopathy Disease Severity Scales

**Ungradable images determined by each family physician

There were wide variety in determining diabetic retinopathy severity by family physicians. The absent of retinopathy was determined ranging from 9.1-60.3%. For mild NPDR, the range was 11.0-19.3%, moderate NPDR, the range was 13.5-48.5%. The range of severe NPDR and PDR were 3.6-35.0% and 2.2-13.8%, respectively. In determining ungradable images, the range was 0-9.1%.

4.5 Grading of diabetic retinopathy by reference standard and interpretation of the photographs by each family physician

Table 9 The distribution of diabetic retinopathy severity in 363 randomly selected eyes based on the dilated indirect ophthalmoscopy and interpretation of fundus photographs by the first family physician

The 1 st family physician interpreted result	The reference standard					Total
	No DR	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	
No DR	179(85.2)	18(48.6)	21(23.1)	0	1(5.9)	219
Mild NPDR	7 (3.3)	13(35.1)	18(19.8)	1(12.5)	1(5.9)	40
Moderate NPDR	1 (0.5)	3(8.1)	39(42.9)	2(25.0)	4(23.5)	49
Severe NPDR	0	0	5(5.5)	5(62.5)	4(23.5)	14
PDR	0	1(2.7)	1(1.1)	0	6(35.3)	8
Ungradable	23(11.0)	2(5.4)	7(7.7)	0	1(5.9)	33
Total	210	37	91	8	17	363

* the numbers in parenthesis are percentage by column

In case of no DR, there were 85.2 % correctly diagnosed, and 3.8 % over-diagnosed. One case of no DR was diagnosed as moderate NPDR because of misinterpretation of drusen as exudates. 35.1 % of mild NPDR were correctly interpreted, 48.6% were under-diagnosed (most from miss of small microaneurysm), and 8.1 % were overdiagnosed as moderate NPDR (because of misinterpretation of drusen as exudates) and 2.7% were diagnosed as PDR (due to asteroid hyalosis). 42.9% of moderate NPDR were accurately interpreted, 42.9% were under-diagnosis by misjudged of exudates and drusen and limited retinal field. 6.6% were over-diagnosis, mostly cause from massive exudates. For severe NPDR, 62.5% were correct, 37.5% were underdiagnosed (due to limited retinal field and poor quality image from cataract) and none was over-diagnosed. In case of PDR, 35.3% were correct and 59.8% were under-diagnosis because of limited retinal field and missing of neovascularization. For the ungradable images judged by the first family physician, 16 of 33 were poor quality and 14 were acceptable images and 3 were PDR with tractional retinal detachment or vitreous hemorrhage.

Table 10 The distribution of diabetic retinopathy severity in 363 randomly selected eyes based on the dilated indirect ophthalmoscopy and interpretation of fundus photographs by the second family physician

The 2 nd family physician interpreted result	The reference standard					Total
	No DR	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	
No DR	148(70.5)	13(35.1)	13(14.3)	1(12.5)	1(5.9)	176
Mild NPDR	19(9.0)	16(43.2)	9(9.9)	1(12.5)	1(5.9)	46
Moderate NPDR	29(13.8)	6(16.2)	54(59.3)	3(37.5)	4(23.5)	96
Severe NPDR	2(1.0)	0	8(8.8)	1(12.5)	2(11.8)	13
PDR	0	0	1(1.1)	2(25.0)	6(35.3)	9
Ungradable	12(5.7)	2(5.4)	6(6.6)	0	3(17.6)	23
Total	210	37	91	8	17	363

* the numbers in parenthesis are percentage by column

In case of no DR, there were 70.5% of cases correctly diagnosed, and 23.8% overdiagnosed. Two cases of no DR were diagnosed as severe NPDR because of misinterpretation of drusen and asteroid hyalosis as exudates. 9% of no DR were diagnosed as mild NPDR. 13.8% of no DR were diagnosed as moderate NPDR due to misinterpretation of drusen as exudates. 43.2% of mild NPDR were correctly interpreted, 35.1% were under-diagnosed (most from limited retinal field and miss of small microaneurysm), and 16.2% were over-diagnosed as moderate NPDR because of misinterpretation of drusen as exudates). 59.3% of moderate NPDR were accurately interpreted, 24.2% were under-diagnosis by misjudged of exudates and drusen and limited retinal field. 9.9% were over-diagnosis mostly caused from massive exudates. For severe NPDR, 12.5% were correct, 62.5% were under-diagnosed (due to limited retinal field and poor quality image from cataract) and 25% were over-diagnosed (misinterpreted of flame-shape hemorrhage as neovascularisation). In case of PDR, 35.3% were correct and 47% were under-diagnosis because of missing of neovascularisation and vitreous hemorrhage and limited retinal field. For the

ungradable images judged by the second family physician, 11 of 23 were poor quality and 6 were PDR with tractional retinal detachment and 6 were acceptable images.

Table 11 The distribution of diabetic retinopathy severity in 363 randomly selected eyes based on the dilated indirect ophthalmoscopy and interpretation of fundus photographs by the third family physician

The 3 rd family physician interpreted result	The reference standard					Total
	No DR	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	
No DR	28(13.3)	2(5.4)	3(3.3)	0	0	33
Mild NPDR	42(20.0)	5(13.5)	4(4.4)	0	0	51
Moderate NPDR	58(27.6)	16(43.2)	16(17.6)	1(12.5)	0	91
Severe NPDR	54(25.7)	12(32.4)	48(52.7)	4(50.0)	9(52.9)	127
PDR	18(8.6)	2(5.4)	15(16.5)	3(37.5)	8(47.1)	46
Ungradable	10(4.8)	0	5(5.5)	0	0	15
Total	210	37	91	8	17	363

* the numbers in parenthesis are percentage by column

In case of absent retinopathy, there were 13.3% correctly diagnosed, and 81.9% over-diagnosed. 13.5% of mild NPDR were correctly interpreted, 5.4% were under-diagnosed (all were from missing of small microaneurysm), and 81% were over-diagnosed. Most of the over-diagnosed images of no DR and mild NPDR were correctly diagnosed by 1st, 2nd and 5th family physician. 17.6% of moderate NPDR were accurately interpreted, 7.7% were under-diagnosis by misjudged of exudates and drusen and limited retinal field. 69.2% were over-diagnosis mostly caused from inconfidence in diagnosis of moderate NPDR in cases of numerous exudates. For severe NPDR, 50% were correct, 12.5% were under-diagnosed (due to limited retinal field) and 37.5% were over-diagnosed by misinterpretation of flame-shape hemorrhage as neovascularization. In case of PDR, 47.1% were correct and 52.9% were under-diagnosed as severe NPDR because of missing of neovascularisation, limited reinal field and tractional retinal

detachment. For the ungradable images judged by the third family physician, 13 of 15 were poor quality and 2 were acceptable images.

Table 12 The distribution of diabetic retinopathy severity in 363 randomly selected eyes based on the dilated indirect ophthalmoscopy and interpretation of fundus photographs by the fourth family physician

The 4 th family physician interpreted result	The reference standard				PDR	Total
	No DR	Mild NPDR	Moderate NPDR	Severe NPDR		
No DR	34(16.2)	1(2.7)	2(2.2)	0	0	37
Mild NPDR	52(24.8)	14(37.8)	3(3.3)	1(12.5)	0	70
Moderate NPDR	87(41.4)	20(54.1)	63(69.2)	1(12.5)	5(29.5)	176
Severe NPDR	5(2.4)	1(2.7)	16(17.6)	5(62.5)	3(17.6)	30
PDR	32(15.2)	1(2.7)	7(7.7)	1(12.5)	9(52.9)	50
Ungradable	0	0	0	0	0	0
Total	210	37	91	8	17	363

* the numbers in parenthesis are percentage by column

In case of no DR, there were 16.2% correctly diagnosed, and 83.8% over-diagnosed mainly from misinterpretation of drusen and media opacity from cataract as exudates and vitreous hemorrhage respectively. 37.8% of mild NPDR were correctly interpreted, 2.7% were under-diagnosed (from limited retinal field), and 59.5% were over-diagnosed. Most of the over-diagnosed images of mild NPDR were correctly diagnosed by 1st, 2nd and 5th family physician. In case of over-diagnosed as PDR, the fundus images revealed peripapillary atrophy with cataract which lead to over-diagnosis by the 3rd family physician and ungradable by the others. 69.2% of moderate NPDR were accurately interpreted, 5.5% were under-diagnosis by misjudged between exudates and drusen and limited retinal field. 25.3% were over-diagnosis from inconfidence in diagnosis of moderate NPDR in cases of numerous exudates and poor quality images. For severe NPDR, 62.5% were correct, 25% were under-diagnosed (due

to limited retinal field) and 12.5% were over-diagnosed as PDR (in case that present of cataract). In case of PDR, 52.9% were correct and 47.1% were under-diagnosed as severe NPDR because of missing of neovascularisation and vitreous hemorrhage and limited retinal field. There were no ungradable images judged by the fourth family physician (even in 19 poor quality retinal images).

Table 13 The distribution of diabetic retinopathy severity in 363 randomly selected eyes based on the dilated indirect ophthalmoscopy and interpretation of fundus photographs by the fifth family physician

The 5 th family physician interpreted result	The reference standard					Total
	No DR	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	
No DR	171(81.4)	11(29.7)	23(25.3)	0	0	205
Mild NPDR	21(10)	18(48.7)	11(12.1)	1(12.5)	2(11.7)	53
Moderate NPDR	5(2.4)	5(13.5)	39(42.9)	2(25.0)	1(5.8)	52
Severe NPDR	0	0	11(12.1)	5(62.5)	4(23.5)	20
PDR	0	0	2(2.2)	0	5(29.5)	7
Ungradable	13(6.2)	3(8.1)	5(5.5)	0	5(29.5)	26
Total	210	37	91	8	17	363

In case of no DR, there were 81.4% correctly diagnosed, and 12.4% over-diagnosed. 10% of no DR were diagnosed as mild NPDR, 2.4% of no DR were diagnosed as moderate NPDR due to misinterpretation of drusen as exudates. 48.7% of mild NPDR were correctly interpreted, 29.7% were under-diagnosed (most from limited retinal field), and 13.5% were over-diagnosed as moderate NPDR (because of misinterpretation of drusen as exudates and blot retinal hemorrhage). 42.9% of moderate NPDR were accurately interpreted, 37.4% were under-diagnosis by misjudged of exudates and drusen and limited retinal field. 14.3% were over-diagnosis mostly caused from massive exudates and misinterpreted of flame-shape hemorrhage as neovascularisation. For severe NPDR, 62.5% were correct, 37.5% were under-diagnosed (due to limited retinal field) and none was over-diagnosed. In case of PDR, 9.5% were

correct and 41% were under-diagnosis because of missing of neovascularisation, and limited retinal field. For the ungradable images judged by the fifth family physician, 14 of 26 were poor quality and 5 were PDR with vitreous hemorrhage and 7 were acceptable images.

4.6 The inter-observer and intra-observer reliability

Table 14 The intraclass correlation for 2 raters of the 5 family physicians (Diabetic retinopathy severity)

Family physician ICC (95% CI)	1 st	2 nd	3 rd	4 th	5 th
1 st	X	0.66 (0.59-0.71)	0.51 (0.43-0.58)	0.40 (0.30-0.48)	0.69 (0.63-0.74)
2 nd	0.66 (0.59-0.71)	X	0.53 (0.46-0.60)	0.43 (0.34-0.51)	0.75 (0.70-0.79)
3 rd	0.51 (0.43-0.58)	0.53 (0.46-0.60)	X	0.36 (0.27-0.45)	0.51 (0.43-0.59)
4 th	0.40 (0.30-0.48)	0.43 (0.34-0.51)	0.36 (0.27-0.45)	X	0.34 (0.25-0.43)
5 th	0.69 (0.63-0.74)	0.75 (0.70-0.79)	0.51 (0.43-0.59)	0.34 (0.25-0.43)	X

Table 15 The intraclass correlation for 2 raters of the 5 family physicians (Referrals to ophthalmologists)

Family physician ICC (95% CI)	1 st	2 nd	3 rd	4 th	5 th
1 st	X	0.61 (0.54-0.67)	0.34 (0.25-0.43)	0.37 (0.27-0.45)	0.67 (0.61-0.72)
2 nd	0.61 (0.54-0.67)	X	0.33 (0.23-0.42)	0.47 (0.38-0.54)	0.62 (0.55-0.68)
3 rd	0.34 (0.25-0.43)	0.33 (0.23-0.42)	X	0.21 (0.11-0.31)	0.32 (0.23-0.41)
4 th	0.37 (0.27-0.45)	0.47 (0.38-0.54)	0.21 (0.11-0.31)	X	0.31 (0.22-0.40)
5 th	0.67 (0.61-0.72)	0.62 (0.55-0.68)	0.32 (0.23-0.41)	0.31 (0.22-0.40)	X

4.6.1 The inter-observer reliability

4.6.1.1 The inter-observer reliability (DR severity)

The ICC of all 5 family physicians was moderate (0.53, 0.49-0.58). The ICC for 2 raters of the first and second family physicians, the first and fifth family physicians, the second and fifth family physicians were good (0.66, 0.69, 0.75, respectively). The ICC for 2 raters of the others were moderate and fair.

4.6.1.2 The inter-observer reliability (Referrals to ophthalmologists)

The ICC of all 5 family physicians was moderate (0.43, 0.38-0.48). The ICC for 2 raters of the first and second family physicians, the first and fifth family physicians, the second and fifth family physicians were good (0.61, 0.67, 0.62, respectively). The ICC of the second and fourth family physicians were moderate (0.47). The ICC for 2 raters of the others were fair.

4.6.2 The intra-observer reliability

Table 16 The intra-observer reliability of the 1st and 3rd family physicians using ICC

Family physician	DR severity	Referrals to ophthalmologists
	ICC (95 % CI)	ICC (95 % CI)
1 st	0.92 (0.87-0.95)	0.87 (0.81-0.92)
3 rd	0.67 (0.53-0.78)	0.60 (0.44-0.72)

The intra-observer reliability by the ICC of the first and the third family physicians were very good (0.92 for DR severity and 0.87 for referrals to ophthalmologists) and good (0.67 for DR severity and 0.60 for referrals to ophthalmologists), respectively.

4.7 The sensitivity, specificity, positive predictive value and negative predictive value of the fundus photographs interpreted by family physicians in DR screening

Table 17 The sensitivity, specificity, positive predictive value and negative predictive value of the fundus photographs interpreted by family physicians in DR screening

Family physician	%Sensitivity (95% CI)	%specificity (95% CI)	% Accuracy (95% CI)	PPV	NPV
1	63.8(54.4,72.5)	87.9(83.1,91.7)	80.2(75.7,84.1)	71.43	84.11
2	77.6(68.9,84.8)	79.4(73.8,84.2)	78.8(74.2,82.9)	63.83	88.29
3	94.0(88.0,97.5)	31.2(25.5,37.4)	51.2(46.0,56.5)	39.07	91.67
4	94.8(89.1,98.1)	40.9(34.7,47.3)	41.9(36.7,47.1)	42.97	94.39
5	68.1(58.8,76.5)	89.5(85.0,93.0)	82.6(78.4,86.4)	75.24	85.66

*Use the referral cut off value at moderate NPDR or greater or ungradable images by family physicians

Table 15 shows the diagnostic diversity of sensitivity, specificity, PPV and NPV in DR classification judged by family physicians. The sensitivity and specificity range from 64.66-94.83 % and 31.17-89.47%, respectively. The PPV and NPV were 39.07-75.24, 84.11-85.66, respectively.