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RESEARCH ARTICLE
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CORRELATION OF CENTRAL MACULAR THICKNESS ON OCT FOLLOWING PANRETINAL PHOTOCOAGULATION WITH HBA1C AMONG DIABETIC PATIENTS

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ABSTRACT

Background: PDR is defined as the formation of new retinal vessels due to poor glycemic control patients with diabetes mellitus .Among the risk factors, one of the most significant risk factor that predicts this complication is the long term hyperglycemia with the long duration of disease, that ultimately causes the development of advance diabetic eye disease .The definite treatment of PDR is via PRP laser , that reduce oxygen demand of retinal tissue and prevents further ischemic mediated damage.

Objective: Find out any change in the CMT and its correlation with HbA1c following PRP by OCT macula among patients with PDR.

Methods: This study was conducted at the department of Ophthalmology, Services Institute of Medical Sciences, Services Hospital Lahore, Pakistan. Study period was of six months from December 2023 to June 2024. This study included a total of fourty eyes from fourty patients with diagnosed proliferative diabetic retinopathy , study participants were divided into two groups, Group mA with HbA1c below 7.5% comprising of twenty patients , and group B comprising of twenty patients with HbA1c between 8.5 and 9.0%, both study groups were treated with pan retinal photocoagulation performed in single session with 1500 laser burn spots This laser treatment was followed by Optical coherence tomography , four weeks after the sessions. Central macular thickness was measured for a change before and after PRP laser sessions.

Results: In our study, patients had a mean age of 48.71±2.42 years, ,the measured mean baseline CMT before the PRP laser sessions was recorded at baseline thickness of 230.45±5.0 and four weeks after the PRP session ,the mean CMT value was 238.50±5.30 among patients in group A and 257±3.5 microns among group B patients. (p-value of 0.001)

Conclusion: There was no statistically proven significant change found in macular thickness before and after PRP session upto to four weeks of follow-up via OCT macula

Keywords: Proliferative diabetic retinopathy (PDR), Optical coherence tomography

INTRODUCTION

Diabetes mellitus is involved in a number of pathological developments in the eye which starts from mild to moderate or background diabetic retinopathy depending upon the classification system used to describe , a progression and development of cataract, development of indexial myopia due to osmotic effects of sorbitol accumulation and proliferative diabetic retinopathy that can lead to the development of advance diabetic eye disease(ADED), vitreous cavity hemorrhage development and/or tractional retinal detachment(TRD) involving or sparing the macula.[2] The progression of PDR and its related complications are mediated by the long term duration of the disease and the long term poor glycemic control among these patients which is represented as the average blood levels of glycosylated heamoglobin or HBA1c, which is a non enzymatic glycation product and is a consequence of long term hyperglycemic metabolic state.[2]

The pathogenesis of proliferative diabetic retinopathy involves microangiopathic changes that are driven by uncontrolled and persistent poor glycemic control and hyperglycemia which leads to cummulative endothelial cell damage associated with pericyte cell dysfunction and ultimately loss of these cells around retinal capillaries endothelial cells which cause the blood retinal barrier to break as the tight junctions between endothelial cells is compromised in neo vessels formed in response to vascular endothelial growth factor as these vessels lack the endothelial linning maturation and are leaky , causing macular edema and pericyte loss leads to the formation of retinal microanuresyms which later on cause thrombosis of looped out microanuresyms and lead to capillary dropout .[4] The thrombosis of retinal microanuresyms lead to disruption of virchows triad and capillary drop out leads to retinal reduced perfussion which leads to ischemia. To develop Vacular endothelial growth factor mediated retinal neo vascularization, at least one fourth of the retina must be ungergoing ischemic changes that leads to the development of PDR mediated by the disturbance of balance between angiogenic and anti- angiogenic VEGF .[5] Various other factors involved in the pathogenesis of PDR are endothelial and pericyte cell damage via advance glycation end products or AGEs, mediated by non enzymatic glycosylation or formation of AGEs products, the non regulated activation of protein kinase C as well as endothelial basement membrane thickeinig in diabetic retinal cappilaries.[6] The definitive treatment for this retinal neovascularization and its root cause of ischemia leading to VEGF production is PRP , involving light energy by using double requency Nd-YAG diode state laser in the visible green spectrum at around 532 nanometers, which by photocoagulation tissue interaction mediates reduced VEGF production and improves retinal oxygen supply that in turn leads to the regression of proliferative vessels indicated by pruning of vessels and reduced venous vasular calliber .Clinical effects pan retinal photocoagulation treatment are indicated by blunting as well as pruning of neo vascula vessel tips, vascular density reduction, retinal and vitreous hemorrhage absorbtion ,reduction in retinal venous tortiosity and venous calliber.

The link between retinopathy and Hba1c was first provided by two landmark trials in the form of DCCT for type 1 diabetc patients and UKPDS for type 2 diabetic patients .According to DCCT intensive therapy for hyperglycemia delays the onset as well as slow down the progression of microangiopathic complications of diabetes including retinopathy,nephropathy as well as neuropathy.Simillarly UKPDS shows that a tight glycemic control in terms of a lower HbA1c reduces microvascular complications like retinopathy, nephropathy and neuropathy in type 2 diabetic patients. Macular OCT is like a noninvasive, optical histopathological biopsy of the retinal layers with a high resolution power that leads to detailed anatomical details of retinal arcitecture and even small changes in the central macular thickness (CMT) can be measured .[7] OCT is based on low coherence interferometery principle and is used for scanning high quality images with a range of spatial

resolution between 8um to 10 µm. A few studies demonstrate change in macular profile after PRP laser in term of thickess increase [2],while other studies did not support such a result.

OBJECTIVE

The objective of this research was to find statistically significant change in macular CMT as well as its correlation with HbA1c in diabetic patients via OCT macula scan among patients diagnosed with PDR undergoing PRP laser treatment.

MATERIALS AND METHODS

Study design: It was designed as a quasi-experimental study.
Study conducted at: Conducted at the department of Ophthalmology, Services Institute of Medical Sciences, Services Hospital Lahore, Pakistan.
Duration of study: A total of Six months, from 1st December 2023 to 30 June 2024.
Sample size: A Sample size of fourty patients was calculated with a 95% confidence interval via online available calculators .
Sample Technique: We used a non probability sampling technique, consecutive sampling.

Inclusion for study: It included patients between 15 - 70 years old , diagnosed with PDR atleast in one eye with no history of ophthalmic surgery and ocular trauma in one year before study period starts .

Exclusion Criteria: Our exclusion criteria included patients with diagnosed vitreous hemorrhage dense enough to occlude retinal view ,mature and dense cataracts, trauma or post scarring corneal opacities, macular involving tractional retinal detachment, any past history ocular trauma including surgery surgery in last one year prceeding study period.
Data Collection : The patients fulfilling our criteria of inclusion had clinical ophthalmic examination via slit lamp biomicroscope, direct and indirect fundoscopic examination with use of 90D condensing lens and an Optical coherence tomography(OCT) scan along with the laboratory diagnostic evaluation including serum HbA1c levels. Patients who took part in this research were explained in detail about the purpose and reason of the study.All patients were explained in advance about no financial or economic gains from this study. Informed consent written in english as well as in the native language(urdu) was signed by the patients after detailed review of the document. Age and gender of the patients was recorded and was analyzed for statistical results via SPSS programme. Detailed clinical examination included unaided visual acuity and BCVA, posterior segment examination on slit-lamp via 78 D lens and intraocular pressure (IOP) measured by slit-lamp mounted applanation tonometry and recorded for data analysis. For assessment of change in CMT and its correlation with HbA1c , OCT macula before and after pan retinal photocoagulation was performed four weeks apart along with serum HBA1c measurement. In our study the mean variation in CMT was examined by finding the difference between OCT based central macular thickness(CMT) after four weeks after PRP laser ,completed via fifteen hundered burns of mild or moderate burn intensity the initial CMT recorded before the laser procedure .
Data Analysis: Our study used the analytical tool of SPSS for the statistical analysis of the recorded patient details. Age of the patients and mean CMT were recorded as standard deviation and mean. For qualitative variables, frequency and distribution were calculated that included the gender of the patients. Paired student t-test with P-value of less than 0.05 was set as a limit for of any result to be considered as a significant one.

RESULTS

In our study, mean patient age was 48.71±2.42 years. From a total of 40 patients, sixteen(40%) were male and twenty four (60%) were female. PRP laser with fifteen hundered burns with light - moderate intensity was performed for each patient. The baseline mean CMT before PRP session was

230.45±5.0,later at four weeks after PRP laser with fifteen hundered burns of mild to moderate intensity ,the mean CMT turned out to be 238.50±5.30 among patients in group A and 257±3.5 microns among patients in group B (p-value=0.001) which was under the lower limit value to be considered as statistically .Table 1

Our patients who aged ≤50 years and had the sessions of PRP laser had a mean CMT at baseline of 238.20±6.63 and later, four weeks following the laser PRP sessions mean CMT was 240.28±6.42. in patients >50 years of age the mean central macular thickness at baseline was found to be 235.37±8.32 after at four weeks of laser session was 241.57±6.44.Across all age groups the mean central macular thickness before and after session of PRP laser was not statistically significant. Male patients had a mean(CMT) befor PRP laser of 236.55±7.22um and after PRP laser session , their CMT was 236.00±6.26 um. Likewise, among female patients had a mean central macular thickness(CMT) at baseline of 238.28±6.21 um and after PRP laser session a CMT of 239.50±4.77um. This change was not statistically significant in mean (CMT) when this data was analysed by gender stratification with a p-value of less than 0.05. Table 3.

Table1: Baseline characteristics

N		40
Age (years)		48.71±2.42
Gender	**Male**	16(40.00%)
	Female	24(60.00%)
Duration after surgery (months)		8.40±1.96
CMT at baseline		230.45±5.0
CMT at 4th week		238.50±6.43
Change in CMT		9.90±0.59*
p-value		0.001

Table 2: Comparison of change in CMT pre laser and post PRP

		At baseline	At 4th week	Change	p-value
Age(years)	**≤50**	238.20±6.63	240.28±6.42	2.08±0.51	**0.001***
	>50	235.37±8.32	241.57±6.44	6.20±0.36	**0.001***
Gender	**Male**	236.55±7.22	238.00±6.26	1.45±0.43	**0.001***
	Female	238.28±6.21	239.50±4.77	1.22±0.35	**0.001***

Table 3: Comparison of change in CMT pre laser and post PRP and its correlation with HbA1c

	Mean CMT at baseline	Mean CMT at 4 weeks of PRP
Group A (HbA1c less than 7.5%)	238.65±6.4	238.50±5.30
Group B (HbA1c between 8.5-9%)	241.45±3.2	257.00±3.5

DISCUSSION

Diabetes mellitus(DM) is a chronic disorder of carbohydrate metabolism including impaired or sub optimal insulin function that manifested clinically as insulin receptor resistance in case of type 2 diabetics where insulin is present and is being secreted by the pancreas but its action at the tyrosine kinase receptor or its down the receptor second messenger function is impaired leading to resistance of insulin function, and in case of type 1 diabetes mellitus, the production of insulin is impaired that leads to impaired carbohydrate metabolism because insulin is required by the GLUT4 receptors to internalize gluscose molecules to be used as fuel for glycolysis and TCA cycle. Depending upon the cause ,the resulting chronic hyperglycemia that remains uncontrolled for long duration leads to formation of advance glycation end products that lead to microangiopathic changes in retinal

vasculature disturbing the virchows triad and cause basement membrane thickening along with loss of pericyte cells around retinal capillaries which cause leakage and breakdown of blood brain barrier , leading to the development of microaneurysms along with capillary out pouching with luminal obliteration by development of abnormal heamodynamics leading to the formation of capillary drop out areas which angiographically corresponds to the hypofluorescence on FFA. The capillary drop out impairs the normal retinal perfusion and cause an imbalance between demand and supply of oxygent to local retinal tissue which in turn leads to the development of retinal ischemia ,this ischemia by upregulation of hypoxiac cell response produces VEGF which have the ability to causes vascular proliferation by new vessel formation.[12]

According to DRS study, the definitive treatment of PDR with neo vascularization is via retinal photocoagulation or PRP laser in which light energy at a specific wavelength is absorbed by RPE (as it contains melanin pigment) and causes local thermal coagulation in response to rise in temperature by protein denaturation process, this PRP laser also cayse induction of heat shock proteins in retinal pigment epithelim and cause proliferation of these cells under local regulator response but ultimately death of RPE cell causes the cell death of attached photoreceptors along with cell death of down the chain bipolar cells and ganglion cells which are connected to that particular RPE cell that has being photocoagulated as a result of PRP laser .[13,15,14]

Optical coherence tomography is non invasive diagnostic method to evaluate retinal micro arcitecture and is identical to histopathological biopsy of the retina and is applied as a diagnostic tool to document central retinal thicknessCMT) with a normal range of 220um to 240um.The resolution and detailed arcitecture scanning of retinal tissue via OCT depend on the specific wavelength of light being used to study the tissue with low coherence interferometry as its basic principle. The pan retinal photocoagulation(PRP) induced rise in tissue temperature produces a local tissue response simillar to sterile inflammation in the retinal layers where it causes the capillary endothelum mediated blood retinal barrier and retinal RPE barrier to become leaky and allow fluid accumulation to develop between layers of retinal tissue ,that can be documented as a variation in CMT profile pre and post PRP sessions[11,12,14].

CONCLUSION

Our study documented no statistically significant change in CMT in baseline and four weeks following the PRP laser treatment performed among patients with PDR with HbA1c below 7.5% and between 8.5 to 9%.

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