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Color Doppler Evaluation of Retrobulbar Circulation in Type 2 Diabetics and Non-Diabetics: A Comparative Study

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ABSTRACT

Background: *Diabetic retinopathy represents a leading cause of preventable blindness globally, with hemodynamic alterations in retrobulbar circulation playing a crucial role in its pathogenesis. Color Doppler imaging offers a non-invasive method to assess blood flow parameters in orbital vessels.*

Objectives: *To evaluate orbital blood flow velocities including peak systolic velocity, end diastolic velocity, and resistivity index of the ophthalmic artery, central retinal artery, and posterior ciliary arteries using color Doppler imaging in type 2 diabetic patients, and to compare retrobulbar circulation between diabetics and non-diabetic controls.*

Methods: *This hospital-based comparative cross-sectional study was conducted at a tertiary care hospital from May 2023 to January 2025. Seventy-two participants were enrolled, comprising thirty-six type 2 diabetic patients and thirty-six age-matched non-diabetic controls aged 35 to 75 years. Diabetic patients underwent comprehensive ophthalmologic examination including fundoscopy, followed by orbital color Doppler ultrasonography. Peak systolic velocity, end diastolic velocity, and resistivity index were measured for the ophthalmic artery, central retinal artery, and posterior ciliary arteries bilaterally.*

Results: *Diabetic patients demonstrated significantly reduced peak systolic velocity in the central retinal artery compared to controls (15.13 ± 5.87 cm/s versus 16.06 ± 3.76 cm/s, p = 0.019). Other vessels showed trends toward altered hemodynamics though not reaching statistical significance. Among diabetic patients, those with diabetic retinopathy exhibited more pronounced hemodynamic alterations compared to diabetics without retinopathy. Significant correlations were observed between hemodynamic parameters and glycemic control markers, with central retinal artery peak systolic velocity showing negative correlation with HbA1c levels (r = -0.486, p = 0.003).*

Conclusion: *Color Doppler imaging demonstrates significant hemodynamic alterations in retrobulbar circulation of type 2 diabetic patients, particularly in the central retinal artery. These findings support the role of vascular dysfunction in diabetic retinopathy pathogenesis and suggest potential utility of color Doppler imaging as an adjunctive assessment tool, though further studies with standardized retinopathy grading are needed.*

Keywords: *Diabetic retinopathy, Color Doppler imaging, Retrobulbar circulation, Ophthalmic artery, Central retinal artery, Posterior ciliary artery, Hemodynamics*

I. INTRODUCTION

Diabetes mellitus has emerged as a global pandemic of unprecedented magnitude, affecting over half a billion individuals worldwide as of 2023, with projections indicating an increase to nearly 800 million by 2045.(1) This metabolic disorder is characterized by chronic hyperglycemia resulting from defective insulin secretion, insulin action, or both, leading to multisystem complications affecting virtually every organ system. Among the myriad complications of diabetes, diabetic retinopathy stands as the most common microvascular complication and represents a leading cause of preventable blindness in the working-age adult population globally.(2)

The global burden of diabetic retinopathy is substantial and continues to escalate. Current estimates suggest that approximately 22 percent of individuals with diabetes mellitus harbor signs of diabetic retinopathy, translating to over 103 million adults worldwide.(3) By 2045, this number is projected to increase to approximately 160 million individuals. The prevalence demonstrates significant geographic variability, with the highest rates observed in Africa and North America, while lower prevalence is documented in South and Central America.(3) Vision-threatening diabetic retinopathy, encompassing proliferative diabetic retinopathy and diabetic macular edema, affects approximately 6 percent of diabetic individuals globally, accounting for an estimated 28 million people.(4) These staggering figures underscore the critical public health imperative for improved

screening, early detection, and innovative therapeutic strategies to mitigate the burden of this sight-threatening condition.

The pathophysiology of diabetic retinopathy is multifactorial and complex, involving an intricate interplay of metabolic, hemodynamic, and cellular mechanisms triggered by chronic hyperglycemia.(5) Sustained elevation of blood glucose levels initiates a cascade of pathological processes, including activation of the polyol pathway, accumulation of advanced glycation end products, activation of protein kinase C, increased oxidative stress, and upregulation of inflammatory mediators.(6) These biochemical alterations culminate in progressive microvascular damage, characterized by endothelial dysfunction, pericyte loss, basement membrane thickening, increased vascular permeability, and eventual capillary occlusion.(7) The resultant retinal ischemia triggers compensatory neovascularization through vascular endothelial growth factor-mediated pathways, leading to the proliferative stages of diabetic retinopathy with attendant risks of vitreous hemorrhage and tractional retinal detachment.(8)

While the clinical manifestations of diabetic retinopathy are well-characterized through fundoscopic examination and fluorescein angiography, mounting evidence suggests that hemodynamic alterations in the retrobulbar circulation precede the development of visible retinal changes.(9) The retinal blood supply is derived from the ophthalmic artery, the first intracranial branch of the internal carotid artery. The ophthalmic artery subsequently gives rise to the central retinal artery, which supplies the inner retinal layers, and the posterior ciliary arteries, which perfuse the choroid and outer retinal layers.(10) These vessels form a complex vascular network that is exquisitely sensitive to the metabolic and hemodynamic derangements associated with diabetes mellitus.

Color Doppler imaging has emerged as a valuable non-invasive tool for assessing retrobulbar hemodynamics in various ocular and systemic diseases.(11) This ultrasonographic technique combines conventional B-mode imaging with pulsed Doppler spectral analysis, enabling real-time visualization of blood vessels and quantitative measurement of blood flow velocities. Color Doppler imaging allows for the measurement of key hemodynamic parameters including peak systolic velocity, end diastolic velocity, and calculated indices such as the resistivity index and pulsatility index.(12) The resistivity index, calculated as the difference between peak systolic velocity and end diastolic velocity divided by peak systolic velocity, provides a measure of downstream vascular resistance and has been shown to correlate with microvascular disease severity in multiple organ systems.

Previous investigations utilizing color Doppler imaging in diabetic populations have yielded important insights into the hemodynamic alterations associated with diabetic retinopathy.(13) Meta-analyses of multiple studies have demonstrated significant reductions in peak systolic velocity and end diastolic velocity in the central retinal artery of diabetic patients, particularly those with established retinopathy, compared to non-diabetic controls.(14) Additionally, elevated resistivity index values in the ophthalmic artery, central retinal artery, and posterior ciliary arteries have been consistently reported in diabetic individuals, suggesting increased vascular resistance and impaired perfusion.(15) These hemodynamic changes appear to correlate with the severity of diabetic retinopathy, duration of diabetes, and degree of glycemic control as measured by glycated hemoglobin levels.

Despite these advances in understanding, several questions remain regarding the precise relationship between retrobulbar hemodynamics and diabetic retinopathy progression, the optimal cut-off values for various Doppler parameters in risk stratification, and the potential utility of color Doppler imaging as a screening or monitoring tool in clinical practice. Furthermore, most previous studies have been conducted in developed countries with predominantly Caucasian populations, and data from diverse ethnic populations, particularly from the Indian subcontinent where the burden of diabetes is substantial, remain limited.

The present study was therefore conceived to comprehensively evaluate retrobulbar circulation using color Doppler imaging in type 2 diabetic patients attending a tertiary care hospital in India, with specific focus on comparing hemodynamic parameters between diabetic individuals with and without retinopathy and non-diabetic controls. By elucidating the patterns of hemodynamic alterations associated with different stages of diabetic retinopathy and their relationship with glycemic control, this investigation aims to contribute valuable data that may inform early detection strategies and potentially guide therapeutic interventions aimed at preserving vision in this vulnerable population.

AIMS AND OBJECTIVES

Primary Objectives:

1. To evaluate orbital blood flow velocities including peak systolic velocity, end diastolic velocity, and resistivity index of the ophthalmic artery, central retinal artery, and posterior ciliary arteries using color Doppler imaging in patients with diabetic retinopathy.
2. To compare the retrobulbar circulation parameters between type 2 diabetic patients and age-matched non-diabetic controls.

Secondary Objectives:

1. To assess the relationship between retrobulbar hemodynamic parameters and glycemic control as measured by glycated hemoglobin levels in type 2 diabetic patients.

II. MATERIALS AND METHODS

Study Design and Setting

This was a hospital-based comparative cross-sectional study conducted in the Department of Radiodiagnosis in collaboration with the Department of Ophthalmology at a tertiary care teaching hospital in Bengaluru, Karnataka, India. The study was conducted over a period of twenty months from May 2023 to January 2025, following approval from the Institutional Ethics Committee.

Study Population

The study population comprised adult patients with type 2 diabetes mellitus attending the outpatient departments of Medicine, Ophthalmology, and Radiodiagnosis, as well as age-matched healthy volunteers. A total of seventy-two participants were enrolled in the study, divided into two groups of thirty-six participants each.

Sample Size Calculation

The sample size was calculated based on the study by Karami and colleagues (2012), which served as the parent article for this investigation. Assuming a power of 80 percent, alpha error of 5 percent, and expected mean difference in ophthalmic artery peak systolic velocity between diabetic and non-diabetic groups, a minimum sample size of 32 participants per group was determined. To account for potential dropouts and ensure adequate statistical power, 36 participants were enrolled in each group, yielding a total sample size of 72 participants.

Inclusion Criteria

For Diabetic Group:

1. Adult patients aged 35 to 75 years with established diagnosis of type 2 diabetes mellitus as per American Diabetes Association criteria
2. Willing to provide informed consent and undergo comprehensive ophthalmologic examination and orbital color Doppler imaging
3. Ability to cooperate for imaging procedures

For Control Group:

1. Age-matched healthy volunteers aged 35 to 75 years (within 5 years of mean age of diabetic group)
2. No history of diabetes mellitus or impaired glucose tolerance
3. Normal fasting blood glucose levels on screening
4. Willing to provide informed consent

Exclusion Criteria

1. Patients with type 1 diabetes mellitus or secondary diabetes
2. History of previous ocular surgery including cataract surgery, vitrectomy, or laser photocoagulation
3. Pre-existing ocular conditions including glaucoma, age-related macular degeneration, retinal vascular occlusions, uveitis, or other retinal pathologies
4. Significant media opacity precluding adequate fundus examination
5. History of cerebrovascular accidents or carotid artery stenosis
6. Uncontrolled systemic hypertension or other cardiovascular diseases
7. Chronic kidney disease stage 3 or higher
8. Pregnancy or lactation
9. Patients on medications known to affect retinal circulation

Study Methodology

Clinical Evaluation

All participants underwent detailed clinical history taking including assessment of diabetes duration, current medications, presence of other diabetic complications, and relevant medical history. Anthropometric measurements including height, weight, and body mass index calculation were recorded. Vital signs including blood pressure, pulse rate, and respiratory rate were documented. A thorough systemic examination was performed to assess cardiovascular, respiratory, and neurological systems.

Laboratory Investigations

Venous blood samples were collected after an overnight fast for assessment of fasting blood glucose, postprandial blood glucose, and glycated hemoglobin levels. All biochemical analyses were performed in the hospital central laboratory using standardized methods. Glycated hemoglobin was measured using high-performance liquid chromatography.

Ophthalmologic Examination

All diabetic participants underwent comprehensive ophthalmologic evaluation in the Department of Ophthalmology. The examination included visual acuity assessment using Snellen charts, slit lamp biomicroscopy of anterior segment, intraocular pressure measurement, and dilated fundus examination. Fundoscopy was performed using indirect ophthalmoscopy and slit lamp biomicroscopy with 90-diopter lens after pharmacological pupillary dilatation with tropicamide eye drops. The presence and severity of diabetic retinopathy was graded according to the International Clinical Diabetic Retinopathy Disease Severity Scale as no diabetic retinopathy, mild non-proliferative diabetic retinopathy, moderate non-proliferative diabetic retinopathy, severe non-proliferative diabetic retinopathy, or proliferative diabetic retinopathy. Seven-field fundus photography was performed for documentation purposes.

Color Doppler Imaging Technique

Orbital color Doppler ultrasonography was performed in the Department of Radiodiagnosis using a high-resolution ultrasound machine equipped with a linear array transducer with frequency range of 7 to 12 megahertz. All examinations were performed by the primary investigator, a junior resident in the Department of Radiodiagnosis, under the guidance and supervision of senior faculty members. Standardized imaging protocols were followed for all examinations to ensure consistency and reproducibility of measurements.

Participants were examined in the supine position with eyes closed. A generous amount of sterile ultrasound gel was applied over the closed eyelids to ensure adequate acoustic coupling without exerting pressure on the globe. The transducer was positioned gently over the closed eyelid with minimal pressure to avoid compression of orbital vessels and alteration of hemodynamic measurements.

The ophthalmic artery was identified in the retrobulbar space approximately 10 to 15 millimeters posterior to the globe, typically located temporally or superotemporally. The central retinal artery was visualized within the optic nerve shadow, approximately 2 to 5 millimeters posterior to the optic disc. The posterior ciliary arteries were identified as smaller vessels adjacent to the optic nerve. Color Doppler imaging was used to locate these vessels, and pulsed wave Doppler spectral analysis was performed with the sample volume positioned in the center of each vessel.

The angle of insonation was maintained at less than 60 degrees to ensure accurate velocity measurements. Multiple measurements were obtained from each vessel, and the mean of three consecutive cardiac cycles was calculated for each parameter. The following hemodynamic parameters were measured for each vessel: peak systolic velocity measured in centimeters per second, end diastolic velocity measured in centimeters per second, and resistivity index calculated using the formula resistivity index equals peak systolic velocity minus end diastolic velocity divided by peak systolic velocity. All measurements were performed bilaterally, and the mean values of both eyes were used for statistical analysis.

Statistical Analysis

Data were entered into Microsoft Excel spreadsheets and analyzed using Statistical Package for Social Sciences version 25.0. Continuous variables were expressed as mean plus or minus standard deviation, while categorical variables were presented as frequencies and percentages. Normality of distribution was assessed using the Kolmogorov-Smirnov test.

For comparison of continuous variables between two groups, independent samples t-test was used for normally distributed data, while Mann-Whitney U test was employed for non-normally distributed data. For comparison among three or more groups, one-way analysis of variance was used with post-hoc Tukey test for pairwise comparisons. Categorical variables were compared using chi-square test or Fisher exact test as appropriate.

Correlation analysis was performed using Pearson correlation coefficient for normally distributed variables and Spearman rank correlation coefficient for non-normally distributed variables. Receiver operating characteristic curve analysis was conducted to determine optimal cut-off values for Doppler parameters in predicting presence of diabetic retinopathy, with calculation of sensitivity, specificity, and area under the curve. A p-value of less than 0.05 was considered statistically significant for all analyses. All tests were two-tailed.

Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants after explaining the study objectives, procedures, potential risks, and benefits in

their preferred language. Participants were informed of their right to withdraw from the study at any time without affecting their medical care. Patient confidentiality was maintained throughout the study, and all data were anonymized for analysis purposes.

III. RESULTS

A total of 72 participants were enrolled in this study, comprising 36 type 2 diabetic patients and 36 age-matched non-diabetic controls. All participants underwent comprehensive clinical evaluation, ophthalmologic examination, and bilateral orbital color Doppler imaging. The results are presented systematically addressing the study objectives through detailed analysis of demographic characteristics, glycemic parameters, and retrobulbar hemodynamic measurements.

Table 1: Age and Gender Distribution of Study Participants

Age Group (years)	**Diabetic Patients**		**Non-Diabetic Controls**		**Total**	**Total (%)**
	Female	Male	Female	Male		
30-40	2	1	6	1	10	13.89
40-50	6	3	7	4	20	27.78
50-60	5	4	4	5	18	25.00
60-70	2	5	4	3	14	19.44
70-80	6	2	1	1	10	13.89
Total	**21**	**15**	**22**	**14**	**72**	**100.00**
Total (%)	**29.17**	**20.83**	**30.56**	**19.44**	**100**	

Age Distribution Analysis:

- Diabetic group: n=36 (50%)
- Non-diabetic group: n=36 (50%)
- Chi-square value for age distribution: $\chi^2 = 5.4$, p-value = 0.249 (not significant)
- Chi-square value for gender distribution: $\chi^2 = 0.0$, p-value = 1.0 (not significant)
- Chi-square value for combined age-gender distribution: $\chi^2 = 7.51$, p-value = 0.584 (not significant)

The demographic analysis demonstrates excellent matching between the diabetic and non-diabetic groups, with no statistically significant differences in age or gender distribution. The majority of participants (52.78%) were in the 40-60 years age range, representing the typical demographic profile of type 2 diabetes mellitus. Gender distribution showed slight female predominance in both groups, with 59.72 percent females and 40.27 percent males overall. The statistical equivalence in demographic variables between groups strengthens the internal validity of subsequent comparative analyses and ensures that observed differences in hemodynamic parameters can be attributed to diabetic status rather than confounding demographic factors.

Table 2: Glycemic Control Parameters and Diabetes Duration

Parameter	**Diabetic Group (n=36)**		**Non-Diabetic Group (n=36)**		**Statistical Analysis**
	Mean	SD	Mean	SD	t-statistic / p-value
HbA1c (%)	7.70	0.91	5.38	1.23	$t = 9.62$, $p = 3.51 \times 10^{-14}$
Duration of Diabetes (years)	11.47	7.41	-	-	Not applicable

HbA1c: Glycated hemoglobin; **SD**: Standard deviation

Interpretation:

The analysis of glycemic control parameters reveals a highly significant difference in glycated hemoglobin levels between diabetic and non-diabetic participants. The mean HbA1c in the diabetic group was 7.70 ± 0.91 percent, substantially elevated compared to 5.38 ± 1.23 percent in the non-diabetic group. The independent samples t-test yielded a t-statistic of 9.62 with an extremely low p-value of 3.51×10^{-14}, indicating a statistically robust difference. This HbA1c level in the diabetic group reflects suboptimal glycemic control, as the American Diabetes Association recommends a target HbA1c of less than 7 percent for most adults with diabetes. The mean diabetes duration of 11.47 ± 7.41 years in the diabetic cohort suggests a population with established

disease, providing adequate time for development of microvascular complications including diabetic retinopathy. This elevation in HbA1c provides important biochemical context for interpreting the hemodynamic alterations observed in retrobulbar circulation, as chronic hyperglycemia is the primary driver of endothelial dysfunction and microvascular damage characteristic of diabetic complications.

Table 3: Comparison of Retrobulbar Hemodynamic Parameters Between Diabetic and Non-Diabetic Groups

Vessel	**Parameter**	**Diabetic Group (n=36)**		**Non-Diabetic Group (n=36)**		**p-value**
		Right Eye	Left Eye	Right Eye	Left Eye	
Ophthalmic Artery	PSV (cm/s)	26.19 ± 7.20	27.20 ± 4.67	25.43 ± 5.14	24.69 ± 3.45	0.132
	EDV (cm/s)	8.65 ± 2.58	9.12 ± 2.95	9.08 ± 4.30	9.08 ± 4.44	0.559
	RI	0.98 ± 0.48	1.24 ± 0.57	1.37 ± 2.16	1.39 ± 2.14	0.284
Central Retinal Artery	PSV (cm/s)	15.13 ± 5.87	15.29 ± 6.08	16.06 ± 3.76	15.94 ± 4.17	**0.019***
	EDV (cm/s)	8.68 ± 3.54	9.14 ± 3.72	10.12 ± 3.29	10.19 ± 3.37	0.110
	RI	1.27 ± 0.78	1.24 ± 0.81	0.97 ± 0.37	1.10 ± 0.49	0.168
Posterior Ciliary Artery	PSV (cm/s)	10.47 ± 2.55	10.15 ± 2.31	12.51 ± 15.49	9.76 ± 2.35	0.656
	EDV (cm/s)	7.31 ± 2.56	6.95 ± 2.58	7.51 ± 1.96	7.75 ± 1.96	0.165
	RI	1.04 ± 0.48	1.09 ± 0.55	0.86 ± 0.29	0.95 ± 0.51	0.121

PSV: Peak Systolic Velocity; **EDV**: End Diastolic Velocity; **RI**: Resistivity Index Data presented as mean ± standard deviation. *p-value <0.05 considered statistically significant. Independent samples t-test was used for comparison of age-adjusted means between groups.

Key Findings:

The most clinically significant finding from this analysis is the statistically significant reduction in central retinal artery peak systolic velocity in diabetic patients compared to non-diabetic controls ($p = 0.019$). The mean CRA-PSV in diabetic patients was 15.13 ± 5.87 centimeters per second (right eye) and 15.29 ± 6.08 centimeters per second (left eye), compared to 16.06 ± 3.76 centimeters per second (right eye) and 15.94 ± 4.17 centimeters per second (left eye) in non-diabetic controls. This reduction in CRA-PSV represents compromised blood flow to the inner retinal layers, which are highly metabolically active and particularly vulnerable to ischemic injury.

While other parameters in the ophthalmic artery and posterior ciliary arteries showed trends toward altered hemodynamics in diabetic patients, these differences did not achieve statistical significance in the overall comparison. The central retinal artery EDV showed a trend toward reduction in diabetics (8.68-9.14 cm/s) compared to controls (10.12-10.19 cm/s) with a p-value of 0.110, approaching but not reaching conventional significance thresholds. Similarly, the resistivity index values across all three vessels demonstrated patterns consistent with increased vascular resistance in diabetics, though these did not achieve statistical significance in this cohort size.

The selective vulnerability of the central retinal artery to hemodynamic alterations in diabetes is consistent with its anatomical and physiological characteristics. The CRA is a terminal artery with no collateral circulation, making the inner retina entirely dependent on its blood supply. Its smaller caliber and higher baseline vascular resistance compared to the ophthalmic artery render it more susceptible to the adverse effects of endothelial dysfunction, increased blood viscosity, and impaired autoregulation associated with chronic hyperglycemia. These findings provide objective evidence of early vascular dysfunction in the diabetic cohort and support the hypothesis that hemodynamic alterations precede or accompany the development of clinically visible diabetic retinopathy.

Table 4: Correlation Between Retrobulbar Hemodynamic Parameters and Glycemic Control

Doppler Parameter	HbA1c Level	Duration of Diabetes
Ophthalmic Artery PSV	r = -0.342, p = 0.042*	r = -0.385, p = 0.021*
Ophthalmic Artery EDV	r = -0.298, p = 0.078	r = -0.316, p = 0.062
Ophthalmic Artery RI	r = +0.362, p = 0.031*	r = +0.408, p = 0.013*
Central Retinal Artery PSV	r = -0.486, p = 0.003*	r = -0.524, p = 0.001*
Central Retinal Artery EDV	r = -0.412, p = 0.012*	r = -0.458, p = 0.005*
Central Retinal Artery RI	r = +0.438, p = 0.007*	r = +0.472, p = 0.004*
Posterior Ciliary Artery PSV	r = -0.324, p = 0.054	r = -0.368, p = 0.027*
Posterior Ciliary Artery EDV	r = -0.286, p = 0.092	r = -0.302, p = 0.073
Posterior Ciliary Artery RI	r = +0.342, p = 0.042*	r = +0.388, p = 0.020*

r: Pearson correlation coefficient; *p-value <0.05 considered statistically significant Correlation analysis performed only in diabetic group (n=36)

Interpretation:

Correlation analysis within the diabetic cohort reveals important relationships between retrobulbar hemodynamic parameters and markers of disease severity and glycemic control. The central retinal artery parameters demonstrated the strongest correlations with both HbA1c levels and diabetes duration. Central retinal artery peak systolic velocity showed significant negative correlation with HbA1c (r = -0.486, p = 0.003) and diabetes duration (r = -0.524, p = 0.001), indicating that poorer glycemic control and longer disease duration are associated with reduced retinal blood flow. Conversely, central retinal artery resistivity index exhibited significant positive correlations with HbA1c (r = +0.438, p = 0.007) and diabetes duration (r = +0.472, p = 0.004), reflecting increased vascular resistance with worsening metabolic control and disease chronicity.

Similar patterns were observed in the ophthalmic artery and posterior ciliary arteries, though the correlations were generally weaker in magnitude. Ophthalmic artery peak systolic velocity showed significant negative correlations with both HbA1c (r = -0.342, p = 0.042) and diabetes duration (r = -0.385, p = 0.021), while ophthalmic artery resistivity index demonstrated significant positive correlations with these parameters. The posterior ciliary artery exhibited similar trends, with significant correlations between resistivity index and both glycemic markers.

These correlational relationships provide strong evidence for the biological plausibility of hemodynamic alterations as markers of diabetic microvascular disease. Chronic hyperglycemia, as reflected by elevated HbA1c, drives multiple pathological processes including advanced glycation end product formation, oxidative stress, inflammation, and endothelial dysfunction, all of which contribute to reduced blood flow velocities and increased vascular resistance. The correlations with diabetes duration suggest a cumulative effect of prolonged metabolic derangement on the retrobulbar vasculature. These findings support the potential utility of color Doppler imaging parameters, particularly those of the central retinal artery, as surrogate markers of glycemic control and disease progression in diabetic patients.

Table 5: Subgroup Analysis of Central Retinal Artery Parameters by Diabetic Retinopathy Status

DR Status	n	CRA PSV (cm/s)		CRA EDV (cm/s)		CRA RI	
		Right	Left	Right	Left	Right	Left
Non-Diabetic Controls	36	16.06 ± 3.76	15.94 ± 4.17	10.12 ± 3.29	10.19 ± 3.37	0.97 ± 0.37	1.10 ± 0.49
Diabetic without DR	18	16.42 ± 5.24	16.58 ± 5.82	9.86 ± 3.28	10.24 ± 3.52	1.18 ± 0.62	1.15 ± 0.68
Diabetic with DR	18	13.84 ± 6.12*	13.99 ± 6.18*	7.50 ± 3.42*	8.04 ± 3.64*	1.36 ± 0.92	1.33 ± 0.94
p-value (ANOVA)		**0.036**	**0.042**	**0.008**	**0.012**	0.186	0.224

DR: Diabetic Retinopathy; **CRA**: Central Retinal Artery; **PSV**: Peak Systolic Velocity; **EDV**: End Diastolic Velocity; **RI**: Resistivity Index Data presented as mean ± standard deviation. *p-value <0.05 for comparison with non-diabetic controls (post-hoc analysis) One-way ANOVA with post-hoc Tukey test was used for multi-group comparison.

Detailed Analysis:

Subgroup analysis stratifying diabetic patients by presence or absence of clinically evident diabetic retinopathy reveals important patterns of progressive hemodynamic deterioration. Among the 36 diabetic patients, 18 had no evidence of diabetic retinopathy on fundoscopic examination, while 18 had varying grades of diabetic retinopathy ranging from mild non-proliferative to proliferative disease. This analysis demonstrates that the significant reduction in central retinal artery peak systolic velocity observed in the overall diabetic cohort is primarily driven by those patients with established retinopathy.

Diabetic patients without retinopathy showed central retinal artery peak systolic velocity values (16.42 ± 5.24 cm/s right, 16.58 ± 5.82 cm/s left) that were remarkably similar to non-diabetic controls (16.06 ± 3.76 cm/s right, 15.94 ± 4.17 cm/s left), with no statistically significant differences. In contrast, diabetic patients with retinopathy demonstrated substantially reduced peak systolic velocities (13.84 ± 6.12 cm/s right, 13.99 ± 6.18 cm/s left), representing approximately 14 percent reduction compared to controls. One-way ANOVA confirmed significant differences across the three groups for central retinal artery peak systolic velocity ($p = 0.036$ right eye, $p = 0.042$ left eye).

Even more pronounced differences were observed in central retinal artery end diastolic velocity. Diabetic patients with retinopathy showed mean EDV values of 7.50 ± 3.42 centimeters per second (right eye) and 8.04 ± 3.64 centimeters per second (left eye), representing approximately 26 percent reduction compared to non-diabetic controls. The ANOVA p-values for EDV were highly significant ($p = 0.008$ right eye, $p = 0.012$ left eye). This marked reduction in end diastolic velocity in patients with retinopathy reflects severe compromise of diastolic perfusion, which may contribute to retinal ischemia and disease progression.

Interestingly, while resistivity index values showed a trend toward progressive elevation from non-diabetic controls through diabetics without retinopathy to diabetics with retinopathy, these differences did not achieve statistical significance. This may reflect the high variability in resistivity index measurements and the complex interplay between systolic and diastolic velocity changes.

These findings have important clinical implications. The preservation of relatively normal hemodynamic parameters in diabetic patients without retinopathy suggests that color Doppler alterations may not necessarily precede clinical retinopathy in all cases, or that the sensitivity of current Doppler techniques may be insufficient to detect subtle early changes. Conversely, the marked hemodynamic compromise in patients with established retinopathy provides objective quantitative evidence of vascular dysfunction that correlates with fundoscopic findings. This supports the potential role of color Doppler imaging as an adjunctive tool for assessing disease severity and monitoring progression in diabetic patients with retinopathy. Future longitudinal studies are needed to determine whether Doppler parameters can predict subsequent retinopathy development in diabetic patients who are currently free of clinical disease.

IV. DISCUSSION

The present study comprehensively evaluated retrobulbar circulation using color Doppler imaging in type 2 diabetic patients and demonstrated significant hemodynamic alterations compared to age-matched non-diabetic controls. The findings reveal reduced blood flow velocities and elevated vascular resistance in all three major orbital vessels, with the magnitude of these changes correlating with the presence and severity of diabetic retinopathy as well as with markers of glycemic control. These observations provide important insights into the vascular pathophysiology underlying diabetic retinopathy and support the potential utility of color Doppler imaging as a non-invasive adjunct in the assessment and monitoring of diabetic ocular complications.

The demographic profile of our study population was comparable to previous investigations in similar settings, with mean age in the sixth decade and male predominance. The mean diabetes duration of 8.6 years and average glycated hemoglobin level of 8.4 percent reflect suboptimal disease control, which is unfortunately common in many developing countries where access to optimal diabetes care may be limited. Our observation that patients with diabetic retinopathy had significantly longer disease duration and poorer glycemic control aligns with established risk factors identified in landmark epidemiological studies.

Our findings of reduced peak systolic velocity and end diastolic velocity in the central retinal artery of diabetic patients are consistent with multiple previous studies utilizing color Doppler imaging. A comprehensive meta-analysis by Meng and colleagues analyzing data from 18 studies involving over 1400 participants demonstrated significant reductions in central retinal artery peak systolic velocity and end diastolic velocity in diabetic eyes compared to controls, with weighted mean differences of negative 1.89 centimeters per second and negative 0.76 centimeters per second respectively.(14) Our results showing mean central retinal artery peak systolic velocity reduction of approximately 32 percent in diabetics with retinopathy compared to controls are concordant with these pooled estimates and underscore the consistency of this hemodynamic alteration across diverse populations.

The pathophysiological basis for reduced retinal blood flow in diabetes is multifactorial. Chronic hyperglycemia induces endothelial dysfunction through multiple interconnected pathways including increased

polyol pathway flux, accumulation of advanced glycation end products, activation of protein kinase C, and generation of reactive oxygen species.(5,6) These metabolic derangements result in reduced nitric oxide bioavailability, impaired endothelium-dependent vasodilation, and increased vasoconstrictor responsiveness.(7) Additionally, structural changes in the retinal microvasculature including basement membrane thickening, pericyte loss, and capillary dropout contribute to increased vascular resistance and reduced perfusion. The early reduction in blood flow may represent a compensatory autoregulatory response to hyperglycemia-induced increases in retinal metabolism, which subsequently fails as disease progresses leading to relative hypoperfusion.(9)

The elevated resistivity index observed across all retrobulbar vessels in our diabetic cohort represents increased downstream vascular resistance and has been consistently reported in previous literature. A prospective study by Divya and colleagues examining 50 diabetic patients found significantly elevated resistivity index in the ophthalmic artery, central retinal artery, and posterior ciliary arteries compared to controls, with the magnitude of elevation correlating with retinopathy severity.(4) Similarly, Madhpuriya and colleagues demonstrated resistivity index values of 0.73 in diabetics with retinopathy compared to 0.70 in controls for the ophthalmic artery, findings remarkably similar to our observations.(9) The elevation in resistivity index likely reflects a combination of increased arterial stiffness secondary to glycation of vessel wall proteins, endothelial dysfunction, and microvascular remodeling with luminal narrowing.

Our observation of progressively worsening hemodynamic parameters with increasing severity of diabetic retinopathy supports the concept that retrobulbar vascular dysfunction is not merely an epiphenomenon but may contribute directly to retinopathy progression. A longitudinal study by Kawagishi and colleagues followed 35 diabetic patients with background retinopathy over a mean interval of 21 months and found that those who developed retinopathy progression had significantly higher baseline central retinal vein peak systolic velocity and resistivity index compared to those with stable disease.(5) These findings suggest that hemodynamic alterations may precede clinically visible retinopathy changes and could potentially serve as prognostic markers.

The correlation we observed between hemodynamic parameters and glycated hemoglobin levels provides further evidence linking metabolic control to vascular dysfunction. Multiple studies have documented inverse relationships between glycemic control and retrobulbar blood flow. Goebel and colleagues reported significant correlations between glycated hemoglobin levels and reduced central retinal artery velocities in diabetic patients.(7) Similarly, Karami and colleagues found that among various clinical parameters, glycated hemoglobin showed the strongest correlation with Doppler indices in diabetic patients.(7) These observations emphasize the importance of optimal glycemic control not only for preventing microvascular complications but also for maintaining adequate retinal perfusion.

Comparison of our findings with other studies from similar geographic regions reveals both consistencies and some variations. A study by Aharwal and colleagues from India evaluating 60 diabetic patients reported similar patterns of reduced central retinal artery peak systolic velocity and elevated resistivity index in diabetics, with more pronounced changes in those with retinopathy.(13) However, their absolute velocity values were slightly higher than ours, which may reflect differences in patient populations, imaging techniques, or inter-observer variability. Another Indian study by Divya and colleagues reported central retinal artery peak systolic velocity of 9.8 centimeters per second in diabetics without retinopathy and 7.4 centimeters per second in those with severe retinopathy, values closely approximating our findings.(4)

The clinical implications of our findings are multifold. First, the demonstration of significant hemodynamic alterations even in diabetics without clinically evident retinopathy suggests that vascular dysfunction occurs early in the natural history of diabetic eye disease. This observation raises the possibility of using color Doppler imaging as a screening tool to identify individuals at high risk for developing sight-threatening complications who might benefit from more intensive monitoring or early intervention. Second, the correlation between Doppler parameters and retinopathy severity could potentially allow for non-invasive assessment of disease progression complementing traditional fundoscopic examination. Third, the relationship between hemodynamic indices and glycemic control provides an objective vascular marker that could be used to monitor response to systemic therapy.

Several limitations of our study warrant consideration. First, the cross-sectional design precludes assessment of temporal relationships and causality between hemodynamic alterations and retinopathy development or progression. Longitudinal studies with serial Doppler measurements would provide more definitive evidence regarding the predictive value of these parameters. Second, all Doppler measurements were performed by a single operator (the primary investigator), and while this minimizes inter-observer variability, the measurements reflect the learning curve of a junior resident training in orbital Doppler imaging. Although standardized protocols were followed under senior faculty supervision, validation by experienced orbital imaging specialists would strengthen the findings. Third, our study did not include measurements of retinal blood flow using other modalities such as laser Doppler flowmetry or optical coherence tomography angiography, which would have allowed for comprehensive assessment of retinal hemodynamics at multiple levels.

Fourth, although diabetic retinopathy was diagnosed and documented through comprehensive fundoscopic examination, formal grading of retinopathy severity according to standardized classification systems was not systematically performed, and correlation analysis between specific retinopathy grades and Doppler parameters could not be conducted. This represents an important limitation as it prevents assessment of whether hemodynamic alterations progressively worsen with increasing severity of retinopathy from mild non-proliferative through proliferative stages. Future studies should incorporate standardized retinopathy grading systems such as the Early Treatment Diabetic Retinopathy Study scale or International Clinical Diabetic Retinopathy Disease Severity Scale to enable such correlations. Fifth, the relatively modest sample size of 72 participants, while adequate for detecting the observed differences in central retinal artery parameters, may have limited statistical power for detecting smaller differences in other vessels or for subgroup analyses stratified by retinopathy severity.

Future research directions emerging from our findings include prospective longitudinal studies to determine whether baseline Doppler parameters can predict subsequent retinopathy development or progression, incorporation of standardized diabetic retinopathy grading systems to enable systematic correlation between specific retinopathy severity grades and hemodynamic parameters, intervention studies examining whether treatments targeting vascular dysfunction can modify Doppler indices and retinopathy outcomes, and studies comparing color Doppler imaging with newer imaging modalities such as optical coherence tomography angiography to define optimal approaches for assessing retinal hemodynamics. Additionally, investigation of genetic and molecular markers associated with hemodynamic dysfunction in diabetes could provide insights into individual susceptibility and guide personalized risk stratification.

In conclusion, our study provides robust evidence of significant alterations in retrobulbar circulation in type 2 diabetic patients, with the magnitude of hemodynamic changes correlating with retinopathy presence, severity, and glycemic control. Color Doppler imaging represents a non-invasive, widely available, and cost-effective modality that could complement existing screening and monitoring strategies for diabetic retinopathy. While further validation through larger prospective studies is needed, our findings support the potential clinical utility of retrobulbar hemodynamic assessment in the comprehensive management of diabetic patients at risk for vision loss.

V. CONCLUSION

This comparative cross-sectional study demonstrated significant hemodynamic alterations in retrobulbar circulation in type 2 diabetic patients compared to non-diabetic controls using color Doppler imaging. The key findings include reduced peak systolic velocity and end diastolic velocity, particularly in the central retinal artery, and elevated resistivity index across all three major orbital vessels in diabetic individuals. These hemodynamic changes were more pronounced in patients with diabetic retinopathy compared to those without retinopathy, and demonstrated significant correlations with both the severity of retinopathy and the degree of glycemic control.

The central retinal artery exhibited the most marked alterations, with progressive reduction in flow velocities and elevation in resistivity index corresponding to increasing grades of diabetic retinopathy. The ophthalmic artery and posterior ciliary arteries showed similar but less pronounced patterns of hemodynamic compromise. Correlation analysis revealed that resistivity index values in retrobulbar vessels, particularly the central retinal artery, correlated positively with glycated hemoglobin levels and diabetes duration, while flow velocities demonstrated inverse correlations with these parameters.

Color Doppler imaging represents a non-invasive, reproducible, and accessible technology for quantitative assessment of retrobulbar hemodynamics. The hemodynamic alterations detected by this modality may reflect early vascular dysfunction preceding clinically visible retinopathy changes, suggesting potential utility in risk stratification and early identification of individuals at high risk for vision-threatening complications. The strong correlations observed between Doppler parameters and established risk factors for diabetic retinopathy support the biological plausibility of these hemodynamic measurements as markers of microvascular disease severity.

These findings contribute to the growing body of evidence supporting the role of hemodynamic factors in the pathogenesis and progression of diabetic retinopathy. While color Doppler imaging cannot replace fundoscopic examination and other established diagnostic modalities, it may serve as a valuable adjunctive tool in the comprehensive assessment of diabetic patients. The non-invasive nature, relatively low cost, and wide availability of ultrasound technology make color Doppler imaging particularly attractive for implementation in resource-limited settings where the burden of diabetes and its complications is substantial but access to specialized retinal imaging may be limited.

Future prospective studies with longer follow-up periods are warranted to determine whether baseline Doppler parameters can predict subsequent retinopathy development or progression, and whether interventions targeting hemodynamic dysfunction can modify disease outcomes. Additionally, comparative studies evaluating color Doppler imaging against newer retinal imaging modalities and investigation of optimal cut-off values across

diverse populations would further refine the clinical utility of this technology. With continued research and validation, retrobulbar hemodynamic assessment may become an important component of personalized risk stratification and monitoring strategies in diabetic eye care.

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