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Original Research Article

Systemic Predictors of Post Laser Visual Prognosis in Diabetic Retinopathy

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Abstract:

Background: Early detection of sight threatening diabetic retinopathy and treatment with laser is the only way to prevent visual deterioration and major visual loss.

Methods: The prospective observational study was conducted at the retina clinic of a tertiary eye care centre in South India from June 2021 to June 2022. A total of 248 eyes of 134 PDR [Proliferative Diabetic Retinopathy] patients requiring PRP [Panretinal Photocoagulation] were included. Patients requiring vitreoretinal surgery or intravitreal anti-vascular endothelial growth factor therapy and those with significant media opacity or other ocular comorbidities affecting assessment of vision were excluded.

Results: Good visual outcome was found in 192 eyes (77.4%) and poor outcome in 56 eyes (22.6%) at 6 months. Patients with poor prognosis had significantly higher levels of baseline and follow-up HbA1c, fasting and postprandial blood sugar, LDL cholesterol, triglycerides, serum creatinine and proteinuria, and lower levels of haemoglobin ($p<0.05$ for all).

Conclusion: Poor glycaemic control, associated systemic comorbidities and female sex were significant predictors of poor visual outcome following panretinal photocoagulation in proliferative diabetic retinopathy.

Keywords: Panretinal Photocoagulation Retinopathy, Proliferative Diabetic Retinopathy, Panretinal Photocoagulation, Visual Prognosis, HbA1c, Diabetic Nephropathy, Dyslipidaemia.

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Introduction

Diabetic Retinopathy [DR] is the leading cause of visual disability in diabetics. The reported prevalence in India ranges from 17.6% to 28.2%. With this prevalence, the number of people with Diabetes Mellitus [DM] is likely to increase to 79.4 million and people with DR is likely to increase to 22.4 million by the year 2030. Both DM and DR are relatively less, between 10% and 12%, in rural India compared to urban India but not small enough to ignore. Considering that prevalence of DR at a moderate level of 20% in urban India and at a lower level of 10% in rural India and assuming that 70% of Indians live in rural areas, the incidence of DR in rural India could rise to 10.97 million by the year 2030. In addition, there is an acute shortage of skilled manpower to screen DR in rural India.[1] DR is one of the major complications of diabetes and is a leading cause of blindness and vision impairment. Approximately 75% of persons suffering from type 1 diabetes develop retinopathy, while approximately 50% of persons with type 2 diabetes may develop retinopathy, and approximately 25% of persons with diabetes may develop macular edema. During the next two decades, over 360 million people worldwide are projected to have diabetes and its complications.[2] Diabetes is a systemic malfunction of carbohydrate, lipid, and protein metabolism that leads to vascular and tissue damage in organs such as the retina resulting in damage to the retinal tissue elements and associated vessels. Functional and anatomic changes occur in the retina before the onset of clinically evident vascular lesions.

Preventive strategies have to be evolved to ensure that blindness due to diabetic retinopathy does not become a public health problem in India. Early detection of sight threatening diabetic retinopathy and treatment with laser is the only way to prevent visual deterioration and major visual loss. Good glycemic control, timely treatment and vitrectomy in advanced stages can together bring visual loss due to diabetic retinopathy under control.[3] A detailed look into the various factors that accelerate this visual loss is absolutely an emergency in the present scenario.

Aims and Objective: The research question was: “What are the systemic predictors of post-laser visual prognosis in diabetic retinopathy?” The aim was to assess the metabolic and systemic factors that influence visual outcomes after panretinal photocoagulation (PRP) in patients with proliferative diabetic retinopathy. The patients were classified based on favorable and unfavorable post-laser visual prognosis.The relationship between demographic and clinical characteristics and visual outcome was analysed by comparing glycaemic, lipid, renal, and hematological investigations between the two outcome groups.

Materials and Methods

This was a hospital-based, prospective observational study conducted in the Retina Clinic of a tertiary eye care center in South India from June 2021 to June 2022. A total of 300 eyes from 150 patients were screened; of these, 248 eyes from 134 patients were included in the study. Best-corrected visual acuity assessment, slit-lamp examination, dilated fundus examination, and fundus fluorescein angiography when needed were done.

Inclusion and Exclusion Criteria: All cases of diabetic retinopathy that required PRP laser treatment were included in the study including patients with diabetic nephropthy, hyperlipidemia and anaemia. All cases of diabetic retinopathy who did not require laser treatment and require surgical treatment like vitrectomy and intravitreal anti VEGF (Vascularendothelial Growth Factor) were excluded. Patients with significant cataract or other nondiabetic ocular diseases, which are likely to interfere with the assessment of visual outcome, are excluded were excluded. Patients with significant cataract or other nondiabetic ocular diseases, which were likely to interfere with the assessment of visual outcome, were excluded.

Sample Size: A Sample Size of 254 was calculated with an event rate of 21 % and exposure variable of 5 and a drop out of 10 %. Multivariate logistic regression assumption used. Modified Odds ratio to calculate sample size. Patients were recruited consecutively into the study.

Methods

All patients underwent dilated ophthalmoscopy, slit lamp biomicroscopy and FFA where indicated. Patients were selected for laser based on ETDRS criteria. Patients selected were investigated for diabetic control by HbA1C and other metabolic risk factors like nephropathy, hyperlipidemia, anaemia and hypertension were evaluated.

A proforma was made and evaluation was done on its basis. Follow up was done at 1 month, 3 month, and 6 month after laser treatment.

All the data were computed and statistical analyses were done using the SPSS version 27. Quantitative variables were summarised as means and categorical variables as proportions. Analysis of Variance was done for quantitative variables and Chi square test for qualitative variables. Logistic Regression analysis was used to assess factors that cause a poor visual outcome following laser therapy. $p<0.05$ was considered to be statistically significant.

Results

Out of the 248 eyes taken for the study,136 (54.8%) were males and 128(51.6%) had systemic diseases in addition to diabetes mellitus. With regards to the mode of treatment taken 126(50.8%) took OHA alone, only 95(38.3%) used insulin alone and the rest 22(8.9%) used both.71 of the patients (28.6%) had diabetes for more than 15 years.101(40.7%) had a baseline BCVA 6/60-6/36.

Table 1: Baseline variables

Variable	Category	n (%)
Sex (N=248)	Male	136 (54.8%)
	Female	112 (45.2%)
%Systemic diseases in addition to Diabetes Mellitus (N=248)	Yes	128 (51.6%)
	No	120 (48.4%)
Treatment (N=243)	OHA	126 (50.8%)
	Insulin	95 (38.3%)
	Both	22 (8.9%)
Diabetes duration (N=248)	Less than 10	101 (40.7%)
	10 to 15	76 (30.6%)
	More than 15	71 (28.6%)
Baseline BCVA (N=248)	6/60-6/36	101 (40.7%)
	6/24-6/18	61 (24.6%)
	>6/18	46 (18.5%)
	<6/60	40 (16.1%)
Baseline proteinuria (N=248)	No	217 (87.5%)
	Yes	31 (12.5%)

The mean age of the population is 56 years with a mean BP of 121/80mmHg.Mean FBS/PPBS was 120/200 g percent. Post LASER BCVA at 6 months was favourable (improved/ stabilised) for 192 patients (77.4%) and unfavourable for 56 (22.6%).

The percentage of Post LASER BCVA at 6months which was favourable (improved/stabilised) in comparison to the sex, age group, duration of diabetes, mode of treatment and the presence of other systemic diseases.

Table 2: Post LASER BCVA at 6 months

Variable	Category	Favourable n (%)	Unfavourable n (%)	Total n (%)	p value
Sex	Female	78 (40.6%)	34 (60.7%)	112 (45.2%)	0.008
	Male	114 (59.4%)	22 (39.3%)	136 (54.8%)	
Age group	<40 years	16 (8.3%)	2 (3.6%)	18 (7.3%)	0.252
	41–60 years	116 (60.4%)	40 (71.4%)	156 (62.9%)	
	>60 years	60 (31.3%)	14 (25.0%)	74 (29.8%)	
Duration of diabetes	<10 years	75 (39.1%)	26 (46.4%)	101 (40.7%)	0.058
	10–15 years	66 (34.4%)	10 (17.9%)	76 (30.6%)	
	>15 years	51 (26.6%)	20 (35.7%)	71 (28.6%)	
Treatment	Both OHA and insulin	15 (8.0%)	7 (12.5%)	22 (8.9%)	0.231
	Insulin	78 (41.7%)	17 (30.4%)	95 (38.3%)	
	OHA	94 (50.3%)	32 (57.1%)	126 (50.8%)	
Systemic disease in addition to DM	Present	85 (44.3%)	43 (76.8%)	128 (51.6%)	<0.001
	Absent	107 (55.7%)	13 (23.2%)	120 (48.4%)	

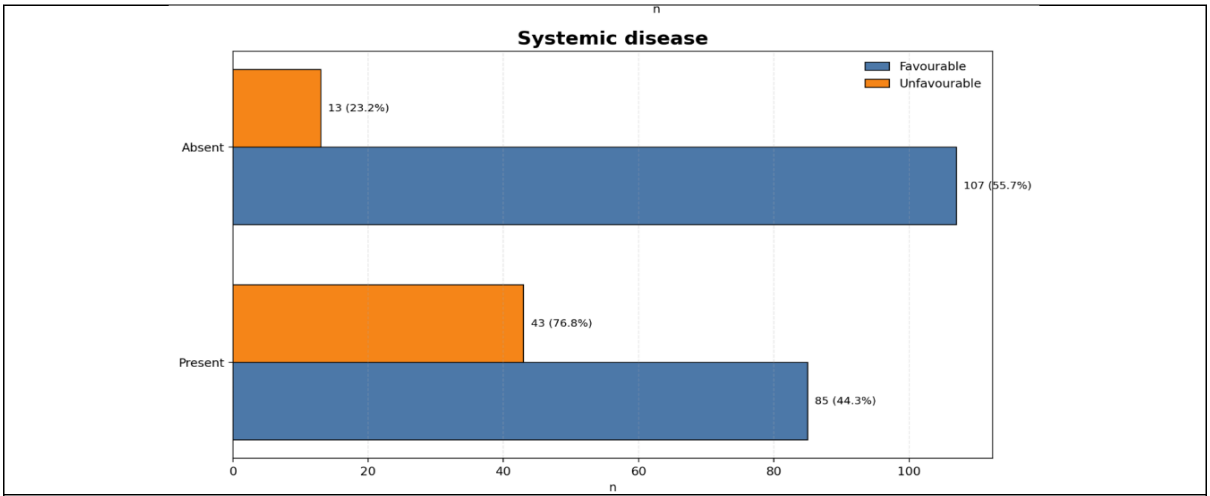

Figure 4: The influence of systemic diseases

The mean values of age of the study population, HbA1C at baseline, 6 months, FBS, PPBS, LDL, TG, Proteinuria, creatinine at 6 months compared with favourable/unfavourable prognosis.

Table 5: Metabolic profile at 6 months

Variable	Favourable prognosis Median (IQR)	Unfavourable prognosis Median (IQR)	Mann–Whitney U	p value
Age, years	56.00 (50.00–62.00)	53.00 (48.50–60.25)	6225	0.072
HbA1c at baseline, %	7.00 (6.00–8.00)	8.00 (7.00–9.35)	2891.5	<0.001
HbA1c at 6 months, %	7.00 (6.00–7.04)	8.00 (7.00–9.00)	2939	<0.001
Fasting blood sugar at 6 months, mg/dL	120.00 (95.00–150.00)	145.50 (120.00– 201.75)	3131	<0.001
Post-prandial blood sugar at 6 months, mg/dL	200.00 (180.00–242.75)	250.00 (210.00– 300.00)	3083	<0.001
LDL cholesterol at 6 months, mg/dL	112.00 (100.00–150.00)	150.00 (120.00– 182.25)	3261.5	<0.001
Triglycerides at 6 months, mg/dL	120.00 (100.00–160.00)	150.00 (116.00– 200.00)	3810	0.001

Proteinuria at 6 months	0.00 (0.00–0.00)	0.00 (0.00–600.00)	3871	<0.001
Creatinine at baseline, mg/dL	0.80 (0.70–1.00)	1.02 (0.90–1.50)	2917	<0.001
Haemoglobin at 6 months, g/dL	13.00 (12.00–14.00)	12.00 (11.00–13.00)	6906.5	0.001

Multivariate Analysis

Figure 5:Independent predictors

Predictor	Category / unit	Adjusted OR	95% CI	p value
HbA1c at baseline	Per 1% increase	1.78	1.40–2.26	<0.001
Systemic disease in addition to Diabetes Mellitus	Present vs absent	3.91	1.87–8.17	<0.001
Sex	Female vs male	2.15	1.09–4.26	0.028
Baseline BCVA code	Per unit increase	1.06	0.76–1.49	0.72
Duration of diabetes	Per unit increase	0.98	0.65–1.49	0.926

A multivariable binary logistic regression model was fitted to identify independent predictors of unfavourable visual prognosis. The model was statistically significant, $\chi^2(5) = 53.871$, $p < 0.001$, and explained 29.7% of the variance in visual prognosis based on Nagelkerke R^2. The model correctly classified 82.3% of cases overall.

Higher baseline HbA1c was independently associated with increased odds of unfavourable visual prognosis (aOR = 1.78, 95% CI: 1.40–2.26, p < 0.001). Presence of systemic disease **in addition to Diabetes Mellitus** was also significantly associated with unfavourable prognosis (aOR = 3.91, 95% CI: 1.87–8.17, p < 0.001). Female sex was independently associated with higher odds of unfavourable prognosis compared with male sex (aOR = 2.15, 95% CI: 1.09–4.26, p = 0.028). Baseline BCVA code and duration of diabetes were not significant independent predictors.

Discussion

In the present study, 77.4% of eyes achieved a favourable visual outcome at six months following laser treatment, whereas 22.6% demonstrated an unfavourable prognosis. Similarly, Rema et al., who observed stabilisation or improvement in vision in the majority of patients following PRP and emphasised the importance of controlling systemic risk factors in determining long-term visual outcomes.[4]

The most important finding of the present study was the strong association between poor glycaemic control and unfavourable visual prognosis. Baseline HbA1c was significantly higher in patients with unfavourable visual outcomes, and multivariate logistic regression demonstrated that each 1% increase in baseline HbA1c increased the odds of poor visual prognosis by 78% (aOR=1.78, 95% CI 1.40–2.26, p<0.001). Similar finding in the landmark Diabetes Control and Complications Trial (DCCT), which demonstrated that intensive glycaemic control significantly reduced the development and progression of diabetic retinopathy.[5-7] The DCCT investigators stressed there is a continuous relationship between HbA1c and retinal complications.[8] The DCCT demonstrated that intensive insulin treatment is associated with a decreased risk of either the development or progression of DR in patients with type 1 diabetes. However even in the intensely treated group retinopathy could not be completely prevented over the 9 year course of the study.[5] Kaiser et al stated that earlier onset of Diabetes, poor vision at presentation were associated with poor outcome.[9] Bek et al stated that high pretreatment visual acuity and low age were strong positive predictors of post-treatment visual acuity.[10] Low levels of hemoglobin glycosylation (A1C <8%) during the pretreatment, treatment, and posttreatment periods are associated with a regression of proliferative diabetic retinopathy after PRP.[11]

Kotoula et al. also demonstrated that patients who maintained HbA1c levels below 8% before and after PRP showed significantly greater regression of proliferative diabetic retinopathy than those with poorer metabolic control.[11] Similarly, Henricsson et al. reported that progression of diabetic retinopathy was closely related to glycaemic control even among patients with relatively mild diabetes.[12] The probable mechanism is persistent hyperglycaemia-induced endothelial dysfunction, capillary basement membrane thickening, oxidative stress, and increased production of vascular endothelial growth factor (VEGF), all of which contribute to retinal ischemia and compromise the beneficial effects of laser treatment. Therefore, strict glycaemic control remains an essential component of successful management of proliferative diabetic retinopathy.

The presence of systemic disease in addition to diabetes mellitus emerged as another significant predictor of poor visual prognosis. Patients with associated systemic illnesses had nearly four-fold higher odds of developing an unfavourable visual outcome after PRP (aOR=3.91, 95% CI 1.87–8.17, p<0.001). Previous studies have demonstrated the coexistence of systemic vascular complications is associated with more severe retinal disease and poorer visual outcomes.

The higher prevalence of systemic disease among patients with unfavourable prognosis in our study suggests that microangiopathy affects visual prognosis following laser treatment. This finding highlights the need for a comprehensive systemic evaluation in patients undergoing PRP. Patients with unfavourable visual outcomes demonstrated significantly higher baseline creatinine levels and proteinuria at follow-up compared to those with favourable outcomes. These findings indicate an important role of renal dysfunction in determining visual prognosis. The association between diabetic nephropathy and retinopathy has been well documented.[8] Patients with renal failure develop worsening of their retinopathy particularly affecting the macula (macular oedema), but are also at risk of PDR. The risk factors of diabetic nephropathy in patients with diabetic retinopathy requiring panretinal photocoagulation (PRP) and the visual prognosis was studied by [Ha M et al]

Manaviat et al. reported a strong relationship between microalbuminuria and diabetic retinopathy among patients with type 2 diabetes.[13] Skyler similarly emphasised that retinopathy and nephropathy share common pathogenic mechanisms involving microvascular damage.[8]

Ha et al. specifically evaluated patients with diabetic retinopathy requiring PRP and found that diabetic nephropathy was associated with more severe disease and poorer prognosis.[14] Renal dysfunction may worsen retinal outcomes through endothelial dysfunction, fluid retention, increased vascular permeability, and aggravation of macular oedema. The significant association observed in the present study, therefore, reinforces the importance of screening for nephropathy and optimising renal function in patients undergoing laser treatment.

The present study demonstrated significantly higher LDL cholesterol and triglyceride levels among patients with unfavourable visual outcomes. Although these variables did not remain independently significant in multivariate analysis, their association in univariate analysis suggests a contributory role. The ETDRS identified elevated serum lipid levels as important risk factors for retinal hard exudates and moderate visual loss.[15] Increased triglyceride levels were also associated with progression to high-risk proliferative diabetic retinopathy.[15] Kim et al. reported significantly elevated serum lipoprotein levels among patients with proliferative diabetic retinopathy, further supporting the role of dyslipidaemia in disease progression.[16] Elevated lipid levels may contribute to retinal vascular leakage, hard exudate formation, and persistent macular oedema, thereby limiting visual recovery following laser treatment. Consequently, lipid control should form an integral part of diabetic retinopathy management.

Haemoglobin levels were significantly lower among patients with unfavourable visual outcomes. Anaemia may aggravate retinal hypoxia by reducing oxygen delivery to ischemic retinal tissue and thereby stimulate the production of angiogenic factors. Reduced haemoglobin levels have previously been implicated in worsening diabetic retinopathy because of impaired retinal oxygenation and increased retinal ischemia. The present findings support the concept that correction of anaemia may improve the retinal microenvironment and potentially enhance treatment response.

Female sex emerged as an independent predictor of unfavourable visual prognosis in the present study, with women having approximately twice the risk of poor visual outcome compared with men (aOR=2.15, 95% CI 1.09–4.26, p=0.028).

Previous studies evaluating visual outcomes following PRP have not consistently identified gender as a significant determinant. Therefore, this finding should be interpreted with caution. The observed association may reflect differences in healthcare access, health-seeking behaviour, socioeconomic factors, disease severity at presentation, or associated systemic comorbidities rather than a true biological effect.

Although a longer duration of diabetes showed a trend toward poorer outcomes, it did not remain significant in multivariate analysis. Similarly, baseline visual acuity was not independently associated with visual prognosis. Kaiser et al. reported that poorer visual acuity at presentation was associated with worse visual outcomes following PRP.[9] Conversely, Bek and Erlandsen found that better pretreatment visual acuity and younger age were significant predictors of improved post-treatment vision.[10] The discrepancy between these studies and our findings may be due to differences in sample size, disease severity, treatment protocols, and adjustment for systemic factors. The effect of baseline visual acuity may become less important once metabolic and systemic variables are taken into account.

The findings of this study emphasise that successful treatment of proliferative diabetic retinopathy extends beyond laser photocoagulation alone. Patients with poor glycaemic control, renal dysfunction, dyslipidaemia, anaemia, and associated systemic diseases are at increased risk of unfavourable visual outcomes despite appropriate laser treatment. A multidisciplinary approach involving ophthalmologists, diabetologists, nephrologists, and primary care physicians is therefore essential to optimise visual outcomes. Early identification and aggressive management of systemic risk factors may improve the effectiveness of PRP and reduce long-term visual disability.

Limitations

The study was conducted in a single tertiary eye care centre and had a relatively short follow-up period of six months. Ocular parameters such as central macular thickness, extent of retinal ischemia and OCT biomarkers were not included in the analysis. Future multicentric studies with longer follow-up and multimodal retinal imaging may provide a more comprehensive understanding of factors influencing post-laser visual prognosis.

The present study demonstrates that poor glycaemic control, associated systemic disease burden, and female sex are significant predictors of unfavourable visual prognosis following PRP for proliferative diabetic retinopathy. Renal dysfunction, dyslipidaemia, and anaemia were also significantly associated with poor visual outcomes. These findings highlight the importance of comprehensive systemic management in addition to retinal laser therapy for achieving optimal visual outcomes in patients with diabetic retinopathy.

Conclusion

1. Higher baseline HbA1c was independently associated with unfavourable visual prognosis (aOR = 1.78, 95% CI: 1.40–2.26, $p < 0.001$).
2. Presence of systemic disease in addition to Diabetes Mellitus was also significantly associated with unfavourable prognosis (aOR = 3.91, 95% CI: 1.87–8.17, $p < 0.001$).
3. Female sex was independently associated with higher odds of unfavourable prognosis compared with male sex (aOR = 2.15, 95% CI: 1.09–4.26, p = 0.028).
4. Baseline BCVA code and duration of diabetes were not significant independent predictors

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