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A study on effect of diabetes mellitus and hypertension on ocular blood flow by colour doppler ultrasonography

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ABSTRACT

BACKGROUND: Diabetes mellitus (DM) and hypertension (HT) have been the two major medical and public health issues for over 40 years worldwide. Colour doppler imaging (CDI) is widely used to evaluate ocular circulation. It is non-invasive, safe, and useful tool, most commonly used to investigate circulatory parameters in retrobulbar blood vessels. The aim was to study ocular blood flow (OBF) velocity in the ophthalmic artery (OA), central retinal artery (CRA) and central retinal vein (CRV) in patients with DM and HT by CDI.

MATERIALS AND METHODS: A cross-sectional observational study was done for 6 months (June 2021–November 2021) on 40 patients of age 40 years and above with DM and/or HT of a minimum 6 months duration. Retrobulbar circulation was assessed in all subjects bilaterally. Subjects were further divided into groups with or without retinopathy.

RESULTS: Of the total number of 40 participants, 26 (65%) were male, and 14 (35%) were female. 16 (40%) participants were diabetics, 8 (20%) were hypertensive, and 16 (40%) had both DM and HT. 57.5% were diagnosed with retinopathy changes. The mean values of the pulsatile index (PI) were: 1.23 in patients with DM, 1.30 in patients with HTN, and 1.33 in patients with DM and HTN.

CONCLUSION: Our study showed reduced blood flow velocity and increased resistivity index (RI) in patients with DM and/or HT. Significant changes were noted in retrobulbar blood flow in patients with retinopathy. These results can potentially provide prognostic values in times to come regarding altered OBF even before retinopathy develops.

KEY WORDS: diabetes mellitus; hypertension; color doppler ultrasonography; ophthalmic artery; central retinal artery

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INTRODUCTION

Diabetes mellitus (DM) and hypertension (HT) have been the two major medical and public health issues for 40 years worldwide. Diabetes affects around 347 million worldwide, of which 37.7 million cases are present in India. Type 2 diabetes (adult onset) is more associated with diabetic retinopathy (DR) and is the leading cause of visual

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impairment. It affects ocular circulation, which may contribute to the development and progression of DR. The exact nature of ocular blood flow (OBF) abnormalities in DM has not yet been established, but increased resistance in peripheral vascular bed is noted even before the appearance of overt DR [1]. Hypertension is estimated to affect 1.13 billion worldwide. Essential HT is frequently encountered in patients with ocular problems like glaucoma, central retinal vein occlusion (CRVO), and DM, with decreased blood flow, noted in central retinal artery (CRA) in patients with HT and peripheral vascular diseases. This information is less known and is essential, as any change in supplying vessels could affect the blood flow to the optic nerve head [2]. Color doppler imaging (CDI) of orbital flow is a non-invasive and safe technique combining B-scan ultrasonography for the visualization and measurement of retrobulbar blood flow velocities [3]. CDI is a widely used method to evaluate the ocular circulation. It is non-invasive, safe, and useful tool and is most commonly used to investigate circulatory parameters in retrobulbar blood vessels. CDI has been employed to study the flow of blood in the ophthalmic and central retinal arteries in various ophthalmic diseases, including glaucoma, age-related macular degenerations, DR, and CRVO [4]. Colour Doppler imaging (CDI) has made it possible to evaluate OBF under real-time and physiological conditions. The literature shows an inverse correlation between diabetic/hypertensive retinopathy severity and flow velocity [5].

The main aim of this study is to study the OBF velocities in the ophthalmic artery (OA), CRA, and central retinal vein (CRV) in patients with DM and HT by CDI.

MATERIAL AND METHODS

A hospital-based cross-sectional study was done in the Outpatient Department (OPD) of the Ophthalmology Department of Rajarajeswari Medical College and Hospital, Bangalore. The study was conducted for 6 months (from June 21 to Nov 21) on 40 patients (80 eyes) of age 40 years and above with DM and/or HT of a minimum 6 months duration. Approval of the Institutional Ethical Committee (no. RRMCH-IEC/27/2021) was obtained then tenets of the Declaration of Helsinki were followed. As the sampling method was used the consecutive sampling technique.

Sample size: 40 (by Yamane Formula):

$$n = \frac{N}{1 + N\,e2} = \frac{80}{1 + 80(0.05)2} = 40$$

Where:
n = sample size
N = known population (80 OPD patients aged 40 years and above)
e = margin of error (for 95% confidence level, margin of error is 0.05).

Patients included in this study had to be fulfilling the following criteria:

- will to give consent attending OPD of the Ophthalmology department of Rajarajeswari Medical College and Hospital;
- above the age of 40 years, DM and/or HT of a minimum 6 months duration.

Criteria of exclusion were aso follows:

- glaucoma;
- age below 40 years.

Informed consent was taken. All selected participants were evaluated with detailed ocular history, ocular examination — visual acuity tests, anterior segment examination done under slit-lamp biomicroscope, and posterior segment examination done using +90 D volks lens and indirect ophthalmoscope. Intraocular pressure was measured using Goldmann applanation tonometer.

Then the same radiologist performed CDI assessing the retrobulbar circulation. The Philips HD11xe ultrasound scanner machine was used. Subjects were imaged in the supine position. The acoustic gel was applied over the closed upper eyelid, and imaging was performed, avoiding any pressure on the globe (Fig. 1–3). OA blood flow was measured about 2 cm posterior to the globe, and CRA was assessed within the retro-laminar part of the optic nerve. Peak systolic velocity (PSV) and end diastolic velocity (EDV) were measured, and resistivity index (RI) [defined as (PSV – EDV/PSV)] was calculated

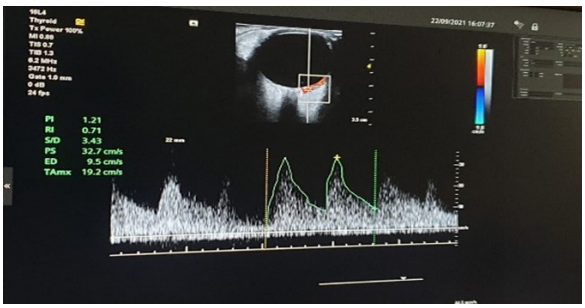

FIGURE 1. Illustration of blood flow velocity parameters seen in the ophthalmic artery in a patient

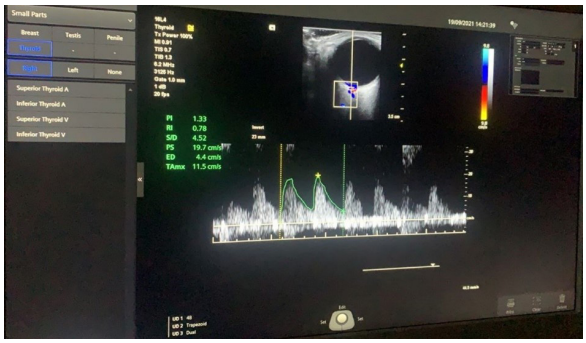

FIGURE 2. Illustration of blood flow velocity parameters seen in a patient's central retinal artery/central retinal vein

FIGURE 3. Color Doppler imaging procedure

for OA and CRA bilaterally. Each measure was repeated 3 times, and the average number was used for calculations.

CDI was performed by a masked, experienced sonologist with a 9–15 broadband MHz linear probe to measure OA and CRA. A 7.5 MHz probe was applied to the closed eyelids using sterile coupling gel in the supine position and fingers resting on the face to avoid probe pressure on the globe. Identification of the ocular vessels was made per the anatomic location and flow characteristics, i.e., arterial flow is pulsatile and is usually red, while venous flow has a continuous spectrum and is blue (away from the probe). The examination was done in medium to low-flow settings, and a sample volume of approximately 1.2 mm was chosen. Examination time for each eye was 10–15 min. Angle correction was applied to minimize errors in the measurement of OBF. If the disease was symmetrical, one eye was chosen randomly, or the eye with more advanced disease was selected for analysis. PSV and EDV were obtained. RI was calculated according to Pourcelot's formula:

$$RI = (PSV - EDV)/PSV$$

The mean velocities (MV) velocities and RI in OA and CRA were compared across the diabetic group (DM group), hypertensive group (HT group), and diabetic plus hypertensive group (DM + HT group) using ANOVA.

RESULTS

Forty patients participated in this study. There were three groups of participants: Group 1 consisted of only diabetic patients (DM group, n = 16), Group 2 consisted of only hypertensive patients (HT group, n = 8), and Group 3 consisted of patients having both DM and HT (DM + HT group, n = 16). Out of 40 patients, 26 (65%) were male patients, and 14 (35%) were female patients (Fig. 4).

46% of males had only DM, 15% had only HT, and 38% had both DM and HT. Females had a more even spread: 28% were diabetic, 28% — hypertensive, and 43% had DM and HT (Fig. 5).

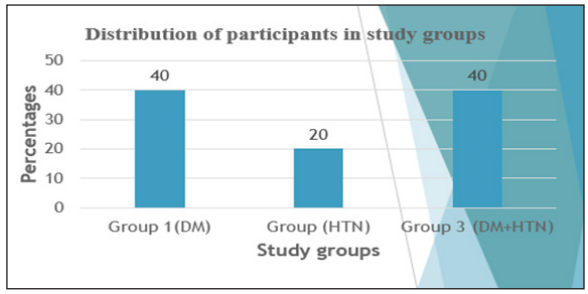

FIGURE 4. Distribution of participants in the groups

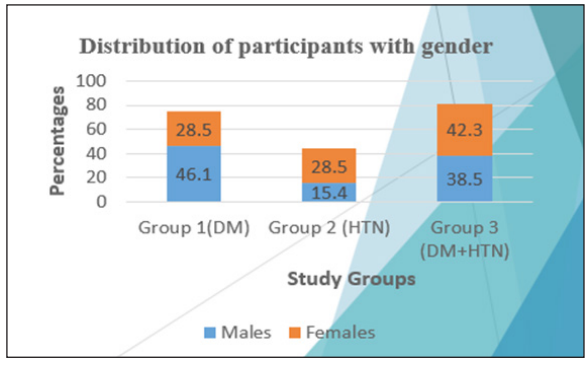

FIGURE 5. Sex distribution in the studied groups

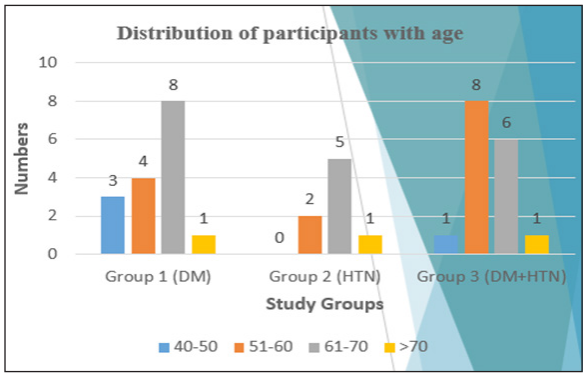

FIGURE 6. Age distribution in the studied groups

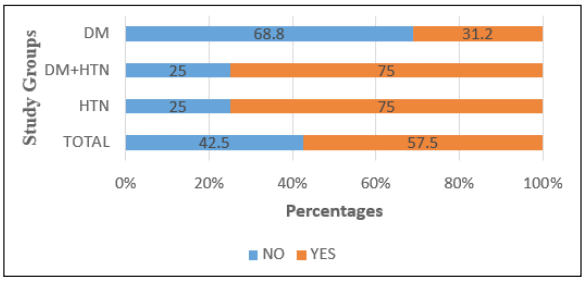

FIGURE 7. Distribution of retinopathy in the studied groups. No — patients without retinopathy. Yes — patients with retinopathy

Group 1 consisted of 8 patients in the age 61–70. In group 2 where 5 patients in the age of 61–70 and 2 patients in the age of 51–60. Group 3 consisted of 8 patients in the age of 51–60 and 6 patients in the age of 61–70 (Fig. 6).

68.8% of patients with DM had DR features, while 31% did not show any DR features. In Group 2 (DM + HTN) 75% of patients did not have diabetic/hypertensive retinopathy features. The same data is shown in Group 3 where patients only had hypertension. In total, 57% of patients in our study showed associated diabetic/hypertensive retinopathy features, while 42% did not show diabetic/hypertensive retinopathy features (Fig. 7).

The mean value of the pulsatility index (PI) was 1.23 in patients with DM, 1.30 — in patients with HTN, and 1.33 — in patients with DM + HTN. The mean PSV in Group 1 was 26.25, in Group 2 — 28.83, and 26.98 in Group 3. The mean EDV in Group 1 was 8.49, in Group 2 — 8.67, and in Group 3 — 7.85. The resistivity index (RI) values were 0.68 in Group 1, 0.71 — in Group 2, and 0.71 in Group 3 (Tab. 1).

The mean values of PI in Group 1 were 1.16, in Group 2 — 1.08, and in Group 3 — 1.23. Mean values of RI were 0.67 in Group 1, 0.67 in Group 2, and 0.68 in Group 3. Mean values in PSV were

Table 1. Comparison of the ophthalmic artery parameters among the groups using ANOVA

OA	Groups	N	Minimum	Maximum	Mean
PI (1.45-1.55)	DM	16	0.71	1.81	1.23 (↓)
	HTN	8	1.13	2.05	1.30 (↓)
	DM+HTN	16	0.72	2.08	1.33 (↓)
RI (0.6) {0.1}	DM	16	0.49	0.85	0.68(↑)
	HTN	8	0.55	0.78	0.71(↑)
	DM+HTN	16	0.51	0.89	0.71(↑)
PSV (37.5) {7.1}	DM	16	15.50	41.40	26.25 (↓)
	HTN	8	21.30	45.80	28.83 (↓)
	DM+HTN	16	17.00	45.60	26.98 (↓)
EDV (9) {2.1}	DM	16	2.90	17.60	8.49 (↓)
	HTN	8	4.80	15.20	8.67 (↓)
	DM+HTN	16	4.10	14.00	7.85 (↓)
TA Max	DM	16	7.00	25.80	16.62
	HTN	8	9.90	26.90	17.19
	DM+HTN	16	10.00	26.70	15.63
S/D (8.6) {3.8}	DM	16	1.97	6.48	3.56 (↓)
	HTN	8	3.01	6.10	3.80 (↓)
	DM+HTN	16	2.01	9.50	4.07 (↓)

PI — pulsatile index; RI — resistivity index; PSV — peak systolic velocity; EDV — end diastolic velocity; DM — diabetes mellitus; HTN — hypertension

Table 2. Comparison of the central retinal artery (CRA) and central retinal vein (CRV) parameters among the groups using ANOVA

CRA	Groups	N	Minimum	Maximum	Mean
PI (1.45-1.55)	DM	16	0.59	1.56	1.16 (↓)
	HTN	8	0.81	1.45	1.08 (↓)
	DM+HTN	16	0.82	1.93	1.23 (↓)
RI (0.6) {0.1}	DM	16	0.43	0.84	0.67 (↑)
	HTN	8	0.53	0.84	0.67 (↑)
	DM+HTN	16	0.42	0.86	0.68 (↑)
PSV (37.5) {7.1}	DM	16	7.10	20.80	14.90 (↓)
	HTN	8	10.20	17.00	16.30 (↓)
	DM+HTN	16	7.40	26.70	15.45(↓)
EDV (9.00) {2.1}	DM	16	1.30	7.10	4.46 (↓)
	HTN	8	2.40	7.90	4.60 (↓)
	DM+HTN	16	2.20	7.30	4.49 (↓)
TA Max	DM	16	3.90	13.20	8.84
	HTN	8	5.30	12.60	9.70
	DM+HTN	16	4.30	14.60	8.77
S/D (8.6) {1.5}	DM	16	1.77	6.00	3.27 (↓)
	HTN	8	2.14	4.21	3.14 (↓)
	DM+HTN	16	1.74	7.35	3.55 (↓)

PI — pulsatile index; RI — resistivity index; PSV — peak systolic velocity; EDV — end diastolic velocity; DM — diabetes mellitus; HTN — hypertension

14.90 in Group 1, 16.30 — in Group 2, and 15.45 in Group 3. Mean values in EDV were 4.46 in Group 1, 4.60 in Group 2, and 4.49 in Group 3 (Tab. 2).

Comparison of ophthalmic artery blood flow velocities in patients with and without retinopathy regarding the studied groups is presented in Table 3.

The comparison of the central retinal artery (CRA) and central retinal vein (CRV) blood flow velocities in patients with and without retinopathy regarding the studied groups was shown in Table 4.

DISCUSSION

Our study shows a clear deviation of blood parameters from normal values in all three groups in both OA and CRA. PSV and EDV values in OA and CRA/CRV were reduced in patients with DM, HTN, and DM + HTN compared to normal patients. RI findings in all three groups showed increased values compared to the normal range. Khandelwal et al. (2020) studied 46 subjects and reported that in OA of DM patients, regardless of the presence or absence of DR, EDV (4.67 ± 1.88) was significantly reduced, and RI (8.49 ± 2.26) was significantly increased than normal, which is similar to our study. Results suggest that it has the potential to provide valuable information related to altered OBF even before the appearance of DR. This also means CDI may have prognostic value in identifying those at risk of developing sightthreatening proliferative diabetes retinopathy (PDR) [1]. A study conducted by Itay Ben Zion et al. in 2007 showed that OBF is associated with systolic and pulsatile components of blood flow velocities in both OA and CRA, suggesting that OBF determinants are influenced by pulsatile components of both choroidal and retinal perfusion, which is similar to observations in our study [6].

A study conducted by Yuksel Sullu et al. in 2005 suggested that blood flow velocities of the OA and CRA were decreased, but RI was increased significantly in PDR patients, which is similar to our results [7]. A study by Mehdi Karami et al. in 2012 proved that the resistivity index in OA and CRA were higher in patients with DR than in healthy individuals, indicating disturbances of retinal and choroidal circulation in patients with DR, which is similar to our study observations [8].

In a study conducted by Berthold Pemp et al. in 2008, the authors proved there is an initial increase in retinal blood flow in the early stages of DM be-

Table 3. Comparison of ophthalmic artery blood flow velocities in patients with and without retinopathy regarding the studied groups

	Normal values	Patients with retinopathy	Patients without retinopathy
Group 1 (n = 16)		n = 5	n = 11
PSV	37.5	27.71	25.6
EDV	9	8.35	8.15
RI	0.6	0.69	0.67
Group 2 (n = 8)		n = 6	n = 2
PSV	37.5	28.78	28.95
EDV	9	8.24	7.97
RI	0.6	0.73	0.63
Group 3 (n = 16)		n = 12	n = 4
PSV	37.5	27.22	26.25
EDV	9	7.50	6.89
RI	0.6	0.73	0.67
Total (n = 40)		n = 23	n = 17

p-value is 0.0232 which is statistically significant as p is at < 0.05; PSV — peak systolic velocity; EDV — end diastolic velocity; RI — resistivity index

Table 4. Comparison of the central retinal artery (CRA) and central retinal vein (CRV) blood flow velocities in patients with and without retinopathy regarding the studied groups

	Normal values	Patients with retinopathy	Patients without retinopathy
Group 1 (n = 16)		n = 5	n = 11
PSV	37.5	16.86	14.01
EDV	9	4.070	4.65
RI	0.6	0.676	0.68
Group 2 (n = 8)		n = 6	n = 2
PSV	37.5	16.45	15.87
EDV	9	4.59	4.62
RI	0.6	0.67	0.65
Group 3 (n = 16)		n = 12	n = 4
PSV	37.5	18.55	14.41
EDV	9	4.91	4.34
RI	0.6	0.69	0.66
Total (n = 40)		n = 23	n = 17

PSV — peak systolic velocity; EDV — end diastolic velocity; RI — resistivity index

fore the onset of DR, with an eventual decline in retinal blood flow in the further course of the disease, which is similar to the results in our study [9]. A study conducted by Lam et al. in 2003 proved that reduction in OBF with age was significant and the most influential factor affecting OBF. PSV in OA also decreased with age [10].

Geyer et al. in 1999 identified the initial decrease in pulsatile OBF with the onset of DM where no DR has occurred. However, as the disease progresses, OBF increases with the severity of DR [11]. A study done by K Divya et al. in 2020 proves that significant changes in RI and flow velocities were observed in retrobulbar vessels, especially in OA in DM, compared to healthy individuals. CDI showing results with increased resistance or decreased flow could be useful to predict individuals at higher risk for developing severe DR [12].

CONCLUSION

Although it was a study with a small sample size, our results suggest that it could provide useful information related to altered ocular blood flow

even before the appearance of retinopathy changes in the patients. This also suggests CDI may have prognostic value in identifying those at risk of developing sight-threatening retinopathy changes.

LIMITATION OF STUDY

The sample size was small.

Patients above the age of 40 with DM and HT of less than 6 months could not be included.

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Conflict of interests

No competing interests.

Financial interests

Nil.

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