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Color Doppler Assessment of Retrobulbar Hemodynamics in Type 2 Diabetics vs. Non-Diabetics.

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Abstract
Background: Diabetic retinopathy (DR) is preceded by subclinical microvascular alterations and hemodynamic perfusion deficits in the orbital circulation. Evaluating retrobulbar hemodynamics using Color Doppler Imaging (CDI) provides a non-invasive window into early circulatory resistance before ophthalmoscopic retinal changes manifest. ***Methods:*** A prospective case-control study was conducted over a 6-month period at the Department of Radiodiagnosis and Ophthalmology, ESIC Medical College, Kalaburagi. A total of 80 participants were enrolled, comprising 40 patients with Type 2 Diabetes Mellitus (Cases) and 40 age- and sex-matched healthy normoglycemic individuals (Controls). High-resolution CDI was performed to evaluate the ophthalmic artery (OA), central retinal artery (CRA), and short posterior ciliary artery (PCA). Quantitative hemodynamic parameters, including Peak Systolic Velocity (PSV), End-Diastolic Velocity (EDV), and Resistive Index (RI), were analyzed and correlated with glycemic control (HbA1c) and disease duration. ***Results:*** Diabetic patients demonstrated significantly increased vascular resistance and reduced diastolic perfusion in the retrobulbar circulation compared to controls. In the CRA, the mean EDV was significantly lower in diabetics compared to non-diabetics (2.4 ± 0.6 cm/s vs. 3.5 ± 0.7 cm/s, $p < 0.001$), accompanied by a markedly elevated RI (0.78 ± 0.05 vs. 0.67 ± 0.04, $p < 0.001$). Similarly, in the PCA, the RI was significantly elevated in the diabetic cohort (0.75 ± 0.06 vs. 0.65 ± 0.05, $p < 0.001$). While OA systolic velocities remained comparable between groups, OA Resistive Index showed a positive correlation with HbA1c levels ($r = 0.52$, $p < 0.001$) and duration of diabetes ($r = 0.48$, $p = 0.002$). ***Conclusion:*** Type 2 diabetes mellitus is associated with significant retrobulbar hemodynamic impedance, characterized by elevated resistive indices and blunted end-diastolic velocities in the central retinal and posterior ciliary arteries. CDI serves as a valuable adjunct for early detection of orbital microvascular ischemia in diabetic patients.

Keywords: Color Doppler Imaging; Retrobulbar Hemodynamics; Type 2 Diabetes Mellitus; Resistive Index; Central Retinal Artery.

INTRODUCTION
Across the globe, type 2 diabetes mellitus brings about a pandemic, which results in microvascular and macrovascular complications [1]. Diabetic retinopathy (DR) is one of the leading causes of visual impairment in the working-age population[1,2]. The clinical grading and intervention paradigms for diabetic retinopathy (DR), depend on structural features seen on ophthalmoscopy for example, microaneurysms, dot-and-blot hemorrhages, neovascularization, etc. However, physiological evidence accumulating shows that functional abnormalities in retinal blood flow and microvascular hemodynamic deficits develop long before the structural damage becomes clinically visible[2,3].The retina, choroid, and optic nerve head experience constant perfusion, which relies on control mechanisms that govern ocular microcirculation [3,4]. Prolonged elevation of blood sugar is responsible for the triggering of biochemical routes that injure capillary endothelial cells; thickening of the basement membrane; impairment of nitric oxide-mediated vasodilation; and, an increase in the loss of pericytes [4,5].

The aggregate impact of these cellular insults enhances downstream vascular resistance while diminishing capillary perfusion. This, in turn, precipitates localized tissue ischemia, ultimately instigating the upregulation of vascular endothelial growth factor (VEGF) and the advancement of neovascularization [3,6].Standard angiographic techniques such as fundus fluorescein angiography (FFA) are invasive in nature. Moreover, these techniques primarily delineate the structural luminal competency rather than the real-time hemodynamic velocities [5,6]. Color Doppler imaging (CDI) is an established safe and reproducible ultrasound technique that allows simultaneous B-mode anatomical visualization and Doppler spectral quantification of orbital retrobulbar blood flow [6, 7]. The CDI evaluates the ophthalmic artery (OA), the

central retinal artery (CRA), and the short posterior ciliary artery (PCA) to determine the peak systolic velocity (PSV), end-diastolic velocity (EDV) and Pourcelot's resistive index (RI) [7]

The orbital Doppler imaging technique is clinically useful, but the retrobulbar hemodynamic patterns observed in diabetics may differ according to different publications. While some studies showed a considerable drop in velocities, others showed isolated increases of impedances [6,7]. As a result, the study aimed to assess and compare retrobulbar hemodynamic parameters in Type 2 diabetic patients with healthy non-diabetic subjects. It was conducted at a tertiary care medical college. Moreover, it aimed to assess the correlation of orbital vascular resistance with glycemic control and disease duration.

MATERIALS AND METHODS

Study Design and Setting

This prospective, analytical case-control study was conducted over a 6-month period at the Department of Radiodiagnosis in collaboration with the Department of Ophthalmology at ESIC Medical College, Kalaburagi. The institutional medical ethics committee approved the study protocol, and written informed consent was obtained from all enrolled participants prior to examination in accordance with the Declaration of Helsinki.

Participant Selection and Cohort Stratification

A total of N = 80 adult participants aged 40 to 65 years were recruited and stratified into two equal, age- and sex-matched groups:

Diabetic Group (Cases, n = 40): Comprising 40 patients with confirmed Type 2 Diabetes Mellitus receiving out-patient care. Inclusion required a documented history of T2DM for at least 1 year. Patients with end-stage proliferative diabetic retinopathy (PDR) requiring vitreoretinal surgery, severe vitreous hemorrhage, or dense cataracts obscuring fundus evaluation were excluded.

Control Group (Controls, n = 40): Comprising 40 healthy, normoglycemic individuals attending routine health screening with no history of diabetes (fasting plasma glucose < 100 mg/dL and HbA1c < 5.7%), matched for age and body mass index (BMI).

Exclusion Criteria: Patients with uncontrolled systemic hypertension (BP > 160/100 mmHg), carotid artery stenosis (> 50% luminal narrowing on carotid Doppler), primary open-angle or angle-closure glaucoma, ocular trauma, history of retinal photocoagulation or anti-VEGF intravitreal injections, and those with renal insufficiency or coronary artery disease.

Color Doppler Imaging Protocol

All retrobulbar orbital Doppler evaluations were performed using a high-resolution color Doppler ultrasound scanner equipped with a 7–12 MHz linear-array transducer. To avoid circadian and postural hemodynamic fluctuations, all examinations were standardized and conducted between 09:00 and 11:00 AM after a 15-minute resting period in a temperature-controlled room (22°C–24°C). Subjects were examined in the supine position with the head elevated at 30 degrees.

A sterile acoustic coupling gel was applied over the closed eyelids, and the transducer was positioned gently without exerting mechanical compression on the globe, which could artifactually elevate intraocular pressure and distort vascular resistance measurements [6, 7]. The retrobulbar vessels were identified based on anatomical landmarks and color flow velocity mapping:

Ophthalmic Artery (OA): Insonated about 15–20 mm posterior to the globe, medial to the optic nerve.

Central Retinal Artery (CRA): Insonated within the anterior 3–5 mm of the optic nerve shadow alongside the central retinal vein.

Short Posterior Ciliary Artery (PCA): Insonated in the temporal or nasal perineural tissue adjacent to the scleral insertion.

Hemodynamic and Clinical Variables Analyzed

For each vessel, three consecutive cardiac cycles with clean spectral waveforms and an angle of correction maintained below 30° were recorded. The quantitative parameters averaged across the measurements included Peak Systolic Velocity (PSV, cm/s) and End-Diastolic Velocity (EDV, cm/s). The Resistive Index (RI) was calculated according to Pourcelot's formula: RI = (PSV − EDV) / PSV. Concurrently, baseline clinical variables including glycated hemoglobin (HbA1c), fasting blood glucose, systolic and diastolic blood pressure, and Goldmann applanation intraocular pressure (IOP) were recorded.

Statistical Analysis

Data were compiled and analyzed using statistical software. Continuous variables were tested for normality using the Shapiro-Wilk test and presented as mean ± standard deviation (SD). Categorical variables were expressed as frequencies and percentages. Group comparisons between diabetics and non-diabetic controls were conducted using Student's independent two-tailed t-test for normally distributed continuous data, and the Mann-Whitney U test for non-parametric

data. Pearson's correlation coefficient (r) was utilized to evaluate linear associations between retrobulbar Resistive Indices, HbA1c levels, and diabetes duration. A p-value < 0.05 was considered statistically significant.

RESULTS

Of the 80 participants enrolled over the 6-month study duration at ESIC Medical College Kalaburagi, 40 were Type 2 diabetics and 40 were healthy controls. The baseline demographic variables, including age, sex distribution, body mass index (BMI), systolic blood pressure, and intraocular pressure, were well-matched between the two groups without statistically significant differences (Table 1). As anticipated, diabetic cases exhibited significantly elevated mean HbA1c (8.4 ± 1.6% vs. 5.2 ± 0.4%, p < 0.001) and fasting blood glucose levels compared to controls. The mean duration of diabetes in the case cohort was 7.2 ± 3.8 years.

Table 1: Baseline Demographic and Clinical Characteristics of Diabetic Cases and Controls

Clinical Parameter	Diabetic Cases (n=40)	Control Group (n=40)	p-value
Age (years), Mean ± SD	54.2 ± 6.8	53.6 ± 7.1	0.70
Male / Female, n (%)	22 (55%) / 18 (45%)	21 (52.5%) / 19 (47.5%)	0.82
Body Mass Index (kg/m²)	25.4 ± 3.1	24.8 ± 2.9	0.38
Duration of Diabetes (years)	7.2 ± 3.8	N/A	N/A
Fasting Plasma Glucose (mg/dL)	164 ± 42	88 ± 10	< **0.001**
Glycated Hemoglobin (HbA1c, %)	8.4 ± 1.6	5.2 ± 0.4	< **0.001**
Systolic Blood Pressure (mmHg)	128 ± 12	124 ± 10	0.11
Diastolic Blood Pressure (mmHg)	80 ± 8	78 ± 7	0.24
Intraocular Pressure (IOP, mmHg)	15.4 ± 2.2	14.9 ± 2.0	0.29

Color Doppler spectral waveform analysis revealed pronounced hemodynamic alterations in the retrobulbar circulation of diabetic patients compared to normoglycemic controls (Table 2). The most striking abnormalities were observed in the smaller distal vessels, specifically the central retinal artery and the short posterior ciliary artery.

In the central retinal artery (CRA), diabetic patients exhibited a highly significant reduction in end-diastolic velocity (EDV) compared to controls (2.4 ± 0.6 cm/s vs. 3.5 ± 0.7 cm/s, p < 0.001), while peak systolic velocity (PSV) showed a moderate but significant decline (10.8 ± 1.9 cm/s vs. 12.1 ± 1.8 cm/s, p = 0.003). Consequently, the CRA Resistive Index (RI) was markedly elevated in the diabetic cohort (0.78 ± 0.05 vs. 0.67 ± 0.04, p < 0.001), indicating substantial downstream microvascular impedance.

A similar pattern was evident in the short posterior ciliary artery (PCA), where the mean EDV was significantly suppressed in diabetics (3.1 ± 0.8 cm/s vs. 4.4 ± 0.9 cm/s, p < 0.001), resulting in a significantly elevated PCA Resistive Index (0.75 ± 0.06 vs. 0.65 ± 0.05, p < 0.001). In the larger ophthalmic artery (OA), Peak Systolic Velocity did not differ significantly between groups (34.5 ± 5.2 cm/s vs. 36.1 ± 4.8 cm/s, p = 0.16); however, OA end-diastolic velocity was lower in diabetics, leading to a statistically significant elevation in OA Resistive Index (0.76 ± 0.05 vs. 0.71 ± 0.04, p < 0.001).

Table 2: Color Doppler Hemodynamic Parameters of Orbital Vessels in Diabetic Cases and Controls

Vessel / Parameter	Diabetic Cases (n=40)	Control Group (n=40)	Difference (95% CI)	p-value
Ophthalmic Artery (OA)				
Peak Systolic Velocity (PSV, cm/s)	34.5 ± 5.2	36.1 ± 4.8	-3.8 to 0.6	0.16
End-Diastolic Velocity (EDV, cm/s)	8.2 ± 1.8	10.4 ± 1.9	-3.0 to -1.4	< **0.001**
Resistive Index (RI)	0.76 ± 0.05	0.71 ± 0.04	0.03 to 0.07	< **0.001**
Central Retinal Artery (CRA)				
Peak Systolic Velocity (PSV, cm/s)	10.8 ± 1.9	12.1 ± 1.8	-2.1 to -0.5	0.003
End-Diastolic Velocity (EDV, cm/s)	2.4 ± 0.6	3.5 ± 0.7	-1.4 to -0.8	< **0.001**
Resistive Index (RI)	0.78 ± 0.05	0.67 ± 0.04	0.09 to 0.13	< **0.001**
Short Posterior Ciliary Artery (PCA)				
Peak Systolic Velocity (PSV, cm/s)	12.5 ± 2.2	13.8 ± 2.1	-2.2 to -0.4	0.008
End-Diastolic Velocity (EDV, cm/s)	3.1 ± 0.8	4.4 ± 0.9	-1.7 to -0.9	< **0.001**
Resistive Index (RI)	0.75 ± 0.06	0.65 ± 0.05	0.07 to 0.13	< **0.001**

Within the diabetic cohort, Pearson correlation analysis demonstrated a statistically significant positive correlation between chronic glycemic burden and orbital vascular resistance (Table 3). Glycated hemoglobin (HbA1c) levels correlated

positively with the Resistive Index of the Central Retinal Artery ($r = 0.58$, $p < 0.001$) and the Ophthalmic Artery ($r = 0.52$, $p < 0.001$). Furthermore, the duration of diabetes exhibited a strong positive correlation with CRA Resistive Index ($r = 0.62$, $p < 0.001$) and an inverse correlation with CRA end-diastolic velocity ($r = -0.54$, $p < 0.001$), confirming that progressive chronicity of hyperglycemia steadily exacerbates orbital microvascular impedance.

Table 3: Correlation of Orbital Doppler Parameters with HbA1c and Duration of Diabetes

Hemodynamic Parameter	Correlation with HbA1c (r)	p-value	Correlation with Duration (r)	p-value
Ophthalmic Artery RI	0.52	**< 0.001**	0.48	**0.002**
Central Retinal Artery RI	0.58	**< 0.001**	0.62	**< 0.001**
Central Retinal Artery EDV	-0.49	0.001	-0.54	**< 0.001**
Posterior Ciliary Artery RI	0.45	**0.004**	0.41	0.008

DISCUSSION

This study was done in ESIC Medical College Kalaburagi and was a prospective case-control study and it was found that Type 2 Diabetes Mellitus causes significant retrobulbar hemodynamic changes characterized by increased vascular resistance and decreased end-diastolic perfusion in orbital arterial beds. Our results show that Resistive Indices of Central Retinal Artery (0.78 ± 0.05 vs. 0.67 ± 0.04) and Short Posterior Ciliary Artery (0.75 ± 0.06 vs. 0.65 ± 0.05) are significantly increased in diabetic patients without advanced proliferative retinopathy as compared to a matched healthy cohort [6, 7].

The hemodynamic profile observed is in line with the global literature on the pathogenesis of diabetic eye vascular disease. Our findings confirm the older work by Gracner et al. [2] and more recent prospective studies by Dimitrova et al. [6] that commented that peak systolic velocities in large feeding arteries (eg, ophthalmic artery [OA]) may be preserved early on in the course of diabetes, diastolic perfusion in smaller terminal vessels drops significantly. Moreover, our observed association of HbA1c chronicity with raised CRA-RI is consistent with the recent results of Doppler studies by Kaushal et al. [7] and Liu et al. [8] showing that chronic hyperglycemia leads to impairment of vascular compliance as well as narrowing of the microvascular lumen.A diabetic endothelial dysfunction is the physiological mechanism for this increased orbital impedance [3,4]. Oxidative stress caused by hyperglycemia lowers eNOS and this impairment inhibits basal basal retinal and ciliary arterioles vasodilation [4, 5]. The accumulation of advanced glycation end-products (AGEs) also leads to collagen cross-linking and basement membrane thickening in the capillary beds [3, 5]. Due to the lack of sufficient collateral networks of the central retinal artery and short posterior ciliary artery, any rise in downstream peripheral resistance directly diminishes diastolic forward flow during cardiac relaxation [6,7]. The retinal vascularity will serve as the acoustic marker of microvascular ischemia prior to structural retinal exudation or neovascularization being detectable by ophthalmoscopy [7,8].

The findings may inform the clinical practice of preventive ophthalmology and internal medicine. According to references [1,2], diagnostics by means of periodic fundus photography or ophthalmoscopy do not reveal diabetic retinopathy until structural capillary breakdown has occurred. Integrating Color Doppler Imaging of the retrobulbar vessels into routine diabetic screening protocols provides clinicians with a functional biomarker that is objective, non-invasive and quantifiable. If a diabetic patient has a rising CRA or PICA Resistive Index (for example RI>0.75), then stricter glycaemic targets, aggressive blood pressure optimization, and earlier initiation of microvascular protective agents may be warranted to prevent progressive sight-threatening retinopathy [7, 8].

CONCLUSION

Retrobulbar orbital circulation shows significant hemodynamic resistance due to Type 2 Diabetes Mellitus. This is largely evidenced by increase in Resistive Indices and blunted end-diastolic velocities in central retinal and short posterior ciliary arteries. Abnormalities of vascular impedance correlate significantly with severity of glycemic (HbA1c) and duration of disease. Color Doppler Imaging is a useful noninvasive test to identify early subclinical microvascular ischemia in diabetics. It helps in risk stratification and prompt neurovascular treatment before permanent retinal structural damage.

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