ORIGINAL ARTICLE

Visual and Anatomical Outcomes of Pars Plana Vitrectomy in Refractory Diabetic Macular Edema

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ABSTRACT

Purpose: To find the visual and anatomical outcomes of pars plana vitrectomy in cases of refractory diabetic macular edema.

Study Design: Quasi Experimental study.

Place and Duration of Study: Department of Ophthalmology, Lahore General Hospital from January 2013 to April 2019.

Material and Methods: Seventy-six patients between the age of 18 and 60 years of both genders having refractory diabetic macular edema with macular thickness of 400 micrometers or more on OCT were enrolled. Informed consent was taken. Detailed preoperative workup including visual assessment, examination on slit lamp using 90D or 78D lens for assessment of macular edema and OCT was done. Patients underwent pars plana vitrectomy, ERM, and ILM peeling. Visual assessment and macular thickness was recorded 4 weeks after surgery.

Results: This study included 76 patients with the mean age of 48.15 ± 8.16 years. Patients were further categorized according to age into 2 groups. The gender distribution of patients showed that most of the participants were female in this study. Mean duration of Diabetes Mellitus was 9.95 ± 6.29 years. Most of the patients did not have previous history of laser and only three patients (3.9%) did not receive Intravitreal Anti-VEGF. Mean preoperative visual acuity was 0.44 ± 0.13 while postoperative visual acuity was 0.876 ± 0.18 (P = 0.000). Similarly, significant decrease in macular thickness was observed after the procedure (P = 0.000).

Conclusion: Pars plana vitrectomy, ERM and ILM peeling can be an effective treatment option for refractory diabetic macular edema.

Key Words: Diabetes Mellitus, Retinopathy, Macular thickness, Visual acuity, Vitrectomy.

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INTRODUCTION

In working age group, diabetic macular edema is one of the leading causes of visual impairment occurring in almost 12% of patients diagnosed with diabetic retinopathy (DRP) and due to which every year more than 10,000 cases of blindness are reported. DME is the result of one of the major complications of DRP[1,2].

The rate of prevalence of DME is directly affected by the type and duration of diabetes. Following the diagnosis of type 1 diabetes in patients, DME can

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develop in the first five years. Within 30 years, the frequency of DME reaches up to 40%[3]. At the time of diagnosis, DME is present in about five percent of patients with type II diabetes. Systemic risk factors include duration of diabetes, gender, cardiovascular disease, proteinuria, abnormal levels of HbA1c, and use of diuretics. DME can occur at any stage of DRP[2-4]. Ocular treatments include administration of Anti VEGF (Vascular Endothelial Growth factor)[5], Triamcinolone acetonide[6] and vitreoretinal surgery[7].

According to clinical trials, macular edema is reduced by doing pars plana vitrectomy (PPV) in selected cases of Diabetic Macular Edema. Proinflammatory substances and traction forces are eradicated by PPV and also increase inner retinal layers oxygenation along with reduction in thickness of macula and gain in visual acuity[8]. In DME cases, the presence of vitreous hemorrhage, hard exudates, and VMT (vitreomacular traction) may be considered as indications for PPV[7]. In a study, mean visual acuity was 0.84 ± 0.32 pre-operatively and 0.72 ± 0.26 postoperatively while Macular thickness was 559 ± 89 µm preoperatively and 354 ± 76 µm postoperatively following Pars plana vitrectomy[9].

Already published literature showed variable results. The purpose of the study is to evaluate the effect of the pars plana vitrectomy in the diabetic patients presenting with macular edema in our population.

MATERIAL AND METHODS

The study was conducted at the department of ophthalmology, Lahore General Hospital, Lahore after Institutional ethical committee approval. A total of 76 patients were included in this study between January 2013 to April 2019. Patients were selected by non-probability convenience sampling. Inclusion criteria comprised of patients having refractory diabetic macular edema with macular thickness of 400 micrometers or more on OCT in diabetics, diagnosed at least 1 year back with previous history of laser or intravitreal anti-VEGF injections. Patients having diabetic macular edema associated with tractional retinal detachment, HbA1c > 8, patients with serum creatinine level of > 1.5 mmol were excluded. Informed consent was taken from all patients**.** Personal profile of the patients including name, age, sex, patient registration number and address was noted. Detailed preoperative work-up including BCVA (best-corrected visual acuity), examination on slit lamp using 90D and 78D lens for assessment of macular edema and tractional retinal detachment was done. OCT was done to confirm and quantify macular edema before undergoing pars plana vitrectomy. Post-operative visual acuity and macular thickness was recorded 4 weeks after surgery.

All data was recorded on a pre-designed proforma and was analyzed using SPSS version 21. Age, Pre-operative BCVA and Post-operative BCVA of patients, Pre-Operative, Post-Operative macular thickness was presented by calculating mean and standard deviation. Categorical variables like gender, previous Laser and previous Intra-vitreal Anti VEGF was presented using frequency and percentages. Data was stratified for age, gender, previous Laser, previous Intra-vitreal Anti VEGF and duration of DM to control effect modifier. Post-stratification t-test was used taking P-value < 0.05 as significant.

RESULTS

Mean age of the patients was 48.15 ± 8.16 years. Most of the participants were female in this study. Mean duration of Diabetes Mellitus was 9.95 ± 6.29 years and is given in table 1. Most of the patients did not have previous history of laser; however, only three patients (3.9%) had not received Intravitreal Anti-VEGF.

Table 1: *Distribution according to duration of Diabetes Mellitus (n = 237).*

Duration of DM	No. of Patients	%
< 5 Years	32	42.1%
≥5.1 Years	44	57.9%
Total	**76**	**100**
Mean ± SD	9.95 ± 6.29 years	

Mean preoperative visual acuity was 0.44 ± 0.13 while postoperative visual acuity was 0.876 ± 0.18. Similarly, significant decrease in macular thickness was observed after the procedure. Comparison of pre-operative and post-operative outcomes as shown in table 2. Stratification of outcome variables (Post-operative Visual acuity and post-operative Macular thickness) was done for age, gender, duration of Diabetes Mellitus, history of previous Intravitreal Anti-VEGF and previous history of laser. All details are summarized in tables 3 and table 4.

Table 2: *Comparison of pre-operative and post-operative findings (n = 76).*

Preoperative Visual Acuity	Postoperative Visual Acuity	P-value
0.44 ± 0.13	0.876 ± 0.181	0.000
Preoperative Macular Thickness	Postoperative Macular Thickness	P-value
554.66 ± 37.01	371.63 ± 32.12	0.000

Table 3: *Stratification of postoperative Visual Acuity with respect to age, gender, duration of Diabetes Mellitus, history of previous Intravitreal Anti-VEGF and previous history of Laser.*

Variables		Post-operative Visual Acuity	P-Value
Age Groups	18-40 Years	0.892 ± 0.173	0.534
	41-60 Years	0.871 ± 0.183	
Gender	Male	0.875 ± 0.177	0.991
	Female	0.876 ± 0.184	
Duration of Diabetes Mellitus	< 5 Years	0.877 ± 0.177	0.924
	≥ 5.1 Years	0.875 ± 0.184	
History of previous Intravitreal Anti-VEGF	Yes	0.876 ± 0.177	0.812
	No	0.860 ± 0.282	
Previous history of Laser	Yes	0.873 ± 0.184	0.920
	No	0.876 ± 0.181	

Table 4: *Stratification of postoperative Macular Thickness with respect to age, gender, duration of Diabetes Mellitus, history of previous Intravitreal Anti-VEGF and previous history of Laser.*

Variables		Post-operative Macular Thickness	P-Value
Age Groups	18-40 Years	373.44 ± 31.72	0.665
	41-60 Years	371.168 ± 32.31	
Gender	Male	372.61 ± 30.98	0.274
	Female	371.01 ± 32.94	
Duration of Diabetes Mellitus	< 5 Years	372.05 ± 31.38	0.445
	≥ 5.1 Years	371.38 ± 32.68	
History of previous Intravitreal Anti-VEGF	Yes	372.13 ± 31.82	0.262
	No	358.85 ± 39.61	
Previous history of Laser	Yes	381.85 ± 26.97	0.050
	No	370.80 ± 32.43	

DISCUSSION

In developed countries, edema secondary to diabetes is primary reason behind visual deficit. With satisfactory results, a lot of therapeutic approaches including grid macular photocoagulation and anti-VEGF (Vascular Endothelial Growth Factor) have been experimented for treating refractory DME. Pars Plana Vitrectomy is controversial and has shown moderate outcomes[10]. This technique depends on the idea that vitreous adhesions could unfavorably have an effect on DME; thus, removing vitreomacular traction would be helpful. Increasing the supply of oxygen to the retina and henceforth improving retinal ischemia. The viscosity of vitreous is 300–2,000 times greater than aqueous viscosity, the diffusion constant of molecules in the vitreous ought to multiply by an analogous magnitude after vitrectomy[11].

Pars plana vitrectomy (PPV) was introduced back in 1971, and it has been employed largely to treat ocular diseases involving the posterior segment and it has been increasingly evolving with smaller and quicker vitrectomy systems. Over the last 10 years, micro-incision suture-less vitrectomy (MISV) instruments i.e. 20-gauge (20G) have provided varied benefits and dramatically simplified vitrectomy procedures, together with diminished postoperative pain, shorter operative time, self-sealing scleral wound and inflammation, reduced astigmatism and quicker visual recovery[12].

Out of the many causes of diabetic macular edema (DME), one is vascular leakage. This is due to compromised blood retinal barrier and number of proinflammatory factors like cytokines, lipoprotein deposition around the fovea and the osmotic gradient. This makes retinal pigment epithelial cells deficient in clearing fluid from the retina and consequently aggravates macular edema. This resists fluid evacuation by the retinal pigment epithelium and consequently increases macular edema. After vitrectomy, the visual improvement in eyes with resolved DME is completely in correlation with the postoperative photoreceptor status of the fovea. Since permanent photoreceptor dysfunction is caused by chronic DME, long standing DME causes irreversible photoreceptor disfunction and disrupts external limiting membrane[13,14].

In patients with diabetes, vision loss is mainly caused by DME and may be refractory to traditional treatment. Vitrectomy is suggested in patients with VMT. In refractory DME cases, the part of vitrectomy without taking into consideration the tractional component is more disputable. Though studies have indicated that peeling of ILM could facilitate getting better results, others studies have depicted similar results by vitrectomy[15].

In a study, mean macular thickness decreased from

baseline 558.27 ± 86.68μm to final 355.97 ± 77.45μm. Same consequences for vitrectomy were reported in patients with refractory diabetic macular edema and no vitreomacular interface abnormality. Intravitreal triamcinolone and macular laser photocoagulation together with vitrectomy in diabetic macular edema patients with no ERM was performed by Kim et al[16] and reported a major decline in macular thickness from 433.7 ± 78.2 μm before surgery to 310.6 ± 80.6 μm six months after procedure. They conjointly noted improvement in thickness three months after surgery. Two teams were formulated, one with cases of diabetic macular edema refractory to standard treatment (macular laser photocoagulation) and the other with diabetic macular edema unresponsive to intravitreal antivascular endothelial growth factor (VEGF) treatment, and deduced that former showed considerably greater decline in macular thickness than latter. The effectiveness of combined vitrectomy, Intravitreal triamcinolone on macular thickness and best corrected visual acuity (BCVA) of forty eyes with refractory diabetic macular edema with a long-run follow-up of three years was evaluated in another study by Kim et al[17]. Throughout the three years post-operatively (decline from 498.1 ± 174.8 μm to 219.4 ± 66.6μm) a major trend towards continued decrease in macular thickness was reported. Once vitrectomy has been performed, similar outcomes concerning changes in macular thickness have been found by similar studies. All this information support that in cases of intractable diabetic macular edema, reduction in macular thickness is effectively caused by vitrectomy.

The impact of vitrectomy on best corrected visual acuity by many reports is heterogenous. We compared our results with other studies showing vitrectomy in refractory diabetic macular edema without vitreomacular interface abnormality. In the last follow-up, insignificant visual acuity improvement was shown by our findings which corresponds to the already reported results in which improvement from 1.00 ± 0.81 log MAR to 0.83 ± 0.18 log MAR was seen. Kim et al[17] reported a major improvement in best corrected visual acuity (from 0.46 ± 0.17 log MAR to 0.37 ± 0.25 log MAR at six months). A mild reduction in best corrected visual acuity was found after 2.5 or 3 months by them and they attributed it to cataract formation. Baseline mean best corrected visual acuity in other studies was significantly higher as compared to ours[18,19].

At least partially, these variations could justify completely different results. However, other studies report significant improvement of BCVA[20] with baseline mean best corrected visual acuities worse than the study mentioned by Kim et al and by a study[17] with a number of patients similar to our study. Moreover, Rosenblatt et al have found worse baseline visual acuity as the only clinical variable that is associated with improvement in postoperative visual acuity[18].

The limitation of the study was the small sample size. Moreover, it was also conducted at one center. More studies are required to obtain more generalizable results.

CONCLUSION

Pars plana vitrectomy, ERM and ILM peeling can be effective treatment options for refractory diabetic macular edema and for improvement of visual acuity.

Ethical Approval

The study was approved by the Institutional review board/Ethical review board.

Conflict of Interest

Authors declared no conflict of interest

Authors' Designation and Contribution

Hussain Ahmad Khaqan; Associate Professor: *Study design, manuscript writing, literature review and final review.*

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