



## FACTORS DETERMINING PROGRESSION OF PROLIFERATIVE DIABETIC RETINOPATHY TO ADVANCED DIABETIC EYE DISEASE DESPITE LASER INTERVENTION

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**ABSTRACT** **Background:** Proliferative diabetic retinopathy(PDR) is a microvascular complication of diabetes mellitus that is associated with severe vision loss.

The purpose of this study was to determine if there are any risk factors that are pertinent to the progression of PDR after photocoagulation

**Methods:** This study involved 72 eyes diagnosed with PDR. All eyes underwent argon laser panretinal photocoagulation (PRP) over one month. They were followed up for six months during which the severity of PDR and its complications were assessed.

**Results:** Out of the 72 eyes, five eyes (6.9%) exhibited signs of progression after PRP and sixty seven eyes (93.1%) showed regression or stabilized. Among the eyes that showed progression, 2.2% were on oral hypoglycaemic agents (OHAs), 10.5% were on insulin and 17.6% were on both medications.

**Conclusion:** We have determined that patients on OHAs or on both medications were associated with higher risk of progression of PDR.

**KEYWORDS :** Proliferative Diabetic Retinopathy, photocoagulation

### INTRODUCTION

Diabetic retinopathy (DR) is the chief cause of blindness among working aged adults around the world<sup>1</sup>. Proliferative retinopathy, a late stage of diabetic retinopathy, is associated with severe vision loss.<sup>2,3</sup> Laser panretinal photocoagulation is an accepted and recommended mode of treatment of PDR. The aim of this mode of treatment is to cause regression of existing neovascular tissue and progressive neovascularisation in the future which can lead to further complications and severe vision loss.

This study aimed to investigate factors that could be related to the progression of PDR in patients treated with photocoagulation and whether they could make a considerable difference.

### MATERIALS AND METHODS

Patients diagnosed with proliferative diabetic retinopathy with or without macular edema were considered for this study. Patients who have had prior treatment with photocoagulation were excluded.

This study was conducted after obtaining approval from the institutional research and ethics committee. A written informed consent was obtained after explaining the procedure and risks involved. A detailed history was taken followed by a complete ophthalmological examination.

The diagnosis of PDR was made either clinically, using direct, indirect ophthalmoscopy, and slit lamp biomicroscopy with +90D lens or using fundus photographs and classified according to modified ETDRS classification.

Lab investigations reports such as Haemoglobin, serum plasma glucose (random, fasting and postprandial), HbA1c, fasting lipid profile, proteinuria, serum urea and serum creatinine were noted.

Patients were then subjected to panretinal photocoagulation after instillation of topical anesthetic. Argon laser was used with laser settings- 1200-3000 burns with spot size of 100-300 microns, duration of 0.05 – 0.1 sec, one half to one spot diameter spacing with enough intensity to whiten the overlying retina which usually requires a power of 200-600 mW with Mainster panfunduscope lens. The lens was placed on the patient's eye with coupling agent like Methylcellulose. The patients underwent 3 sittings of laser by a single surgeon over 1 month after which patients were then followed up regularly for six

months during which the severity of PDR and its complications were assessed and whether there was a need for surgery.

Progression was defined as development of fundus obscuring vitreous hemorrhage or performance of vitrectomy.

Regression was defined as blunting of vessel tips, shrinkage or disappearance of new vessels, regression of IRMA, decreased venous changes and absorption of hemorrhages.

In this study laser treatment was considered for patients with non high risk PDR who were type 2 diabetics, had impending cataract surgery, poor follow-up compliance, renal disease, severe disease in the fellow eye or had evidence of retinopathy progression.

The analysis of the data was done by SPSS software version 19 using Fischer exact test, chi square test and t test. A p value of  $\leq 0.05$  was taken as significant.

### RESULTS

This study analysed the correlation of factors, such as age, gender, duration of diabetes, blood pressure, baseline severity of retinopathy, and various biochemical parameters such as haemoglobin, serum plasma glucose, HbA1c, fasting lipid profile, serum urea, serum creatinine and proteinuria, to the progression of PDR after treatment with panretinal photocoagulation.

This was a hospital based prospective nested case-control study that included 72 eyes of 45 known diabetic patients who were diagnosed with PDR.

Out of the 72 eyes, five eyes (6.9%) exhibited signs of progression after laser photocoagulation. The eyes that showed progression were taken as cases while the remaining sixty seven eyes (93.1%) were the controls.

The majority of the patients (76.4%) belonged to the male gender.

The majority the patients belonged to the age group 41 to 60 years (59.7%) in this study.

A majority of the patients in this study (65.3%) had duration of diabetes ranging from 10 to 20 years. The mean duration was 13.57 years. 80%

of the eyes that had a duration of DM of 10-20 years progressed while 64.2 % of patients with similar duration showed no progression. Duration of diabetes was not found to be statistically significant in this study.

A total of 30(66.67%) patients had hypertension. 9.1% of eyes that showed progression belonged to hypertensive patients which was not statistically significant.

In this study 14(46.67%) patients had hypertension for less than 5 years, 13(43.33%) for 5 to 10 years and 3(10%) for more than 10 years. This was not found to be statistically significant.

A total of 31 eyes (43%) of patients in this study were on oral hypoglycaemic agents(OHAs) alone. Out of the eyes that showed progression, none were on OHAs, 8.3 % were on insulin and 17.6 % were on both. The Fishers exact test p value obtained was 0.044 which was significant.

33.3% of the eyes included in this study belonged to patients on insulin. 8.3% of the eyes that showed progression belonged to patients on insulin. Ap value of 0.743 was obtained and was insignificant.

23.6% of the eyes included in this study belonged to patients on both OHAs and insulin. Out of this 60% showed progression compared to 21% who did not. Ap value of 0.047 was obtained and was significant.

Out of these OHAs and OHAs + insulin were found to be significant. OHAs seemed to reduce the progression as these patients had better glycaemic control compared to those who were on OHAs + insulin in this study.

15.3% eyes included in this study belonged to patients with coronary artery disease. Out of these none of them showed progression of PDR. This was found to be statistically insignificant.

20.8% of eyes included in this study belonged to patients with nephropathy. Out of these 20% of them showed progression of PDR. A chi-square value of 0.962 was obtained was insignificant.

11.1% of total number of eyes included in this study showed high risk characteristics compared to 88.9% which did not. Among them 80% of them showed progression of PDR after laser photocoagulation. A p value of 0.000 was obtained and was highly significant.

The patients who showed progression had a mean systolic BP of 166 +/- 30.50 mmHg compared to a mean of 144.15 +/- 24.82 mmHg among those who did not. The p value was 0.81 which was not significant.

The patients who showed progression had a mean diastolic BP of 96.00 +/- 11.40 mmHg compared to a mean of 85.19 +/- 16.00 mmHg among those who did not. The p value was 0.079 which was not significant.

A hemoglobin value of 9.50 +/- 1.38 g/dl was observed in patients who showed progression of PDR compared to 10.85 +/- 1.94 g/dl in patients who did not. The p value was 0.123 which was insignificant.

A mean FBS of 104.80 +/- 39.07 g/dl was observed in patients who showed progression of PDR compared to 182.28 +/- 85.04 g/dl in patients who did not. The p value was 0.015 which was significant.

The mean HbA1c levels in patients who showed progression of PDR was 8.80 +/- 2.49 compared to a mean of 9.03 +/- 2.46 in those patients who did not. The p value was 0.567 which was insignificant.

The mean total cholesterol levels in patients who showed progression of PDR was 205.40 +/- 31.33 mg/dl compared to a mean of 194.94 +/- 42.97 mg/dl in patients who did not. The p value was 0.400 which was insignificant.

The mean HDL and LDL levels in patients who showed progression of PDR was 37.20 +/- 8.64 mg/dl and 137.56 +/- 32.37 mg/dl compared to a mean of 38.30 +/- 10.33 mg/dl and 130.39 +/- 42.06 mg/dl in patients who did not. The p values were 0.527 and 0.816.

The mean VLDL and TG levels in patients who showed progression of PDR was 32.84 +/- 11.09 mg/dl and 145.40 +/- 45.47 mg/dl compared to

a mean of 30.84 +/- 11.17 mg/dl and 161.03 +/- 50.67 mg/dl in patients who did not. The p values were 0.54 and 0.572.

The mean serum urea and creatinine levels in patients who showed progression of PDR was 38.60 +/- 9.33 mg/dl and 1.20 +/- 0.71 mg/dl respectively compared to a mean of 44.88 +/- 22.81 mg/dl and 2.00 +/- 1.66 mg/dl in patients who did not. The p values were 0.947 and 0.227. A total of 56.9% showed proteinuria 60.0% of whom had progression of PDR compared to 56.7% of those who did not. The chi-square value was 0.886 which was insignificant.

## DISCUSSION

Diabetic retinopathy is one of the major causes of preventable blindness. It is caused by microangiopathy. Damage is due to microvascular leakage and occlusion.

Various risk factors have been associated to the onset and progression of diabetic retinopathy in diabetic individuals. It is, thus, important to screen all diabetics and assess whether these risk factors are present and if so whether they can be modified..

In this study only 6.9% of eyes with PDR progressed despite photocoagulation with 93.1% of eyes having stabilized or improved. In a study by Taylor, neovascularisation of the disc regressed in five out of thirty-one eyes post photocoagulation<sup>4</sup>. Another study by Dobree et al. showed that more than 50% of patients retained good vision for longer after treatment with photocoagulation.<sup>5</sup>

In this study 80% of the eyes that had duration of DM of 10-20 years progressed while 64.2% of patients with similar duration showed no progression. However this finding was not found to be statistically significant. Longer duration of diabetes is one of the major risk factors for the development and progression of DR which was dissimilar to the findings in this study.

A total of 28(63.6%) patients in this study were on OHAs. Out of the eyes that showed progression, 2.2% were on oral hypoglycaemic agents, 10.5% were on insulin and 17.6% were on both medications. Out of these the values of patients who were on OHAs and OHAs + insulin were found to be significant.

In this study FBS was found to be a significant risk factor in the progression of PDR but was inversely related. This may be attributed to these patients being on closer followup and stricter glycaemic control. This finding is similar to that in the DCCT trial which showed a transient early worsening of retinopathy during the first year of intensive therapy.<sup>6</sup>

The mean HbA1c in this study was 8.8 and 9.03 in those who progressed and those who did not. This result was not statistically significant. This finding is in contrast to multiple studies which report HbA1c as a significant factor in the progression of DR.<sup>(6,7,8)</sup>

The mean hemoglobin level in this study was 9.50 +/- 1.38 g/dl in the cases that progressed with no statistical significance. This finding is not similar to a study by Sepulveda et al which showed anemia as a significant factor in the progression of PDR.<sup>9</sup>

The association between serum lipids and DR has been investigated and have shown conflicting results.

This study showed no correlation between lipid levels and progression of PDR. These findings are similar to Cetin et al, where there was no significant association between serum lipids and the severity of DR.<sup>10</sup>

## CONCLUSION

There was statistically significant positive correlation between the risk of progression of PDR and presence of high risk characteristics. We have determined from our study that patients who were on oral hypoglycaemic agents or on a combination of insulin with OHAs were associated with higher risk of progression of PDR.

Thus, laser panretinal photocoagulation continues to be an effective treatment modality for PDR and prevents its progression to advanced diabetic eye disease.

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