• Investigation •

Demographic features and visual outcomes of patients presenting to diabetic photo-screening and treated for sight threatening retinopathy in Fiji

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Abstract

• AIM: To describe the demographic features and visual outcomes of patients presenting to photo-screening services, and treated for sight threatening retinopathy (STR) in a low resource setting, Fiji.

• METHODS: A retrospective review of all new patients who presented for diabetic photo-screening at the Diabetic Eye Clinic, Suva in 2010. Fundus images were graded using standardised guidelines. Patient demographics, retinopathy grading and visual acuity data were extracted from the database and analyzed. Patients that received laser therapy and still attending follow up in 2012 were examined for disease progression

• RESULTS: Totally 2236 patients were photo-screened, 87% (3870/4472) of images were gradable. STR was observed in 26% (988/3870) with advanced STR (proliferative retinopathy/severe maculopathy) in 10% (385/3870). Of those with STR, 59% had BCVA ≥6/18, 31% with advanced STR were <6/60. Male gender [odds ratio (OR) 1.59; 1.20-2.12], history of hypertension (OR 1.36; 1.03-1.80) and peripheral neuropathy (OR 1.41; 1.01-1.95) were predictive of advanced STR. In 2012, 32% (315/988) attended follow up with 69% exhibiting advanced STR compared with 53% of the same cohort in 2010. Laser photocoagulation was administered to 212 eyes (212/3870, 5%) with retinopathy and maculopathy progression observed in 52% and 33% respectively. BCVA ≥6/18 was noted in 67% (143/212) of treated eyes. Improved glycaemic control (OR 46.52; 1.50-1441.90) amongst those with advanced STR was predictive of eyes that maintained good vision.

• CONCLUSION: In Fiji, a quarter of new patients presenting to photo-screening have STR with a third of those with advanced STR having already loss vision. Improved glycaemic control and timely treatment of patients with sight threatening complications is important in halting disease progression.

• KEYWORDS: diabetic retinopathy; sight threatening; photocoagulation; pacific islands; developing countries
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INTRODUCTION

Diabetic retinopathy is a well-recognised cause of visual impairment and irreversible blindness worldwide but is now increasingly identified in the Western Pacific Region. A population based survey in Fiji found 27% of 424 diabetic eyes had evidence of retinopathy or maculopathy[1]. In 2012, 27% of a cohort of 522 new patients presented with sight threatening retinopathy (STR)[2].

The Pacific Eye Institute (PEI) Diabetic Eye Clinic in Suva, established in 2009, is currently the largest photo-screening facility in Fiji. During the study period it provided photo-screening and laser treatment, but no anti-VEGF or vitreo-retinal services. The Standardised Pacific Guidelines-a version of the New Zealand. Diabetic Photo-screening Guidelines modified for low resource settings- are used in the PEI[3].

All eyes with STR should have referral for urgent specialist assessment and treatment. However, within the category of STR the spectrum of disease, and the consequent prognosis, is wide. Advanced STR with vitreous haemorrhage, tractional retinal detachment and severe exudative maculopathy has a poor prognosis in low resource settings. In an environment where the disease burden is escalating and services are limited, there is a constant need for treatment and outcomes to be evaluated to ensure optimal resource allocation. The aim of this study is to describe the presenting features and outcomes of patients presenting to photo-screening services with STR and try to identify patient cohorts who do best with laser treatment.

Table 1 Peripheral diabetic retinopathy grading

Grade	Description	Clinical signs
R0	No retinopathy	No abnormalities
R1	Minimal	<5 microaneurysms and/or dot haemorrhages
R2	Mild	>4 microaneurysms and/or dot haemorrhagesand/orexudates >2 disc diameters from the centre of the macula If more than 20 microaneurysms and/or haemorrhages per photographic image, then upgrade to R3
R3	Moderate	Any features of R2 mild plus up to 3 quadrants of blot or larger haemorrhages and/or up to 1 quadrant of venous beading
R4	Severe	One or more of: definite IRMA, 2 quadrants or more of venous beading, 4 quadrants of blot or larger haemorrhages
R5	Proliferative	One or more of neovascularisation, sub-hyaloid or vitreous haemorrhage, traction retinal detachment or retinal gliosis
RT	Stable, treated diabetic retinopathy	

Table 2 Diabetic maculopathy grading

Grade	Description	Clinical signs
M0	No macular disease	No microaneurysm, haemorrhage or exudate within 2 DD of centre of the macula
M1	Minimal	Microaneurysms and/or haemorrhages within 2 DD of the centre of the macula No exudates No retinal thickening No reduction in visual acuity
M2	Mild	Exudates and/or retinal thickening within 2 DD of the centre of the macula, but outside 1 DD of the centre
M3	Moderate	Exudates or retinal thickening within 1DD of the centre of the macula Foveola not involved No reduction in visual acuity
M4	Severe	Either microaneurysms and/or haemorrhages within 1 DD of the centre of the macula, reduction in visual acuity or exudates and/or retinal thickening involving the foveola, reduction in visual acuity

DD: Disc diameters.

SUBJECTS AND METHODS

Using a retrospective study design, the computerised database used at the Pacific Eye Institute Diabetic Eye Clinic was searched to identify the cohort of all new patients presenting to photo-screening services between January and December 2010. The database records patient age, gender, ethnicity, duration of diabetes, subjective assessment of glycaemic control, medical history (hypertension, dyslipidaemia, nephropathy, neuropathy), visual acuity, retinopathy/maculopathy grade, and clinical findings written in free text. Typically, patients with diabetes are referred to the photo-screening service by their general practitioner, hospital or community physician.

Visual acuity was measured using a Snellen chart. Pinhole acuity, recorded as "best corrected vision", was measured when unaided vision was less than 6/12. For the purposes of this study, "best corrected acuity" was used. Visual acuity was categorised as ≥6/18 (good), 6/24-6/60 (moderate), or <6/60 (poor). The level of glycaemic control, as volunteered by the patient, was graded as good (<6.99 mmol/L), moderate (7-9 mmol/L) or poor (>9.1 mmol/L)[3]. Random blood glucose levels were taken and recorded by a registered nurse. HbA1c recordings were not performed routinely and have not been included in the analysis.

Fundal photographs were taken with a 45 degree non mydriatic digital retinal camera. Mydriasis was used if the initial images failed to meet quality criteria. If the images were ungradable, a slit lamp examination was performed by an ophthalmologist. Supplementary images of the nasal, superior and inferior retina were obtained if retinopathy was detected, images were analyzed by a certified grader with a Postgraduate Certificate in Diabetes Eye Care (PGCDEC). Grading was performed according to the guidelines with retinopathy and maculopathy were graded separately, and follow up arranged based on grading outcome. A summary of the grading criteria used is presented in Tables 1, 2. Those requiring urgent laser were referred for treatment within a week of screening.

All new patients presenting in 2010 with STR, defined as R4 (severe non-proliferative diabetic retinopathy, NPDR), R5 (proliferative retinopathy), M3 (macula exudates or retinal thickening <1 disc diameter from the fovea with no reduction in vision) or M4 (M3 with reduction in visual acuity) were identified. Those still in attendance in 2012 were also

identified. Data from the earliest and latest clinic visits between 2010 and 2012 respectively were extracted. Information regarding patient demographics, retinopathy grading, best corrected vision and details of any administered treatments were analyzed.

Progression of disease was defined as an increase in retinopathy or maculopathy grade. For patients with advanced STR (R5 and/or M4) recorded at baseline, progression was confirmed from clinical records as required. The efficacy of laser treatment was evaluated based on changes to retinopathy grading and documented clinical changes.

Validation of Photo-grading Fortnightly internal audits of 20 photographs are undertaken by the lead Ophthalmologist (Sikivou B) at the Diabetic Eye Clinic to ensure reliability of grading. In addition, a sample of 100 fundus images (10%) taken of eyes presenting in 2010 were independently graded by the primary author. A high level of agreement (99%) was observed, indicating adequate reliability of photo-screening.

Ethics Ethical approval was obtained from the Fiji Ministry of Health to access the diabetic photo-screening database at the Pacific Eye Institute, and for the results to be published. An application for approval was also submitted to the University of Auckland Human Participants Ethics Committee, who advised that ethical approval was not required for this study due to its retrospective nature.

Statistical Analysis All values were entered into an Excel database (Microsoft Office 2013, Redmond, WA, USA) and statistical analysis performed using SPSS (IBM statistics software v22, Chicago, IL, USA). All reported tests were two-tailed using Chi square analysis with *P*-values <0.05 indicating statistical significance. Binary logistic regression was performed to identify if age, duration of diabetes, ethnicity, hypertension, dyslipidemia, nephropathy, neuropathy, insulin therapy, subjective glycaemic control, presenting blood sugar level were predictive of severity of retinopathy and maculopathy as well as treatment response. An automatic backward selection procedure, based on likelihood ratio tests with a 0.05 significance level cut-off, was used to determine the significant variables that remained in the model.

RESULTS

In 2010, 2236 new diabetic patients presented to the photo-screening service. Of the 4472 eyes screened, 14% (606/4472) were ungradable, almost exclusively due to cataract. Of the 3870 gradable eyes (1956 patients), retinopathy was observed in 55% (2114/3870), STR in 26% (988/3870) and advanced STR in 10% (385/3870).

Including all new diabetic patients (2236), 71% (1590/2236) were Indo-Fijian and 24% (532/2236) Fijian. Twenty-eight percent (636/2236) of patients had STR in at least one eye and 16% (356/2236) had bilateral disease. A description of the clinical cohort with STR is presented in Table 3. Subjective glycaemic control was reported as poor in 45% (287/636) patients with a random blood sugar level of equal or greater than 10 mmol/L noted in 46% (293/636). A significant association (χ^2, P<0.01) was observed between subjective glycaemic control and random blood sugar level taken at screening, with 75% of those with random blood sugar level (BSL) ≥10 mmol/L admitting to poor control.

Table 3 Cohort characteristics of patients with sight threatening diabetic retinopathy (636 patients)

Characteristics	Values
Median age (a, range)	61 (29-86)
Gender, *n* (%)	
F	406 (64)
M	230 (36)
Ethnicity, *n* (%)	
Indo-Fijian	457 (72)
Fijian	149 (23)
Other	30 (5)
Diabetes type, *n* (%)	
Type 1	39 (6)
Type 2	467 (73)
Unknown	130 (20)
Median duration of diabetes (a, range)	10 (1-27)
Subjective diabetic control, *n* (%)	
Good	159 (25)
Moderate	197 (31)
Poor	280 (44)
Treatment, *n* (%)	
Diet controlled	27 (4)
Oral medication	501 (79)
Insulin	108 (17)
Hypertension, *n* (%)	337 (53)
Peripheral neuropathy, *n* (%)	203 (32)
Dyslipidaemia, *n* (%)	54 (8)
Nephropathy, *n* (%)	26 (4)

Subgroup analysis between advanced STR and other STR.

Of 3870 gradable eyes, 3% were R4 (severe NPDR), 7% R5 (proliferative), 17% M3 (moderate maculopathy) and 8% M4 (advanced maculopathy).

The presenting grades of 988 eyes with STR are listed in Table 4.

Multivariate logistic regression analysis showed male gender, history of hypertension and peripheral neuropathy to be predictive of eyes with advanced STR compared to those other forms of STR (Table 5).

Visual Acuity Of 988 eyes with STR, 59% (581/988) presented with visual acuity of ≥6/18, 28% (274/988) were 6/18-6/60 and 13% (133/988) <6/60. With regression analysis,

Table 4 Presenting grades of 988 eyes with sight threatening retinopathy

Retinopathy	Maculopathy		
	Mild (M0-2)	Moderate (M3)	Severe (M4)
Mild-moderate NPDR (R0-3)	-	54%	7%
Severe NPDR (R4)	2%	6%	5%
Proliferative DR (R5)	2%	6%	18%

DR: Diabetic retinopathy; NPDR:Non-proliferative diabetic retinopathy.

Table 5 Predictors of advanced sight threatening retinopathy

Variable	OR	95%CI	*P*
Gender			
F	-	-	
M	1.59	1.20-2.12	0.01
Hypertension			
No	-	-	-
Yes	1.36	1.03-1.80	0.03
Neuropathy			
No	-	-	-
Yes	1.41	1.01-1.95	0.04

OR: Odds ratio.

advanced maculopathy (OR 12.58; 6.96-22.74; $P<0.03$) was predictive of cases with <6/60 compared to those with vision ≥6/18. Of the 385 eyes presenting with advanced STR, 38% (144/385) had moderate vision (6/18-6/60) while 31% (118/385) were <6/60.

Follow-up In 2012, 28% (180/636) of patients from the original cohort with STR in at least one eye were still attending follow up. Of the 315 eyes with STR, 92% (291/315) still had STR in 2012 and 69% (217/315) had advanced STR compared to 53% (167/315) of the same cohort in 2010. Sixty-six percent (207/315) of eyes had ≥6/18 vision (65% in 2010) while 21% (65/315) were <6/60 (11% in 2010). Poor subjective glycaemic control (>10 mmol/L) was noted in 57% (179/315) compared to 47% (149/315) in 2010. A median random blood sugar level of 10.6 mmol/L was noted in 2012 compared to 10 mmol/L in 2010. No significant favourable predictors were identified for eyes that maintained good vision after two years. There was no significant association between good random BSL (<10 mmol/L) at initial and follow up visits, and good vision at two years.

Outcomes Following Laser Treatment Laser photocoagulation was administered to 5% (212/3870) of eyes. This represented 21% of eyes with STR (212/998,147 patients) that received treatment in at least one eye in 2010 and were still attending follow up in 2012. Of those treated, the median age was 61y (29-78y), 60% were female (128/212) and 83% (177/212) Indo-Fijian. Fifty-six percent (118/212) eyes underwent macula laser (focal or grid) alone, 28% (60/212) Pan Retinal photocoagulation (PRP) alone and 16% (34/212) received both types of treatment with a median of two treatments (range one to five) per eye. Of the 152 eyes that received macula laser, including those that also received PRP, 73% had initially presented with moderate maculopathy (M3). Of the 94 eyes that underwent PRP, including those who also received macula laser, 62% had presented with proliferative disease (R5). Progression of retinopathy occurred in 52% (49/94) following PRP and maculopathy progression in 33% (50/152). Of those with advanced STR, progression occurred in 47% (46/97) despite treatment. Amongst those with advanced STR, those on insulin therapy (OR 6.06; 2.02-18.21; $P=0.01$) were likely to progress despite laser treatment. BCVA ≥6/18 was noted in 67% (143/212) of lasered eyes. Of treated eyes with advanced STR, 57% (24/42) that presented with ≥6/18 vision were able to maintain this level of vision after two years. Improved glycaemic control, defined as >20% reduction of random BSL between 2010 and 2012, was identified as a favourable prognostic factor for those with advanced STR that maintained good vision between 2010 and 2012 (OR 46.52; 1.50-1441.90; $P=0.03$). Of eyes with advanced STR presenting with <6/60 vision in 2010, 50% (7/14) had no improvement in vision, however no prognostic associations or predictors were identified.

DISCUSSION

Diabetes is a significant health problem for developing countries including the Islands of the Western Pacific[4-5]. In Fiji the prevalence of type 2 diabetes is increasing and it is projected to affect 15%-25% of the population by the year 2020[6]. In our cohort, 55% of gradable eyes had retinopathy, 26% had STR and 16% of patients presented with bilateral STR. The prevalence of STR is higher than reports from high resource settings in Europe and North America (6%-8%)[7]. Other low resource settings such as Malawi have reported DR prevalence at 33% and STR at 20%[8].

The majority of patients with STR were Indo-Fijian females. Over half of eyes with STR presented with moderate macula disease and mild-moderate diabetic retinopathy with 59% having best corrected vision ≥6/18. Of the 10% that presented with advanced STR, 3% had already lost vision from retinal detachment, vitreous haemorrhage, diabetic macular edema or rubeotic glaucoma. Male gender, history of hypertension and neuropathy were identified as significant predictors of more advanced disease in eyes presenting with STR which is consistent with other studies[9-10]. Furthermore, recent studies have shown an increase in prevalence of hypertension for both ethnic groups over the past 30y[11]. In contrast to earlier studies, duration of diabetes and insulin use were not identified as significant predictors of STR[3]. The protective effect of glycaemic control is well established. Random blood sugar levels were routinely taken with 49% of patients with STR presenting with elevated blood sugar levels, which

suggest inadequate glycaemic control amongst the cohort. Unfortunately, HbA1c was not routinely performed and this represents a weakness of our study, especially when analysing the variables involved in disease progression.

The majority of diabetic patients in Fiji have type two diabetes and many are still diagnosed when they present to medical services with systemic and ocular diabetic complications[12-13]. Even amongst those diagnosed, the lack of systematic evaluation, monitoring and inadequate referral systems resulted in delays in specialist assessment similar to those reported in other developing countries[14]. Patient factors, specifically access to and compliance is an issue with only 21% were still attending photo-screening follow up in 2012. With the population in Fiji spread over 330 islands scattered across 1.3 million square kilometres of ocean (equivalent in size to the Northern Territory in Australia) there are significant travel costs as well as loss of income associated with attending follow up visits a barrier to accessing health services. This is significant as 35% of the population in Fiji are thought to live in poverty (below the basic needs poverty line-World Bank)[15]. Laser photocoagulation is proven to help prevent visual loss from diabetic retinopathy[16-17]. In Fiji, a low resource setting, it is still the main treatment option. Of the 212 eyes that underwent laser, progression was halted in 67% receiving macula laser and 48% receiving PRP. The differences in outcomes are likely to be attributed to the closer follow up of those with moderate maculopathy and early treatment. Furthermore, we found that laser treated patients with improved glycaemic control were able to maintain good vision at two years. These findings emphasise the importance of early referral, close follow up and improved glycaemic control as favourable prognostic factors for diabetic retinal disease. We also found that patients with advanced STR on insulin therapy were at greater risk of disease progression. This may reflect patients with difficult control, unfortunately we cannot prove this as HbA1c blood tests were not routinely performed. Unfortunately eyes with STR and vision worse than 6/60 at presentation (133/988) requiring surgical intervention are unlikely to regain vision, especially in a low resource setting with no vitreo-retinal surgical service. Only those patients who can afford to travel overseas for surgical treatment have a chance to regain their vision. Likewise anti-VEGF treatment, used extensively in the developed world for the treatment of sight threatening retinopathy, is notreadily accessible in this low resource setting[18-20]. A single injection of Bevacizumab supplied from New Zealand costs 185 FJD, which is well out of reach for most household where the average income is 60 FJD per week[15].

In conclusion, more than a quarter of all new patients present to screening services Fiji present with sight threatening retinopathy in a least one eye. The chasm between current best practice in a high resource setting and a low resource one is alarming and ever deepening. In a low resource setting where treatment options are limited, metabolic control of risk factors is essential in reducing the development and progression of diabetic retinopathy. Furthermore, timely early referral of all diabetic patients is essential in both the diagnosis, and application of effective sight preserving laser treatment, to eyes with sight threatening retinopathy.

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