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Original Article

Visual Outcomes Following Grid Photocoagulation in Non-Proliferative Diabetic Retinopathy with Diabetic Macular Edema: Correlation with Systemic Factors

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ABSTRACT

Background: Diabetic macular edema (DME) is a leading cause of visual impairment in patients with diabetes, particularly those with non-proliferative diabetic retinopathy (NPDR). This study aims to evaluate the visual outcomes following grid photocoagulation in patients with DME and to assess the correlation with systemic factors.

Methods: A prospective study was conducted involving 30 eyes of 19 patients diagnosed with Type 2 diabetes mellitus and DME. After obtaining informed consent, patients received grid laser photocoagulation according to Early Treatment Diabetic Retinopathy Study (ETDRS) protocols. Pre-laser evaluations included best-corrected visual acuity (BCVA), intraocular pressure assessments, and imaging studies. Post-treatment follow-ups were conducted at 3, 6, and 9 months to assess changes in visual acuity and central macular thickness through optical coherence tomography (OCT).

Results: The study found that 60% of patients improved or retained vision post-treatment, with 23% to 60% showing stability at 12 weeks. However, 40% experienced worsened vision, primarily linked to uncontrolled glycemia (mean HbA1c: 8.9%). The average participant age was over 60, with 70% having hypertension. Visual acuity improved significantly in the first 3 months, with mean BCVA increasing from 0.5 to 0.7 (Snellen). Systemic factors like blood pressure and serum lipids showed no significant impact on outcomes.

Conclusion: Grid photocoagulation enhances visual acuity in DME patients, requiring strict glycemic control and regular ophthalmological evaluations for early detection and management of vision-threatening complications.

Key-words: Diabetic Macular Edema (DME), Glycemic Control, Grid Photocoagulation, Non-Proliferative Diabetic Retinopathy (NPDR), Visual Acuity

INTRODUCTION

Diabetic macular oedema is the leading cause of impaired visual acuity in diabetes patients, with an incidence ranging from 13.9 to 25.4% over 10 years [1].

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Macular oedema is a common cause of vision loss in nonproliferative diabetic retinopathy. Diabetic Retinopathy affects 17.6% of the population, whereas Diabetic Macular Oedema affects 5% [2]. The oedema is generated primarily by a breakdown of the inner blood-retinal barrier at the retinal capillary endothelium, which allows fluid and plasma contents to flow into the surrounding retina [3].

Diffuse macular oedema is caused by a broad collapse of the inner blood-retinal barrier, in which not only microaneurysms but also retinal capillaries and arterioles leak diffusely [4]. Since this issue develops extremely slowly, close management is required. The fluorescein angiography is typically used to guide treatment. This makes it possible to locate the leak and target specific spots with treatment. Modern imaging techniques like OCT and more recent treatments like intravitreal anti-vascular endothelial growth factors (VEGFs) are two developments that have had a big impact on our knowledge of DME and treatment [5-7].

The gold standard for treating non-center DME is still laser photocoagulation, even with the advent of novel and intriguing drugs [8]. For DME, a focused laser or grid-pattern laser photocoagulation treatment has been assessed in several investigations. These trials demonstrated a propensity for macular oedema to resolve as visual acuity improved [9]. Results from macular grid laser treatment have improved dramatically, according to recent clinical trials carried out by the Diabetic Retinopathy Clinical Research Network (DRCRN) [10,11]. These positive outcomes have been ascribed to improvements in laser technology, stringent glycaemic control, and blood pressure management [12]. The purpose of this study is to determine how grid photocoagulation affects diabetic macular oedema in our configuration.

MATERIALS AND METHODS

This prospective study was conducted at the Retina Clinic of the Karnataka Institute of Medical Sciences in Hubli from January 2015 to August 2016. The first 30 patients' eyes that met the selection criteria were included in the study after obtaining informed consent. They were treated with grid laser photocoagulation as recommended by EDTRS.

Inclusion criteria- Patients diagnosed with Type 2 Diabetes Mellitus, regardless of the duration of their disease were included in the study. Specifically, participants were required to have non-proliferative diabetic retinopathy accompanied by diabetic macular edema. The diagnosis was initially made clinically and subsequently confirmed through fluorescein angiography and OCT. Additionally, a central 10-2 field analysis was conducted to evaluate macular function.

Exclusion criteria- Participants were excluded if they had proliferative diabetic retinopathy with macular edema, ischemic maculopathy, or macular edema attributed to causes other than diabetes. Additionally, individuals who had received prior treatment with panretinal photocoagulation (PRP), experienced retinal detachment or trauma, or had undergone laser photocoagulation at any other institution were not eligible. Other exclusion factors included the presence of an epiretinal membrane, any media opacities such as cataract or vitreous hemorrhage, chronic kidney disease, and patients currently on pioglitazone medications.

Methodology

Pre-laser evaluation- Pre-laser evaluation involves a comprehensive assessment of various ocular parameters to ensure the appropriate treatment of patients. Best corrected visual acuity was measured using the Snellen visual acuity chart, while intraocular pressure was assessed with an applanation tonometer. A thorough slit lamp examination and retinal examination were conducted using indirect ophthalmoscopy, as well as slit lamp biomicroscopy with +90D and 78D lenses. Additionally, fundus fluorescein angiography and OCT were performed in all cases before the laser therapy. To further evaluate the macular function, a central 10-2 field analysis was also conducted.

Procedure of grid photocoagulation- The procedure for grid photocoagulation was carried out in a meticulous grid pattern under topical anesthesia, following the protocols established by ETDRS. The modified ETDRS grid laser treatment utilized the APPASAMY AMOGH PLUS, a diode-pumped green laser operating at a wavelength of 532 nm. This approach ensured precise delivery of the laser energy to the targeted retinal areas, effectively addressing the clinical needs of patients with diabetic macular edema.

Laser parameters used for grid photocoagulation- The laser parameters used for grid photocoagulation were meticulously defined to ensure optimal treatment outcomes. A Mainster grid laser lens was employed, with a spot size ranging from 50 to 75 µm. The burn intensity for the grid laser was kept barely visible, resulting in a light gray appearance. The power of the laser was adjusted between 80 and 100 mW, depending on the condition of the laser, media opacities, and background pigmentation. Each laser burn had a duration of 100 milliseconds, with a total of 100 to 150 spots applied.

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Laser burns were strategically placed at least one burn width apart, with wider spacing utilized in areas of less severe thickening. The grid laser treatment extended up to two-disc diameters superiorly, inferiorly, and temporally from the center of the macula, while avoiding treatment within 500 microns of the disc margin or the center of the macula.

Follow-up- For the follow-up of patients undergoing grid photocoagulation, visual acuities and fundoscopic findings were meticulously recorded at 3 months, 6 months, and 9 months post-treatment. These assessments were utilized for qualitative analysis of the treatment outcomes. Additionally, OCT was performed to quantitatively evaluate macular edema during the follow-up visits. In selected cases, fundus photography was also conducted post-laser treatment to provide a comprehensive review of the retinal condition and the effects of the intervention.

Statistical Analysis- Both descriptive and inferential analyses were conducted. Continuous data were reported as Mean±SD (min-max), while categorical data were expressed as numbers and percentages. Significance was assessed at a 5% level using Fisher's exact test (two-tailed). Results were classified as significant ($0.01<p\leq0.05$) or strongly significant ($p\leq0.01$). Data analysis was performed using IBM SPSS v20, with Microsoft Word and Excel for tables and graphs.

RESULTS

This prospective study evaluated visual outcomes following grid photocoagulation in 30 eyes of 19 patients with diffuse diabetic macular edema at Karnataka Institute of Medical Sciences, Hubli. Patients were followed up at 3-, 6-, and 9-months post-treatment. Among the 30 eyes, 20 (66.66%) belonged to males and 10 (33.33%) to females. Most patients (18) were over 60 years old, and all had Type 2 Diabetes Mellitus, with 18 having diabetes for 6–10 years. Hypertension was present in 21 patients (70%). Baseline visual acuity ranged from 6/18 to 6/60 in 27 patients (90%). Moderate NPDR with macular edema was observed in 20 eyes (67%), while mild and severe NPDR cases accounted for 6 (20%) and 4 (13%), respectively. After nine months, 7 patients (23%) improved, 11 (37%) maintained, and 12 (40%) experienced worsening visual acuity. Glycemic control significantly influenced outcomes—95% of patients with normal HbA1c retained or improved vision, whereas all with altered HbA1c levels experienced deterioration (Fig. 1).

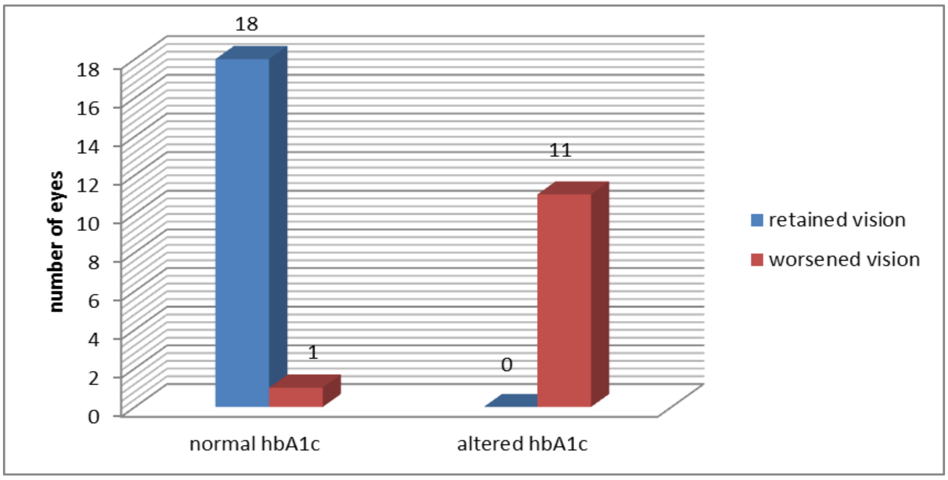

Fig. 1: Distribution of eyes showing the correlation between baseline HbA1c levels and visual acuity at the end of 9 months post laser treatment.

Fig. 2 presents the distribution of eyes based on the correlation between baseline serum triglyceride (TG) levels and visual outcomes at the end of nine months post-laser treatment. The data reveals that among patients with normal baseline triglyceride levels, a significant portion—11 out of 13 eyes (84%)—retained or improved their visual acuity. In contrast, only 7 out of 16 eyes (43.75%) with altered triglyceride levels showed similar outcomes, indicating a notable difference in visual prognosis based on baseline triglyceride status.

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Furthermore, the table indicates that 3 eyes (16%) with normal TG levels experienced worsened vision, while a higher proportion of patients with altered levels—9 eyes (47.35%)—reported a deterioration in their visual acuity. The p-value of 0.071 suggests that while the correlation is not statistically significant, the trend indicates a potential relationship between higher baseline triglyceride levels and poorer visual outcomes.

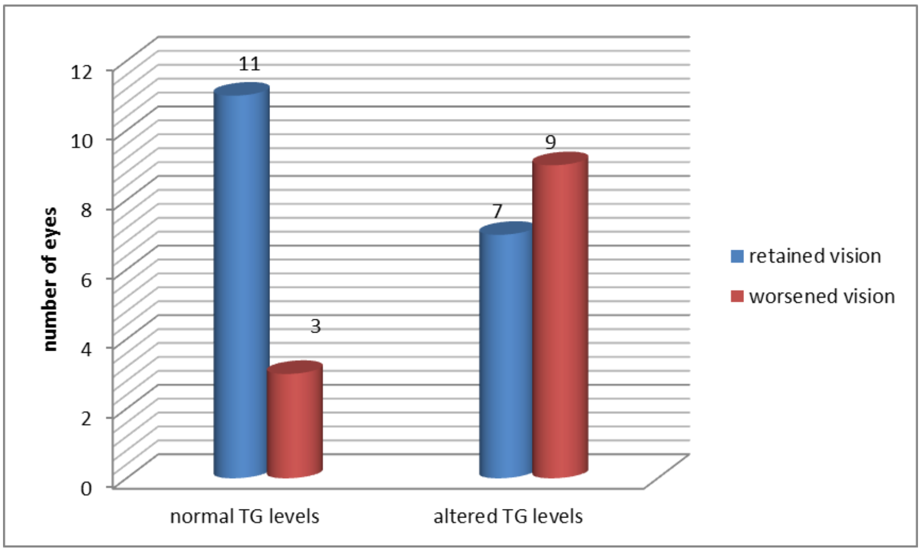

Fig. 2: Distribution of eyes showing correlation between baseline serum triglycerides (TG) levels and visual outcome at the end of nine months post laser treatment.

The correlation between baseline urine albumin levels and visual outcomes at nine months post-laser treatment was analyzed. All patients with albuminuria showed poor visual prognosis, with 12 eyes (100%) worsening and none improving or retaining vision. In contrast, no patients without albuminuria experienced vision deterioration. Although the p-value (1.000) indicates no statistically significant difference, the presence of albuminuria consistently correlated with poorer visual outcomes.

Table 1 summarizes visual acuity changes over time. Initially, 63% of patients had 6/12 to 6/24 vision, and 27% had 6/36 or worse. At three months, 18% achieved 6/9 or better, but this figure remained stable at 20% at six and nine months. Meanwhile, patients with 6/36 or worse vision increased from 36% at three months to 57% at nine months, highlighting a progressive decline in visual acuity.

Table 1: Distribution of eyes as per visual acuity during follow up.

BCVA	Pre-treatment	3 months	6 months	9 months	Change (%)
6/9 and better	0	5(18%)	6(20%)	6(20%)	+20%
6/12-6/24	19(63%)	14(46%)	12(40%)	7(23%)	-40%
6/36 and worse	11(27%)	11(36%)	12(40%)	17(57%)	+30%
Fisher’s exact value	-	650.000	576.127	527.93	-
p-value	-	0.0001	0.0001	0.0006	-

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Univariate analysis of systemic prognostic factors for visual gain post-macular laser treatment revealed a strong association with glycemic control. All 18 patients who retained or improved vision had baseline HbA1c≤6.5%, while 11 of 12 patients with HbA1c>6.5% experienced worsening vision (p=0.0001). Similarly, all patients with random blood sugar<200 mg/dl showed improvement, whereas only 1 of 12 with levels above this threshold improved (p=0.0001). Other factors, including diabetes duration, blood pressure, serum triglycerides, urine albumin, and total cholesterol, showed no statistically significant impact on visual outcomes (p>0.05). This analysis underscores the critical role of glycemic control in achieving better visual prognosis post-laser treatment (Table 2).

Table 2: Univariate analysis of the prognostic systemic factors for gain in vision after macular laser treatment.

Systemic factors	Improved/retained N=18	Worsened N=12	p-value	f-exact value
HbA1c <= 6.5% >6.5%	 18 0	 1 11	0.0001	281.95
Duration of diabetes <10years >=10 years	 13 5	 8 4	1	98.98
Random blood sugar levels <200mg/dl >=200mg/dl	 18 0	 1 11	0.0001	281.95
Blood pressure <=140/90 >140/90	 18 0	 10 2	0.151	187.36
Serum triglycerides <200mg/dl >200mg/dl	 11 7	 3 9	0.71	199.20
Urine albumin Absent present	 0 18	 0 12	1	78
Serum total cholesterol <250mg/dl >=250mg/dl	 11 7	 5 7	0.45	1.094

DISCUSSION

In our study, after a follow-up period of nine months, we observed that among the 30 eyes treated with grid laser, visual acuity improved in 7 eyes (23%), remained unchanged in 11 eyes (37%), and worsened in 12 eyes (40%). When comparing our results with those from other studies, we found that Shresta *et al.* [13] reported that 50.6% of eyes improved, 39.5% retained their vision, and only 9.9% experienced worsening. Other studies reported varying outcomes: Zaidi and Jacob [14] noted 35.6% improvement and 29.7% retention; Diabetic Retinopathy Clinical Research Network [15] documented 14.4% improvement and 60.9% Diabetic Retinopathy Clinical Research Network [16] observed 17% improvement with 52% retention; while the Diabetic Retinopathy Clinical Research Network [17] study found 36% improvement combined with a 55% retention rate. In contrast, Scott *et al.* [18] reported an 18% improvement with a 50% retention rate, and Ophir *et al.* [19] indicated 44.5% improvement with an equal percentage of retention. Notably, Shimura *et al.* [20] recorded 43% improvement and 47% retention, and McDonald and Schatz found a high 67% improvement rate but only 24% retention [9].

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Our study's finding that 40% of patients experienced a decline in visual acuity is significant when viewed against the backdrop of these other studies. A common factor among these patients who saw worsening vision was their uncontrolled glycemic levels, as reflected by a mean HbA1c of 8.9%, which is considered elevated. This relationship leads us to conclude that poor glycemic control played a crucial role in contributing to the worsening of macular edema and, consequently, the decline in visual acuity at the end of the nine months. Our results highlight the importance of managing blood glucose levels effectively to improve visual outcomes following laser treatments in patients with diabetic retinopathy.

It is important to note that all participants in our study underwent only a single session of focal/grid photocoagulation laser treatment. This decision was made due to potential side effects associated with multiple treatments, such as laser scar expansion, paracentral scotoma, elevation of central visual field thresholds, and the risk of secondary choroidal neovascularization and subretinal fibrosis [21].

In our study, we observed that 23% to 60% of eyes continued to improve or retain their vision at the 12-week follow-up, a result that aligns closely with findings from the Diabetic Retinopathy Clinical Research Network (DRCRN) report, which indicated that 23% to 63% of eyes maintained or improved their visual acuity following a single laser treatment at the 16-week follow-up and continued to be assessed until the 48-week mark, including later retreatment evaluations [17]. Notably, we reported no complications associated with the laser treatment in our study, likely due to the adaptation of a modified ETDRS protocol for grid laser treatment that resulted in mild blanching. Furthermore, the DRCRN study highlights significant improvements in outcomes related to macular laser treatment, attributing these positive results to advancements in laser technology as well as enhanced management of glycemia and blood pressure control [11].

Recent studies indicate a decline in the prevalence of diabetic retinopathy when compared to the Wisconsin Epidemiologic Study of Diabetic Retinopathy published in 1984, which is attributed to improved control of systemic factors [22,23]. In our study, we found that patients with normal baseline HbA1c levels (<6.5%) exhibited a positive correlation with improved visual acuity following laser treatment, with a statistically significant p-value of 0.0001. This suggests that maintaining lower HbA1c levels is crucial for preventing maculopathy and enhancing outcomes after maculopathy treatment. Additionally, the CURES Eye Study demonstrated a linear trend in the prevalence of retinopathy corresponding to increasing quartiles of HbA1c; specifically, the prevalence rose from 8.1% in individuals with HbA1c levels below 6.9% to 31.7% in those with levels exceeding 10.3%, with a trend Chi-square value of 51.6 and p<0.001 [2].

Clinical trials and epidemiological research provide compelling evidence that hypertension is a significant modifiable risk factor for diabetic retinopathy (DR). The UKPDS study demonstrated that tight blood pressure control reduced the risk of retinopathy progression by approximately one-third, visual loss by one-half, and the need for laser treatment by one-third in patients with Type 2 Diabetes Mellitus [24]. Similarly, other studies such as the EUCLID study [25], DIRECT study [26], and RASS study [27] have shown positive outcomes regarding the impact of antihypertensive medications on reducing retinopathy risk. Additionally, the CURES Eye study identified major systemic risk factors for both the onset and progression of DR, which include the duration of diabetes, degree of glycaemic control, and hyperlipidaemia. There is also a notable correlation between microalbuminuria and DR; research conducted by Singh *et al.* [27], Mohan *et al.* [28] and findings from the WESDR studies indicated that the prevalence of proliferative retinopathy was significantly higher in Type 2 diabetic patients from South India with macroproteinuria (35%) compared to those with microproteinuria (4%) [29].

In our study, we found that systemic factors such as systolic arterial blood pressure, serum lipid levels, and altered renal function did not have a statistically significant effect on visual outcomes following laser treatment. These findings align with those of Jyoti and Sivaprasad, who assessed the impact of these systemic factors on visual outcomes over five years [30]. Similarly, a study conducted by Aiello *et al.* as part of the DRCRN reported comparable results after evaluating these systemic factors for two years post-laser treatment [31]. While it is important to note that optimal control of these systemic factors is crucial for reducing the risk of developing DR and maculopathy, our current study indicates that they do not influence the outcomes of laser treatment. This conclusion is further supported by

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analyses from both the DRCRN group and the studies conducted by Jyoti and Sivaprasad [30,31].

CONCLUSIONS

In our study, we found that overall, 60% of the patients either improved or retained their vision following grid laser treatment, indicating that grid photocoagulation is beneficial for maintaining vision and resolving diffuse diabetic macular edema without serious complications. This treatment effectively regresses macular edema and halts visual deterioration, making it preferable to no treatment. Moreover, timely administration of laser therapy significantly enhances visual prognosis, and when performed correctly, it rarely results in serious complications. However, potential complications can include worsening of macular edema, retinal hemorrhages, scotoma, and vitreous contraction. Achieving strict glycemic control and maintaining normal arterial blood pressure further contribute to better visual outcomes alongside laser treatment. In conclusion, regular ophthalmic check-ups for diabetic patients are essential to identify vision-threatening complications of diabetic retinopathy at early stages, and timely intervention can help preserve vision and prevent deterioration.

CONTRIBUTION OF AUTHORS

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Materials- Deepthi Prabhakar Iyer
Data collection- Deepthi Prabhakar Iyer
Data analysis and interpretation- Deepthi Prabhakar Iyer
Literature search- Deepthi Prabhakar Iyer
Writing article- Deepthi Prabhakar Iyer
Critical review- Rajashekar Dyaberi
Article editing- Deepthi Prabhakar Iyer
Final approval- Yallappa Bhajantri, Rajashekar Dyaberi

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