**COMPARATIVE STUDY OF RETROBULBAR HEMODYNAMICS IN HYPERTENSIVES WITH RETINOPATHY AND HYPERTENSIVES WITHOUT RETINOPATHY IN IBADAN, NIGERIA**

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**Abstract**

**Background:** Essential hypertension is a multisystemic disorder that may cause retinopathy. Doppler ultrasonography of the retrobulbar arteries is an established imaging modality that detects early vascular changes in hypertensive retinopathy, thus ensuring timely institution of care and prevention of end-organ damage.

**Aim and objectives:** To compare the retrobulbar arterial flow parameters in hypertensive adults with and without retinopathy with flow parameters in normotensive subjects using Doppler ultrasonography.

**Setting:** Departments of Radiology and Ophthalmology**,** University College Hospital, Ibadan, Nigeria.

**Methodology:** This was a prospective, cross-sectional study among 120 subjects, comprising 60 hypertensives (Group 1; subgroup 1a- subjects without retinopathy (*n* = 30), and subgroup 1b-subjects with retinopathy, *n* = 30) and 60 age-sex-matched non-hypertensive subjects (Group 2), conducted at the University College Hospital, Ibadan. Demographic information and clinical data were obtained from the participants and their case files. All participants had fundoscopy, intraocular pressure measurements, and ophthalmic artery (OA), and central retinal artery (CRA) colour Doppler ultrasound. Data were analyzed using SPSS version 23.

**Results:** The PSV and EDV of the CRA in the healthy controls (10.8±2.54cm/s and 4.56 ± 1.32cm/s) were significantly higher than those of group 1a (9.04±1.93cm/s and 3.29±1.12cm/s: P=0.02 and <0.001) and Group 1b cases (5.55±1.32cm/s and 2.48±0.84cm/s: both P<0.001). Additionally, there was also significant difference in the PSV and EDV between groups 1a and 1b (both P<0.001).

Also, the PI and RI in healthy controls (0.93±0.17 and 0.57 ± 0.007) were significantly lower than those of group 1a (1.12±0.25 and 0.63±0.09: P=0.005 and P<0.001) but showed no significant difference from those of Group 1b (0.92±0.25 and 0.53±0.10;P=0.961 and P=0.106). However, the PI and RI in Group 1a were significantly higher than those in Group 1b (P=0.014 and P=<0.001, respectively).

In the Ophthalmic artery, the PSV in healthy controls (14.5±4.54cm/s) was not significantly different from that of group 1a (15.4±7.0cm/s: P=0.847) and Group 1b cases (12.0±4.71cm/s; P=0.107). However, the value in Group 1a was significantly higher than that in group 1b (P=0.045). Furthermore, the RI in healthy controls (0.63±0.08) was significantly lower than that of group 1a (0.68±0.08; P=0.015), but not different from that in 1b (0.63±0.09; P=0.998); the RI in groups 1a and 1b were not significantly different (P=0.060). No significant differences were observed, between the three groups, in the mean values for EDV (p=0.128) and PI (p=0.402) in the ophthalmic artery.

Significant positive correlations were found between PSV and EDV of CRA and duration of hypertension in group 1b (r = 0.395, P = 0.031; r = 0.445, P = 0.014, respectively) but not in 1a.However, there was no significant correlation between RI and degree of retinopathy in group 1b.

**Conclusion:** The CRA PSV and EDV were significantly higher in healthy controls than in hypertensives, and hypertensives without retinopathy had higher values than those with retinopathy. The PI and RI in healthy controls and hypertensives with retinopathy were not significantly different but both were lower than the values in hypertensives without retinopathy. In the Ophthalmic Artery there were no significant differences in EDV and PI between the three groups but PSV was significantly higher in hypertensives without retinopathy compared to those with retinopathy. Although there was no significant difference in the RI between the two groups of hypertensives, those without retinopathy had higher values than normal controls. Increased retrobulbar Doppler resistance and reduced flow velocities may be the earliest Doppler changes in hypertension without retinopathy, while reversal of these parameters may indicate longstanding hypertensive retinopathy. The positive correlation between the retrobulbar Doppler flow and the duration of disease in hypertensives with retinopathy may help to ascertain longstanding cases of hypertensive retinopathy.

 **Keywords**: Hypertension, retinopathy, central retinal artery, ophthalmic artery, ultrasonography.

**Introduction**

Hypertension is a common systemic condition that is associated with significant morbidity and mortality.1,2 It is known to act as a silent killer many years before overt end-organ damage is clinically apparent.3 The complications of hypertension account for 9.4 million deaths worldwide.2

Africa has the highest prevalence of hypertension, affecting about 46% of adults older than 25 years4, and has become a public health issue in sub-Saharan Africa.5,6 Sustained systemic hypertension causes end-organ complications such as myocardial infarction, cardiac failure, renal failure, as well as retinopathy.7,8

Hypertension is a multisystem disease, and in the eye, it is associated with pathological changes in the vessels in the retina. 9, 10 Hypertensive retinopathy, the spectrum of vascular changes that occur in the retina in hypertensive individuals9,10,are sequelae of longstanding hypertension. Previous studies show strong, graded, and consistent association of hypertensive retinopathy with blood pressure9-15, and a link between hypertensive retinopathy and risk of cardiovascular events.16,17

Besides, population studies also validate that change in retinal vessel caliber is related to hypertension, left ventricular hypertrophy (LVH), stroke, and myocardial infarction.18-21

The underlying pathology in systemic hypertension is the series of pathophysiological changes that occur in response to high blood pressure.22 Primarily, there is retinal arteriolar vasoconstriction, followed by disruption of the blood-retinal barrier, increased vascular permeability, and secondary arteriosclerosis in sustained hypertension. On fundoscopy, features commonly described in hypertensive retinopathy include focal and generalized arteriolar narrowing, microaneurysms, intraretinal hemorrhages, cotton-wool spots, hard exudates, and optic disc swelling. As well as changes of secondary arteriosclerosis, which include arteriovenous nipping, arteriolar sheathing as well as occlusion.22

Ultrasonography is now an established imaging technique for the evaluation of ocular changes associated with hypertension. Doppler (color and pulsed wave Doppler) ultrasonography provides both quantitative and qualitative evaluation of the Peak Systolic Velocity (PSV), End Diastolic Velocity (EDV), Pulsatility Index (PI) and Resistive Index (RI).23,24 There is scientific evidence that ocular Doppler changes are more reliable than traditional fundoscopy in the evaluation of hypertension-induced retinal damage, and the assessment of cardiovascular risk.25

Although there are several Doppler studies on the central retinal and ophthalmic artery in other parts of the world, there is a paucity of literature on ocular Doppler changes in hypertensive individuals, despite the high prevalence of hypertension in our environment.

**Patients and Methods**

**Study design and study site**

This study was a prospective, cross-sectional comparative study. The study site was the Department of Radiology, University College Hospital (UCH), a tertiary hospital with 850-bed spaces located in Ibadan, Oyo State, South-Western Nigeria. The Radiology Department provides services to in-patients and outpatients from General and Specialist Outpatient Clinics.

**Study population and duration**

Approval from the Ethical Review Committee of the University College Hospital/the University of Ibadan was obtained for this study. Sixty hypertension cases: 30 cases with retinopathy and 30 cases without retinopathy enrolled from the outpatient Cardiology Clinic of UCH, according to the selection criteria. Consecutive participants were enrolled until the sample size was reached. Similarly, sixty (60) age and sex-matched control subjects (men and women) without hypertension were enrolled from healthy adult volunteers from the general outpatients' department of the hospital who met the inclusion criteria and without past or present history or clinical evidence of cardiovascular diseases were selected by systematic sampling.

All participants had Ophthalmic and central retinal artery Doppler velocimetry. The study spanned a period of six (6) months from August 2017 to January 2018.

**Sample size calculation**

The sample size was estimated using the formula for comparison of means between two groups.26

n = 2σ2 (Zα + Zβ) 2. where n is the minimum sample size for each group,

σ is the standard deviation of the resistivity index (RI) of the ophthalmic artery in hypertensive patients without retinopathy = 0.0827,

Zα is the desired level of statistical significance (5%) =1.96.

Zβ is the desired power (90%) = 1.28

 - 2 is theexpected minimum difference between the two groups= 0.05 for RI 27.

n = 2 X 0.082 (1.96 + 1.28)2 ÷ 0.052 = 54.

Considering that there might be non-responders, 10% was added to make the sample size of sixty (60) participants for each of the two groups. A total of one hundred and twenty (120) participants - 60 hypertensive patients and 60 controls- were recruited for this study.

**Inclusion criteria**

Adults over 18 years with hypertension were included in the study group. Controls were healthy normotensive (BP <130/90mmHg), normoglycemic subjects having normal lipid profile, and body mass index.

**Exclusion criteria**

Subjects with co-morbidities such as diabetes mellitus (defined as Fasting Blood Sugar, FBS ≥ 7.0 mmol/l or 126mg/dl), heart failure, atrial fibrillation, renal failure, Sickle Cell Disease (SCD), vascular disorders, glaucoma, or other medical disorders. Also excluded were cases of previous intraocular surgeryand non-consenting subjects. Healthy subjects with a history of or on medication for cardiovascular disease, or deranged lipid profile were excluded from this study.

**Clinical evaluation**

Adult patients who met the inclusion criteria and had signed the informed consent form participated in this study. Information regarding risk factors was obtained from history and examination of the subjects and documented into personal data forms.

Physical examination included documentation of pulse characteristics (rate, volume, variability) and blood pressure measurement using a mercury sphygmomanometer (Acoson mercury sphygmomanometer, manufactured by Accoson, Model- Dekamet desk, Country- England). We evaluated the blood pressure (BP) while the subject was at rest in a sitting position and the arm supported on a level surface. The cuff was placed around the upper arm and secured. The bell of the stethoscope was placed over the brachial artery in the cubital fossa to listen to pulse sound. The cuff was inflated slowly until the pulse disappeared and then slowly deflated. Readings were based on Korotkoff first (the blood pressure reading when the pulse reappeared) and the fifth phase (the reading when the pulse disappeared) sounds, which correspond to the systolic BP and diastolic BP, respectively. In this study, hypertension was systolic blood pressure greater than or equal to 140 mmHg and diastolic blood pressure greater than or equal to 90mmHg or the use of antihypertensive medications by the patients.

Height was measured in meters (m) using a Stadiometer. At the same time, the weight was measured in kilograms (kg) using the Seca weighing scale, model number 755 1321994, and manufactured in 2010 by Seca GmbH & Co. Kg. in Hamburg, Germany, which was zero corrected.

All subjects had ocular examinations performed by an experienced ophthalmologist (OAO). Parameters such as intraocular pressures, presence or absence of retinopathy, the grade of retinopathy, if present, and the cup-to-disc ratio in each eye documented.

**Laboratory evaluation**

A drop of capillary blood was obtained by finger prick with a sterile lancet after cleaning with a methylated spirit swab and placed on a disposable test strip using Accu-check Active glucometer, serial number GU 21660419, manufactured by Roche in Mannheim, Germany. It was read in mg/dl to document Fasting blood glucose.Participants with normal fasting glucose and without evidence of hyperlipidemia, as documented in the case files, were recruited into the study. Also for controls, the lipid levels in their case notes were taken into account where available and those with hyperlipidemia or on medication for dyslipidemia were excluded.

**Ultrasound evaluation**

Ocular Color and Pulsed Wave Doppler ultrasound examination of the central retinal and ophthalmic arteries was done on all the participants using 5-14 MHz linear transducer of Sonic Touch ultrasound machine, serial number SXTCH2.0-1008.0682; manufactured in 2009 by Ultrasonix Medical Corporation in Richmond, BC, Canada.

All patients were examined in the supine position following the technique described by Schmetterer et al.28. With both eyes closed, a modest amount of standard water-soluble coupling gel was applied to the closed eyelids to provide adequate contact between the transducer and the skin and thus facilitate the transmission of the sound wave to the globe. Excessive compression of the eyelid with the transducer was avoided in order to avoid putting mechanical force on the globe, which could increase intraocular pressure 28. Both globes were scanned in orthogonal (sagittal and transverse) planes while the participants directed the eyes straight ahead with the eyelids closed but without squeezing them. A single examiner performed the color Doppler imaging to identify the central retinal and the ophthalmic arteries after the exclusion of orbital pathologies, such as orbital tumours, uveitis, and drusen,by the B-mode scan. The ophthalmic artery was identified at approximately 15mm from the posterior margin of the globe with a colour Doppler ultrasound to localize the artery. The sample volume box was centered on the vessel, with the angle set parallel to the vessel to account for the Doppler angle28. The CRA and OA also were assessed with the optic nerve taken as a reference. Blood flow velocities in the CRA were measured within the optic nerve head shadow 3-5 mm behind the posterior margin of the globe.

In order to ensure reproducibility, the Doppler wall filter was at 50Hz, and the pulse repetitive frequency for the CRA and OA set at 2.5 kHz and 3.3 kHz, respectively, and the Doppler sample volume adjusted to 2mm.

The value of PSV, EDV, RI, and PI from three (3) consecutive spectral waveforms of the assessed vessels were measured for every participant, and the average of 3 readings recorded. Each participant had both eyes examined, and the mean values of the two were calculated and documented in the datasheet. The average duration of the ultrasound procedure was about twenty (20) minutes.

**Data management and analysis**

The sociodemographic, anthropometric, clinical information from the patient's case files, ophthalmological as well as retrobulbar Doppler data collected were documented in a datasheet. The data was entered and analyzed using Statistical Package for Social Sciences (SPSS Inc. Chicago, IL USA), version 23.

The Doppler parameters (PSV, EDV, PI, and RI), as well as the sociodemographic characteristics of the population, were described using means and standard deviations, proportions, frequencies, and charts.

Student's t-test was used to compare the mean ages of hypertensive and control subjects. Chi-square test was used to compare the sociodemographic characteristics between hypertensive and control subjects. Analysis of variance was used to compare anthropometric, laboratory, and clinical characteristics between hypertensive subjects with retinopathy, those without retinopathy and controls, as well as compare the retrobulbar arterial blood flow Doppler indices between the study groups. Where the ANOVA revealed significant differences, post-hoc analyses (Sidak post hoc test, or Games Howell post hoc test were used as appropriate) were performed to determine where the difference(s) lay, especially with the Doppler blood flow parameters.

Correlation between the duration of hypertension and Doppler parameters, as well as between Doppler parameters and grades of hypertensive retinopathy, were determined through Spearman's rank test. Statistical significance was set at p<0.05.

**Results**

**Sociodemographic, Anthropometric, Laboratory and Clinical Characteristics**

The mean age of the hypertensive subjects, 51.0 ± 9.5 years, (range 29-70 years) was not significantly different from the mean age of the controls, 50.3 ± 9.8 years (range 27-70) (p= 0.671). As expected, there was no significant difference in the sex ratios between the hypertensives and normotensives; however, there were more females, 68 (56.7%), than males 52 (43.3%) in the whole group. The hypertensives had significantly higher levels of education than the normotensives. There were no significant differences in ethnicity or occupations between the two groups. (Table 1)

The systolic blood pressure (SBP) of the participants was 118.6 ± 9.74 mmHg, 135.7±20.3mmHg, and 191.1±25.3 mmHg in the controls, hypertensive subjects without retinopathy (Group 1a), and hypertensive subjects with retinopathy (Group 1b) respectively (P<0.001).

There was also a significant difference in the mean diastolic blood pressure (DBP) of the controls (73.6 ± 8.10 mmHg), group 1a (79.1 ± 12.6 mmHg), and 1b cases (117.8 ± 16.0 mmHg) (P < 0.001) [Table 2].

 Majority of the participants with hypertension, group 1a, 17 (56.7%) and 1b, 19 (63.3%) had been diagnosed with hypertension from 1 to 4 years. There was no significant difference in the median duration of hypertension since diagnosis between patients in group 1a (median = 2 years, interquartile range = [1.0; 4.25] years) and patients in group 1b (median = 1.5 years, interquartile range = [1.0; 3.0] years), p= 0.278 (Table 3).

**Ocular examination findings**

The mean intraocular pressure (IOP) was 15.1 ±2.44mmHg and 15.0 ± 2.42mmHg in the right and left eyes in the controls. The mean IOP was 14.9 ± 2.74mmHg and 14.9 ± 2.58mmHg in the right and left eyes respectively in Group 1a and 14.8 ± 3.14mmHg and 14.9 ± 2.88mmHg in the right and left eyes in group 1b cases. There was no significant difference in the IOP in the right and left eyes between the three groups (P>0.05). The mean cup to disc ratios were not different between the three groups: it was 0.27±0.09 in the controls, 0.29±0.09 in group1a, and 0.29±0.11 in group 1b subjects (p=0.48).

**Doppler sonographic parameters of the study population**

**Central retinal artery**

The mean PSV of Central retinal artery (CRA) among controls, group 1a, and group 1b subjects was 10.8 ± 2.54cm/s, 9.04 ± 1.93cm/s, and 5.55 ± 1.32cm/s respectively. The differences in the average PSV of CRA among the three groups were statistically significant (P < 0.001); post-hoc analyses showed that the value for the controls was significantly higher than those for group 1a (P=0.002) and group 1b (p<0.001), while that for group 1a was significantly higher than that for group 1b (p<0.001).

The differences in the mean EDV of CRA among controls, group 1a and group 1b, 4.56 ± 1.32cm/s, 3.29 ± 1.12cm/s and 2.48 ± 0.84cm/s respectively were statistically significant (P<0.001). Post-hoc analyses revealed that the mean for the controls was significantly higher than those for Group 1a (p<0.001) and group 1b (p<0.001), while that for group 1a was significantly higher than that for 1b (p=0.022).

Concerning CRA PI the mean values, 0.93 ± 0.17 for controls, 1.12 ± 0.29 for group 1a and 0.92±0.25 for group 1b were significantly different (P =0.005). Post-hoc analyses indicated that the mean PI for group 1a was significantly higher than those for group 1b (p=0.014) and the controls (p=0.005); there was however no significant difference in the means for group 1b and controls (p= 0.961)

The mean CRA RI among controls, group 1a and group 1b, 0.57±0.07, 0.63±0.09 and 0.53±0.10 respectively, were significantly different (P < 0.001) as shown in Table 3. On post-hoc analyses the mean for group 1a was significantly higher than the means for group 1b (p<0.001) and the controls (p= 0.002); there was no significant difference between the mean values for group 1b and the controls, p=0.106 (Table 4).

**Ophthalmic artery Doppler**

The mean ophthalmic artery PSV were 14.5±4.54cm/s, 15.4±7.0cm/s and 12.0±4.71cm/s in controls, group 1a and 1b respectively (p= 0.037). There was no significant difference, on post-hoc analyses, between the means of group 1a and controls (p= 0.847) or between group 1b and controls (p=0.107); the mean of group 1a was however significantly higher than that of group 1b (p= 0.045).

No significant differences were observed, between the three groups, in the mean values for EDV (p=0.128) and PI (p=0.402) for the ophthalmic artery.

The mean OA RI was 0.63±0.08 for controls, 0.68±0.08 for group 1a and 0.63±0.09 for group 1b (P= 0.014). On post-hoc analyses, there was no significant difference between group 1a and 1b (p= 0.060) or between group 1b and controls (p=0.998); the mean for group 1a was significantly higher than that for controls, p=0.015 (Table 4).

There was no significant correlation between the duration of hypertension and retrobulbar arterial flow Doppler velocimetry indices in group 1a. In contrast, the central retinal artery PSV (r = 0.395, p = 0.031) and EDV (r = 0.445, p = 0.014) had statistically significant positive correlations with duration of hypertension among group 1b cases. Furthermore, there was no significant correlation between duration of hypertension and PI or RI of the central retinal artery, and neither was there any correlation with ophthalmic artery Doppler indices in group 1b patients (Table 5).

Out of the 30 hypertensive patients with retinopathy, 17 (56.7%) had grade one retinopathy, 10 (33.3%) grade 2, while 3 (10%) had grade 3 retinopathy. There was a statistically significant negative correlation between retinopathy grades and the central retina artery PSV (r = - 0.309, P = 0.040) and EDV (r = - 0.483, P = 0.002), indicating that the CRA PSV and EDV decrease as retinopathy worsens. However, there was no significant correlation between the grade of retinopathy and PI or RI of the central retinal artery, and neither was there any correlation with ophthalmic artery Doppler indices. (Table 6).

**Discussion**

Reduction in retrobulbar arterial blood flow velocities (PSV and EDV) are documented complications of systemic hypertension that have been attributed to increased resistance (typified by the RI and PI) and reduced posterior circulation 27-29.

The observed differences in systolic and diastolic BP between hypertensive subjects with retinopathy and those without were similar to the findings of higher systolic and diastolic B.P. among the hypertensive subjects with retinopathy studied by Akal et al. 27.

However, there is paucity of literature regarding retrobulbar Doppler blood flow studies in hypertensive patients with or without retinopathy, with the commonly cited study in this regard being the one by Akal et al.27.

Most of the literature on retrobulbar Doppler in retinopathy patients is from studies in diabetics with or without retinopathy30,31,32. However most of the authors agreed that the retrobulbar hemodynamics are not yet fully understood.

Meng et al.31, in a metanalytical study of retrobulbar blood vessels hemodynamic changes, using colour Doppler imaging, in diabetic patients without or with retinopathy, showed that compared to controls, in eyes without retinopathy, the PSV and EDV were lower in the CRA, but in the OA, the PSV, and the RI were higher. In eyes with retinopathy compared to controls, the PSV, EDV were reduced in CRA, and the EDV reduced in the OA, while the RI was increased in the OA. Also, the ophthalmic artery PSV was lower in eyes with retinopathy than eyes without, and the central retinal artery PSV and EDV were significantly decreased in eyes with retinopathy compared to eyes without.

The findings in our study, of reduced PSV and EDV with higher RI and PI in the CRA, increased RI in OA in hypertensives without retinopathy, and also decreased PSV and EDV in CRA in hypertensives with retinopathy, compared to controls showed some agreement with the pattern reported by Meng et al.31, howbeit, in diabetic retinopathy cases. Furthermore, their report of significantly decreased PSV and EDV in the central retinal artery in eyes without retinopathy was suggested to be due to underlying ischemia and insufficient perfusion in the central retinal artery present before the onset of the clinical features of diabetic retinopathy. We believe this may be also true in this present study. Our observation of increased RI and PI in in the CRA among group 1a cases is in agreement with the report of Reddy in young hypertensives in the year 2019 33. This we propose may be due to the established vasospasm or peripheral vascular resistance and reduced blood flow, in the literature, in hypertensives 30,33.

In contrast, among the hypertensives with retinopathy in our study compared to controls, we also observed reduction in PSV, and no significant differences in PI and RI in the CRA, and no significant differences in ophthalmic artery PSV, EDV, RI and PI.

Another study by Kerami et al. 32 in diabetic retinopathy also reported that the OA's PI and RI were higher in retinopathy patients, while the OA PSV and EDV as well as CRA Doppler parameters were not significantly different from the normal group.

Dimitrova et al.34 in a follow-up study on the assessment of the ocular blood haemodynamics in diabetic patients over a 21-month duration reported no significant change in Doppler parameters in the CRA and the posterior ciliary artery in retinopathy cases.

However, a 10-year follow-up study on retrobulbar blood flow changes in eyes with diabetic retinopathy by Neudorfer et al35 gave a different insight into the retrobulbar blood flow changes in retinopathy cases. They suggested from their findings that the initial increase of the resistance in the retrobulbar vessels, as part of the retinopathy changes, can lessen over time and may even be reversed, which they noted was contrary to the general belief that the RI increases as part of the deterioration that takes place during the disease process 35.

We believe that similar vascular pathophysiological pathway through atherosclerosis, which with time leads to obstruction to flow, compromised perfusion, and tissue ischemia36, also leads to vascular changes in hypertensive retinopathy. So that the reported initial blood flow reduction and resistance increase, with progression to no vascular flow differences between cases of retinopathy and controls to eventual increase in blood flow with reduction in resistance parameters over a long time in diabetic retinopathy patients35, possibly occur in hypertension with retinopathy, thereby responsible for our observations in this study.

Comparing the hypertensives without retinopathy and those with retinopathy in our study, our observation of decreased PI and RI of the CRA and reduced PSV of OA in retinopathy group while the EDV, PI and RI showed no difference from that of the group without retinopathy, partly agrees with the study of Akal et al.27, which showed no statistical difference in the RI of both CRA and OA between the hypertensives with and those without retinopathy 27.We believe, this may be due to similar phenomenon where the duration of the retinopathy had an effect on the retrobulbar parameters 32.

The Ophthalmic artery supply the orbital contents via the retinal artery and the ciliary branches. The ciliary circulation, compared to the central retinal artery, is a low vascular resistance bed which receives about 90% of the orbital blood flow and supplies the choroid layer of the eye30,37. Our observation of very little differences in PI and RI in the ophthalmic artery between the 3 groups compared to that of the CRA might be due to the anatomical and structural differences between these vessels.

Another proposed reason may be because the CRA directly supplies the retinal layer, it better reflects the circulatory changes in the retina, in line with the report that the CRA is more sensitive in the detection of haemodynamic changes in diabetic retinopathy cases 31.

Although there is paucity of data on IOP in hypertensives with/without retinopathy, it has been suggested that IOP may have an impact on retinal blood flow and velocity due to the retinal vasculature having a direct contact with the intraocular pressure (IOP) 38. In our study, there are no significant differences in the intraocular pressures and cup to disc ratios of both eyes among hypertensive subjects with or without retinopathy and their controls.

Furthermore, the positive correlation between the duration of hypertension and retrobulbar Doppler flow velocities (PSV and EDV) in the CRA but not with RI or PI in hypertensives with retinopathy may suggest that the blood flow velocities increase with the duration of hypertensive retinopathy, in accordance with the report of Neudorfer et al.35 However, Reddy reported a positive correlation between RI and duration of hypertension in a colour Doppler study of orbital vessels in young adult hypertensiveIndians aged 19 to 39 years33. Akal et al also reported a positive correlation between duration of hypertension and RI among a geriatric population in India.27 The differences in the study population may be responsible for this observation. Another possibility is that this finding may be related to adequacy of drug control of hypertension, which was beyond the scope of this study.

A previous study by Goebel et al39, reported a decrease in the mean value of PSV and EDV in the CRA with increased severity of diabetic retinopathy and suggested an inverse correlation between flow velocity in the CRA and the progression of diabetic retinopathy. In agreement, this current study, although in hypertensives with or without retinopathy, also showed that as hypertensive retinopathy grade increased, the CRA blood flow velocities also decreased.

Further studies to validate the observations of this study as regards duration of hypertensive retinopathy and retrobulbar Doppler hemodynamics is suggested.

**Conclusion**

Compared to controls, the retrobulbar blood flow resistance indices increased in hypertensives without retinopathy but not in those with retinopathy.

Increased retrobulbar Doppler resistance and reduced flow velocities may be the earliest Doppler changes in hypertension without retinopathy, while reversal of these parameters may indicate longstanding hypertensive retinopathy. The positive correlation between the retrobulbar Doppler flow and the duration of disease in hypertensives with retinopathy may help to ascertain longstanding cases of hypertensive retinopathy.

**Limitations of the study**

The study did not discriminate between patients already on antihypertensive medications and those who were yet to commence therapy. Inadvertent application of great pressure by the transducer could lead to a decrease in CRA flow36, and this was carefully avoided as much as possible during the Dopplerscan.

**Recommendation**

Colour Doppler imaging of the retrobulbar arteries should be part of the ophthalmologic workup on hypertensive adults. We suggest further studies to assess the effect of antihypertensive therapy on retrobulbar hemodynamics and the progression of retinopathy**.**

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**Table 1:** **Sociodemographic characteristics of the study subjects**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Hypertensives (%)** | **Controls (%)** | **P -value** |
| Age, Mean±SD (years) | 51.0 ± 9.5 | 50.3 ± 9.8 | 0.671**#** |
| Gender Male  Female | 26 (43.3)34 (56.7) | 26 (43.3)34 (56.7) | 1.000 |
| Educational Status None Primary Secondary Tertiary  | 1 (1.7)5 (8.3)11 (18.3)43 (71.7) | 3 (5.0)15 (25.0)14 (23.3)28 (46.7) | 0.016**\*** |
| Occupation Unemployed Employee Self-employed Retired  | 5 (8.3)31 (51.7)19 (31.7)5 (8.3) | 2 (3.4)21 (35.0)32 (53.3)5 (8.3) | 0.085 |
| Ethnicity Yoruba Others | 53 (88.3)7 (11.7) | 58 (96.7)2 (3.3) | 0.163 |
| Cigarette smoking No Yes  | 57 (95.0) 3 (5.0) | 59 (98.3)1 (1.7) | 0.619**\*** |

*#student independent t-test; \* Fisher's exact test (X2)*

**Table 2:** **Anthropometric, laboratory and clinical characteristics of the study subjects**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **VARIABLE** | **Hypertensive Subjects** | **Control****(Group 2)** | **P-value** | **Post hoc Test**  |
| **Group 1a** | **Group 1b** |
| Mean ± SD | Mean ± SD | Mean ± SD |  |  |
| Age (years) | 51.2 ± 9.3 | 50.8 ± 9.9 | 50.3 ± 9.8 | 0.906 |  |
| Body weight (Kg) | 69.5 ± 11.9 | 77.3 ± 17.0 | 72.4 ± 12.5 | 0.131 |  |
| Height (m) | 1.63 ± 0.07 | 1.67 ± 0.08 | 1.61 ± 0.09 | 0.012 | 1b > 2 |
| Body mass Index (Kg/m2) | 26.1± 4.10 | 28.0± 6.67 | 27.9± 4.87 | 0.161 |  |
| Systolic blood pressure (mmHg) | 135.7 ± 20.3 | 191.1 ± 25.3 | 118.6 ± 9.74 | <0.001 | 1b > 1a > 2  |
| Diastolic blood pressure (mmHg)  | 79.1± 12.6 | 117.8 ± 16.0 | 73.6 ± 8.10 | <0.001 | 1b > 1a & 2 |
| Fasting blood glucose (mg/dl) | 87.3 ± 9.2 | 89.4 ± 11.1 | 85.7 ± 15.8 | 0.449 |  |

*Group 1a - hypertensives without retinopathy; Group 1b- hypertensives with retinopathy.*

**Table 3: Duration of disease in hypertensives with or without retinopathy**

|  |  |  |
| --- | --- | --- |
| Duration of Hypertension  |  Hypertensive Subjects | P-value |
| Group 1a | Group 1b |
| < 1 year | 6 (20.0) | 6 (20.0) |  |
| 1 to 4 years | 17 (56.7) | 19 (63.3) | 0.801 |
| ≥ 5 years  | 7 (23.3) | 5 (16.7) |  |

*Group 1a - hypertensives without retinopathy; Group 1b- hypertensives with retinopathy.*

**Table 4: Comparison of retrobulbar arterial blood flow Doppler Indices between the three groups**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **Hypertensive Subjects** | **Control** **(Group 2)** | **P- value** | **Post hoc Test** |
| **Group 1a** | **Group 1b** |
| **Mean ± SD** | **Mean ± SD** | **Mean ± SD** |  |  |
| **CRA**  |
| PSV (cm/s) | 9.04 ± 1.93 | 5.55 ± 1.32 | 10.8 ± 2.54 | <0.001 | 2 > 1a > 1b |
| EDV (cm/s) | 3.29 ± 1.12 | 2.48 ± 0.84 | 4.56 ± 1.32 | <0.001 | 2 > 1a > 1b |
| PI | 1.12 ± 0.29 | 0.92 ± 0.25 | 0.93 ± 0.17 | 0.005 | 1a > 1b & 2  |
| RI | 0.63 ± 0.09 | 0.53 ± 0.10 | 0.57 ± 0.07 | <0.001 | 1a > 1b & 2  |
| **OA**  |
| PSV (cm/s) | 15.4 ± 7.0 | 12.0 ± 4.71 | 14.5 ± 4.54 | 0.037 | 1a > 1b  |
| EDV (cm/s) | 4.71 ± 2.00 | 4.37 ± 1.97 | 5.20 ± 1.77 | 0.128 |  |
| PI | 1.26 ± 0.35 | 1.16 ± 0.37 | 1.16 ± 0.34 | 0.402 |  |
| RI | 0.68 ± 0.08 | 0.63 ± 0.09 | 0.63 ± 0.08 | 0.014 | 1a > 2  |

*Group 1a - hypertensives without retinopathy; Group 1b- hypertensives with retinopathy; CRA= Central Retinal Artery; PSV= Peak systolic Velocity; EDV= End Diastolic Velocity; PI= Pulsatility Index; RI= Resistivity Index; OA= Ophthalmic artery.*

**Table 5:** **Correlation between duration of hypertension and retrobulbar arterial flow Doppler Indices**

|  |  |  |
| --- | --- | --- |
| **Variable** | **Hypertension without retinopathy** | **Hypertension with retinopathy** |
| **Correlation coefficient (r)** | **P-value** | **Correlation coefficient (r)** | **P-value** |
| **CRA**  |  |
| PSV (cm/s) | -0.076 | 0.691 | 0.395 | 0.031 |
| EDV (cm/s) | -0.087 | 0.648 | 0.445 | 0.014 |
| PI | -0.128 | 0.502 | -0.076 | 0.690 |
| RI | -0.082 | 0.666 | -0.147 | 0.438 |
| **OA**  |  |
| PSV (cm/s) | 0.006 | 0.976 | -0.129 | 0.496 |
| EDV (cm/s) | 0.203 | 0.281 | -0.099 | 0.601 |
| PI | -0.208 | 0. 271 | 0.191 | 0.117 |
| RI | -0.173 | 0.359 | 0.100 | 0.601 |

**Table 6:** **Correlation between hypertensive retinopathy grades and retrobulbar arterial flow Doppler Indices**

|  |  |  |
| --- | --- | --- |
| **Variable** | **Correlation coefficient (r)** | **P-value** |
| **CRA**  |
| PSV (cm/s) | -0.309 | 0.040 |
| EDV (cm/s) | -0.483 | 0.002 |
| PI | 0.249 | 0.096 |
| RI | 0.162 | 0.281 |
| **OA**  |
| PSV (cm/s) | 0.012 | 0.935 |
| EDV (cm/s) | -0.153 | 0.309 |
| PI | 0.227 | 0.128 |
| RI | 0.218 | 0.149 |