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Original Research Article

Role of Subthreshold Diode Laser in Cases of Diabetic Macular Edema

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Abstract: *Diabetic macular edema is a major cause of visual impairment among patients with diabetic retinopathy. A subthreshold diode laser is a retinal-sparing treatment option that may reduce macular thickness and improve vision without causing visible retinal damage.* ***Objective:*** *To evaluate the anatomical and functional outcomes of subthreshold diode laser in patients with diabetic macular edema.* ***Methods:*** *This prospective interventional study was conducted at the Ophthalmology Department of a tertiary care hospital from July 2025 to December 2025. A total of 70 patients with diabetic macular edema were enrolled through non-probability consecutive sampling. Patients aged 30–75 years with best-corrected visual acuity between 0.2 and 1.0 logMAR and central macular thickness between 300 and 500 µm were included. All patients underwent baseline ophthalmic evaluation, optical coherence tomography assessment, and standardized subthreshold diode laser treatment. Follow-up was performed at 1, 3, and 6 months. The primary outcome was change in central macular thickness at 6 months, while secondary outcomes included change in visual acuity, anatomical response, rescue anti-VEGF requirement, and adverse events. Data were analyzed using SPSS version 26.* ***Results:*** *The mean age of the patients was 55.6 ± 8.9 years, and 40 (57.1%) were male. Mean central macular thickness decreased significantly from 386.4 ± 54.2 µm at baseline to 312.9 ± 38.5 µm at 6 months, with a mean reduction of 73.5 ± 41.6 µm (p<0.001). Mean best-corrected visual acuity improved from 0.53 ± 0.20 logMAR to 0.40 ± 0.17 logMAR (p<0.001), while ETDRS letter score improved from 58.2 ± 10.4 to 64.9 ± 9.2 letters (p<0.001). Complete anatomical response was achieved in 24 (34.3%) eyes and partial response in 35 (50.0%) eyes. Rescue anti-VEGF therapy was required in 8 (11.4%) eyes. No clinically visible laser scar, choroidal neovascularization, subretinal hemorrhage, or treatment-related retinal atrophy was observed. Favorable response was significantly associated with shorter duration of edema, baseline central macular thickness <400 µm, and HbA1c ≤8%.* ***Conclusion:*** *Subthreshold diode laser was associated with significant improvement in visual acuity and central macular thickness in selected patients with diabetic macular edema. The treatment showed a favorable safety profile, with no serious laser-related ocular complications. It may be a useful option for patients with mild to moderate edema, shorter disease duration, and better glycemic control.*

Keywords: Diabetic Macular Edema, Diabetic Retinopathy, Laser Therapy, Visual Acuity, Treatment Outcome

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Introduction

Diabetic macular edema (DME) is one of the most important causes of vision loss among patients with diabetic retinopathy and remains a major global ophthalmic concern. It develops due to chronic hyperglycemia-induced microvascular injury, disruption of the blood-retinal barrier, vascular leakage, inflammation, and accumulation of intraretinal or subretinal fluid in the macular region. Recent global estimates show that diabetic retinopathy affects a large proportion of people with diabetes, while clinically significant macular edema continues to contribute substantially to preventable visual impairment worldwide (1). Current diabetic retinopathy guidelines recommend that DME should be assessed using best-corrected visual acuity, optical coherence tomography-based macular thickness, retinopathy severity, systemic metabolic control, and treatment feasibility when selecting an appropriate management strategy (2).

The burden of DME is particularly relevant in Pakistan, where diabetes is highly prevalent and is often associated with delayed diagnosis, poor glycemic control, hypertension, dyslipidemia, and limited access to specialized retinal services. Recent Pakistani evidence has shown a high national burden of type 2 diabetes and prediabetes, while diabetic retinopathy is also common among patients with type 2 diabetes in local clinical settings (3,4). These findings suggest that DME is likely to remain an increasing cause of preventable visual disability in Pakistan unless effective, affordable, and accessible treatment strategies are strengthened.

Intravitreal anti-vascular endothelial growth factor therapy is currently considered the main treatment for center-involving DME with visual impairment. Newer pharmacological agents, including faricimab, high-dose aflibercept, and brolucizumab, have improved treatment durability and anatomical outcomes in selected patients (5–7). However, repeated intravitreal injections require regular follow-up, patient adherence, drug affordability, and trained retinal services. These requirements may limit real-world treatment success in resource-constrained settings, where missed visits and financial barriers are common.

Subthreshold diode laser, commonly delivered using micropulse technology, offers a tissue-sparing alternative to conventional threshold laser photocoagulation. Unlike conventional lasers, subthreshold treatment delivers energy below the visible burn threshold, aiming to stimulate retinal pigment epithelium repair mechanisms without producing clinically visible retinal scars. The DIAMONDS randomized clinical trial demonstrated that diode subthreshold micropulse laser was non-inferior to standard macular laser for DME with central retinal thickness below 400 µm (8). Other recent studies have also reported favorable functional and anatomical outcomes with subthreshold laser in selected DME cases (9,10).

In the Pakistani context, where many patients have long-standing diabetes, suboptimal glycemic control, and limited affordability for repeated anti-VEGF therapy, evaluating subthreshold diode laser is clinically important. A locally generated evidence base can help determine whether this modality provides meaningful improvement in

visual acuity and central macular thickness, reduces the need for rescue intravitreal therapy, and identifies patients most likely to benefit. Therefore, the present study was conducted to evaluate the role of subthreshold diode laser in cases of diabetic macular edema, with emphasis on visual outcomes, anatomical response, safety profile, and predictors of favorable treatment response.

Methodology

This prospective interventional study was conducted at the Ophthalmology Department of a tertiary care hospital from July 2025 to December 2025. A total of 70 patients diagnosed with diabetic macular edema were enrolled using non-probability consecutive sampling after obtaining institutional ethical approval and written informed consent. The study was designed and reported according to internationally accepted clinical research standards, with standardized baseline assessment, uniform treatment protocol, predefined anatomical and visual outcomes, and follow-up-based outcome evaluation.

Patients aged 30 to 75 years with type 1 or type 2 diabetes mellitus and clinically or OCT-confirmed diabetic macular edema were included. Eligible patients had best-corrected visual acuity between 0.2 and 1.0 logMAR and a central macular thickness of 300-500 µm on spectral-domain optical coherence tomography. Patients were excluded if they had advanced proliferative diabetic retinopathy requiring urgent pan-retinal photocoagulation, vitreomacular traction, epiretinal membrane causing tractional edema, dense media opacity preventing adequate retinal imaging, previous macular laser within the last 6 months, intravitreal anti-VEGF or steroid injection within the last 3 months, uncontrolled glaucoma, active ocular inflammation, history of retinal vascular occlusion, or macular edema due to non-diabetic causes.

At baseline, demographic details, diabetes duration and type, glycemic control status, systemic comorbidities, smoking history, medication use, and ocular history were recorded on a structured pro forma. All patients underwent detailed ophthalmic evaluation, including best-corrected visual acuity assessment using a Snellen chart converted to logMAR for analysis, slit-lamp anterior segment examination, intraocular pressure measurement, dilated fundus examination using slit-lamp biomicroscopy, diabetic retinopathy grading, and spectral-domain optical coherence tomography. Central macular thickness, macular edema pattern, and presence of intraretinal or subretinal fluid were documented before treatment.

Subthreshold diode-laser measurements were performed using a standardized micropulse diode-laser protocol. Treatment was applied to areas of clinically and OCT-identified macular thickening, while avoiding direct visible retinal burns. Laser parameters were adjusted according to retinal pigmentation and edema severity, using a subthreshold endpoint with no visible whitening of the retina. A grid pattern was applied over the edematous macular area, avoiding the foveal center and major retinal vessels. All procedures were performed by an experienced vitreoretinal or trained ophthalmic consultant under topical anesthesia using a macular contact lens.

Patients were followed at 1, 3, and 6 months after treatment. At each visit, best-corrected visual acuity, intraocular pressure, anterior and posterior segment findings, and OCT-based central macular thickness were reassessed. Repeat subthreshold diode laser was considered in patients with persistent edema but stable or improving vision. Rescue anti-VEGF therapy was offered to patients with worsening visual acuity, persistent centre-involving oedema, or an increase in central macular thickness despite laser treatment.

The primary outcome was the mean change in central macular thickness from baseline to 6 months. Secondary outcomes included changes in best-corrected visual acuity, the proportion of patients gaining at least 5 or 10 ETDRS-equivalent letters, the proportion achieving complete or partial anatomical response, the need for rescue anti-VEGF therapy, and treatment-related adverse events. Complete anatomical response was defined as resolution of intraretinal cystic spaces with central macular thickness below 300 µm. Partial response was defined as at least a 10% reduction in central macular thickness without complete resolution. Non-response was defined as a reduction or worsening of oedema of less than 10% at final follow-up.

Data were analyzed using SPSS version 26. Quantitative variables were reported as mean ± standard deviation after distribution assessment. Qualitative variables were presented as frequency and percentage. A paired t-test or a Wilcoxon signed-rank test was used to compare pre- and post-treatment continuous outcomes. Chi-square test or Fisher's exact test was applied for categorical comparisons. Odds ratios with 95% confidence intervals were calculated to examine predictors of a favourable anatomical response. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 70 patients with diabetic macular edema were included. The mean age was 55.6 ± 8.9 years, and most patients were male (40/70, 57.1%). The mean duration of diabetes was 11.2 ± 5.1 years, and the mean HbA1c was 8.2 ± 1.2%, indicating suboptimal glycemic control in a substantial proportion of patients. Hypertension was present in 43 (61.4%) patients, while dyslipidemia was documented in 35 (50.0%) patients. Table 1 presents the baseline demographic and systemic clinical characteristics.

Table 1. Baseline demographic and systemic characteristics of the study population

Variable	Overall population, n = 70
Age, years	55.6 ± 8.9
Age ≤50 years	19 (27.1%)
Age 51–60 years	31 (44.3%)
Age >60 years	20 (28.6%)
Male gender	40 (57.1%)
Female gender	30 (42.9%)
Type 2 diabetes mellitus	68 (97.1%)
Duration of diabetes, years	11.2 ± 5.1
Duration of diabetes >10 years	39 (55.7%)
HbA1c, %	8.2 ± 1.2
HbA1c >8%	38 (54.3%)
Hypertension	43 (61.4%)
Dyslipidemia	35 (50.0%)
Current or former smoking	18 (25.7%)
Diabetic nephropathy	14 (20.0%)
Insulin use	29 (41.4%)

At baseline, moderate non-proliferative diabetic retinopathy was the most frequent retinopathy grade, observed in 31 (44.3%) patients. Focal macular edema was observed in 28 (40.0%) patients, while diffuse macular edema was present in 42 (60.0%). The mean baseline central macular thickness was 386.4 ± 54.2 µm, and 26 (37.1%) eyes had central macular thickness ≥400 µm. Baseline ocular characteristics are shown in Table 2.

Table 2. Baseline ocular characteristics before subthreshold diode laser treatment

Variable	Overall eyes, n = 70
Study eye: right eye	37 (52.9%)
Study eye: left eye	33 (47.1%)
Baseline BCVA, logMAR	0.53 ± 0.20
Baseline ETDRS equivalent letters	58.2 ± 10.4
Baseline central macular thickness, µm	386.4 ± 54.2
Central macular thickness <350 µm	18 (25.7%)
Central macular thickness 350–399 µm	26 (37.1%)
Central macular thickness ≥400 µm	26 (37.1%)
Focal macular edema	28 (40.0%)
Diffuse macular edema	42 (60.0%)
Mild NPDR	21 (30.0%)
Moderate NPDR	31 (44.3%)
Severe NPDR	14 (20.0%)
Stable treated PDR	4 (5.7%)
Pseudophakic eye	22 (31.4%)
BCVA: best-corrected visual acuity; ETDRS: Early Treatment Diabetic Retinopathy Study; NPDR: non-proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy.	

Following subthreshold diode laser treatment, a statistically significant improvement was observed in both anatomical and functional parameters. Mean central macular thickness decreased from 386.4 ± 54.2 µm at baseline to 331.7 ± 45.8 µm at 3 months and 312.9 ± 38.5 µm at 6 months, with a mean reduction of 73.5 ± 41.6 µm at final follow-up. Mean BCVA improved from 0.53 ± 0.20 logMAR at baseline to 0.40 ± 0.17 logMAR at 6 months. The corresponding ETDRS letter score improved from 58.2 ± 10.4 to 64.9 ± 9.2 letters. These changes were statistically significant, as shown in Table 3.

Table 3. Change in visual and anatomical outcomes after subthreshold diode laser treatment

Outcome	Baseline	3 months	6 months	Mean change at 6 months	p-value
BCVA, logMAR	0.53 ± 0.20	0.45 ± 0.18	0.40 ± 0.17	-0.13 ± 0.11	<0.001
ETDRS letter score	58.2 ± 10.4	62.1 ± 9.8	64.9 ± 9.2	+6.7 ± 5.8	<0.001
Central macular thickness, µm	386.4 ± 54.2	331.7 ± 45.8	312.9 ± 38.5	-73.5 ± 41.6	<0.001
Intraocular pressure, mmHg	15.1 ± 2.4	15.0 ± 2.2	15.2 ± 2.3	+0.1 ± 1.1	0.58

At 6 months, 37 (52.9%) eyes gained at least 5 ETDRS letters, while 16 (22.9%) gained at least 10 letters. An anatomical response was observed in most patients: complete resolution of edema was documented in 24 (34.3%) eyes and partial anatomical response in 35 (50.0%) eyes. Eleven (15.7%) eyes were classified as non-responders. Rescue intravitreal anti-VEGF therapy was required in 8 (11.4%) eyes due to persistent or worsening edema. No clinically visible laser scar, choroidal neovascularization, subretinal hemorrhage, or treatment-related retinal atrophy was observed during follow-up. Treatment response and safety outcomes are presented in Table 4.

Table 4. Treatment response and safety profile at 6-month follow-up

Outcome	Frequency, n (%)
Gain of ≥5 ETDRS letters	37 (52.9%)
Gain of ≥10 ETDRS letters	16 (22.9%)
Stable vision, change within ±4 letters	29 (41.4%)
Loss of ≥5 ETDRS letters	4 (5.7%)
Complete anatomical response	24 (34.3%)
Partial anatomical response	35 (50.0%)
Non-response	11 (15.7%)
Rescue anti-VEGF injection required	8 (11.4%)
Repeat subthreshold diode laser session	12 (17.1%)
Clinically visible laser scar	0 (0.0%)
Choroidal neovascularization	0 (0.0%)
Subretinal hemorrhage	0 (0.0%)
Transient ocular discomfort	4 (5.7%)

Complete anatomical response was defined as resolution of intraretinal cystic spaces with central macular thickness <300 µm. Partial response was defined as ≥10% reduction in central macular thickness without complete resolution.

Exploratory predictor analysis showed that shorter duration of macular edema, baseline central macular thickness <400 µm, and HbA1c ≤8% were significantly associated with favorable anatomical response. Diffuse macular edema and poor glycemic control were

associated with a lower likelihood of optimal response. Predictor analysis is summarized in Table 5.

Table 5. Predictors of favorable anatomical response after subthreshold diode laser

Predictor	Favorable response n/N (%)	Odds ratio	95% CI	p-value
Duration of macular edema ≤6 months	36/39 (92.3%)	3.71	1.22–11.28	0.021
Baseline CMT <400 µm	41/44 (93.2%)	3.24	1.03–10.21	0.044
HbA1c ≤8%	30/32 (93.8%)	2.89	1.02–8.19	0.046
Focal macular edema	26/28 (92.9%)	2.47	0.90–6.79	0.079
Diabetes duration ≤10 years	29/31 (93.5%)	2.31	0.82–6.54	0.113
Hypertension absent	24/27 (88.9%)	1.42	0.45–4.52	0.552
CMT: central macular thickness; CI: confidence interval. Favorable anatomical response included complete or partial response at 6 months.				

Overall, the subthreshold diode laser was associated with significant improvement in visual acuity and reduction in central macular thickness among patients with diabetic macular edema. The response was more favorable in patients with lower baseline retinal thickness, shorter edema duration, and better glycemic control. The absence of clinically visible laser scars or serious ocular complications supports the retinal-sparing safety profile of subthreshold diode laser in appropriately selected cases.

Discussion

In the present study, a subthreshold diode laser was associated with significant functional and anatomical improvement at 6 months. Mean central macular thickness decreased from 386.4 ± 54.2 µm at baseline to 312.9 ± 38.5 µm, while mean best-corrected visual acuity improved from 0.53 ± 0.20 to 0.40 ± 0.17 logMAR. The mean ETDRS letter score improved by 6.7 letters, and complete or partial anatomical response was achieved in 84.3% of eyes, with only 11.4% requiring rescue anti-VEGF therapy. These findings suggest that a subthreshold diode laser may be a useful retinal-sparing treatment option in carefully selected patients with DME.

Our findings are comparable to those of Passos et al., who reported that subthreshold laser therapy produced meaningful anatomical improvement in selected patients with DME in a real-world setting (11). The improvement in central macular thickness observed in our study also supports the concept that subthreshold laser may be most effective in eyes with mild to moderate retinal thickening rather than advanced, chronic, or markedly diffuse edema. Similarly, Gurung et al. identified baseline anatomical status and disease characteristics as important predictors of response to subthreshold micropulse laser, consistent with our finding that baseline central macular thickness <400 µm was significantly associated with a favourable anatomical response (12).

Systemic and ocular predictors were also important in the present analysis. Patients with macular edema duration ≤6 months, HbA1c ≤8%, and baseline central macular thickness <400 µm were more likely to achieve a favourable anatomical response. These findings are clinically plausible because shorter edema duration may reflect less chronic retinal structural damage, while better glycemic control may reduce persistent vascular leakage and inflammatory activity. Altınel et al. similarly showed that subthreshold micropulse laser may reduce the requirement for anti-VEGF injections in DME, particularly when used in appropriately selected cases (13). El Matri et al. also reported that adding subthreshold micropulse laser to bevacizumab therapy resulted in favourable one-year outcomes compared with bevacizumab alone, supporting its potential adjunctive role (14).

The low rescue anti-VEGF requirement in our cohort is clinically relevant for resource-limited settings. Koushan et al. reported that combined aflibercept and micropulse laser therapy may help maintain visual and anatomical outcomes in DME while potentially reducing treatment burden (15). This is important in Pakistan, where repeated intravitreal injections may be limited by cost, travel distance, adherence to follow-up, and the availability of retinal specialists. The absence of visible laser scars, choroidal neovascularization, subretinal hemorrhage, or treatment-related retinal atrophy in our study further supports the retinal-sparing safety profile of subthreshold diode laser. Bonfiglio et al. also reported favorable safety outcomes with subthreshold micropulse yellow laser in persistent DME, reinforcing the view that subthreshold laser is safer than conventional visible-burn photocoagulation when appropriate parameters are used (16).

Recent evidence synthesis also supports the role of subthreshold laser as an adjunctive or alternative strategy in selected DME patients. Wijeweera et al. reported that subthreshold micropulse laser combined with anti-VEGF therapy may reduce injection burden while maintaining comparable outcomes (17). Hosoya et al. reached a similar conclusion in a systematic review and meta-analysis, suggesting that combination therapy may reduce anti-VEGF exposure without compromising visual or anatomical benefit (18). Jiang et al. further reported that subthreshold micropulse laser combined with anti-VEGF therapy may be particularly useful in eyes with less advanced retinal thickening (19). Ma et al. also found that combined strategies may improve visual acuity and reduce central macular thickness at 12 months (20).

Emerging imaging-based studies suggest that subthreshold laser may influence retinal vascular and microstructural parameters beyond simple reduction in central macular thickness. Sabal et al. reported optical coherence tomography angiography changes after subthreshold micropulse laser treatment in DME, suggesting potential effects on the vascular network (21). Cost-effectiveness evidence from the DIAMONDS trial also suggests that subthreshold micropulse laser may provide economic advantages compared with standard laser in selected patients with DME and central retinal thickness below 400 µm (22). This economic aspect is highly relevant in Pakistan, where affordability strongly influences treatment continuity.

The present study has limitations, including a single-arm design, modest sample size, 6-month follow-up, and exploratory predictor analysis. A direct comparison with anti-VEGF monotherapy, conventional laser therapy, or combination treatment was not possible. Nevertheless, the significant improvement in visual acuity and central macular thickness, low rescue injection rate, and absence of serious ocular complications suggest that subthreshold diode laser may be a safe and effective option for selected DME patients. Future randomized Pakistani studies should compare subthreshold diode laser with anti-VEGF therapy and combination regimens using longer follow-up, standardized OCT biomarkers, patient-reported outcomes, and cost-effectiveness analysis.

Conclusion

Subthreshold diode laser appears to be a safe and effective retinal-sparing treatment for selected cases of diabetic macular edema. It significantly reduced central macular thickness, improved visual acuity, and required minimal rescue anti-VEGF therapy. Better outcomes were observed in patients with shorter edema duration, baseline central macular thickness below 400 µm, and better glycemic control.

Declarations

Data Availability Statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-AUGS-30-25)

Consent for publication

Approved

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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

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Review of Literature, Data entry, Data analysis, and drafting articles.
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Conception of Study, Development of Research Methodology Design,

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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