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Original Research Article

Doppler ultrasound features of ophthalmic artery in diabetic retinopathy in a Nigerian Teaching Hospital

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ABSTRACT

Background: Diabetes mellitus is a metabolic disease characterized by elevated blood glucose level due to impaired insulin secretion, insulin action or both with diabetic retinopathy being the most common microangiopathic complication. A comparative, cross- sectional study aimed at evaluating Doppler blood flow indices in the ophthalmic artery in diabetic retinopathy and non-retinopathy patients when compared to normal controls in a Nigerian tertiary hospital.
Methods: Data were collected over 7 months (April 2017-October 2017) in Lagos University Teaching Hospital, Idi-Araba Lagos, Nigeria. Sixty-five diabetic retinopathy patients, 65 diabetic patients without retinopathy and 65 non-diabetic controls had their ophthalmic artery Doppler indices assessed for comparison.
Results: The end diastolic velocity (EDV) of the ophthalmic arteries in the diabetic patients were significantly lower than those of control group (EDV=5.84±2.59 cm/s, $p<0.001$ bilaterally). In diabetic patients with retinopathy, the end diastolic velocity of the ophthalmic arteries was significantly lower than those of diabetic patients without retinopathy (EDV=5.84±2.59 cm/s right eye, EDV=5.75±2.39 left eye, $p<0.001$ bilaterally). The resistivity index (RI) of the ophthalmic arteries was significantly higher in both diabetic patients with retinopathy and those without retinopathy compared to control group (RI=0.92±0.07 right eye, $p=0.044$ right eye, $p<0.001$ left eye) with resistivity index of diabetic retinopathy respondents significantly higher than the diabetic patients with no retinopathy.
Conclusions: The study showed that Doppler is a useful screening parameter in identifying eyes at risk of developing sight threatening proliferative disease in diabetic patients. Significant differences exist in ophthalmic artery Doppler flow indices of diabetics with retinopathy compared to the healthy controls.

Keywords: Diabetic retinopathy, Doppler ultrasound, Resistivity index, Ophthalmic artery

INTRODUCTION

Diabetes mellitus is a metabolic disease characterized by chronic hyperglycemia and disorders in the carbohydrate, lipid, and protein metabolism due to impaired insulin secretion and activity. The disease is caused by multiple factors including genetic, environmental and lifestyle factors.[1] There are two broad aetio-pathogenic categories of diabetes mellitus. Type 1 diabetes is caused by an absolute deficiency of insulin secretion. The other more prevalent category, Type 2 diabetes also called "adult-onset diabetes" is caused by a combination of resistance to insulin action and an inadequate compensatory insulin secretory response.[2]

Diabetes mellitus is an important health problem worldwide due to high urban growth rates, dietary changes, reduction in physical activity, and increasing

incidence of obesity. It is estimated that the prevalence of diabetes may triple within the next 25 years in Nigeria.[3] The prevalence of diabetes mellitus worldwide is projected to increase from 382 million in 2013 to 592 million in 2035.[3] India and other parts of Asia will have the highest number of people with diabetes by 2035, but the highest percentage increase will be in the Middle Eastern Crescent (+96%) and Sub- Saharan Africa (+109%).[3] Currently, the prevalence of diabetes mellitus in Nigeria is 3.3% with those above 80 years having the highest prevalence of 8.1%.[3] The economically active age group of Nigeria have a prevalence of 2.9%.[4]

The complications related to diabetes include acute life-threatening metabolic disturbances and chronic complications which predominantly involves both small and large blood vessels in addition to the nervous system. Macrovascular disease like coronary artery disease, peripheral artery disease and stroke or microvascular diseases like diabetic nephropathy, neuropathy and retinopathy could arise. The risk of vascular complication increases with the duration of the disease.[4]

Diabetic retinopathy generally appears after an average of 5-10 years after the diagnosis of diabetes mellitus and is the most common occular complication of diabetes.[5] Prevention of diabetic retinopathy is becoming increasingly important from a public health standpoint. There is therefore the need for more effective diagnosis and therapeutic techniques to reduce the burden of this sight threatening condition.[4]

Diabetic retinopathy is said to account for 12% of new cases of blindness in the USA and 11.9% of all blind registrations in those aged 16–64 years in the United Kingdom.[6,7] The proportion of persons with diabetes who have diabetic retinopathy varies in different populations, being 33% among adults in Mauritius.[8] Those aged 40 years and above in Latinos in Los Angeles, United States (47%), Singaporean Malays (35%), Singaporean Indians (30%), and the Handan Chinese (45%) have an increased rate of developing diabetic retinopathy.[9-12] Similarly, those aged 50 years and above in Saudi Arabia (37%) and Mexico (39%) have a higher rate of developing diabetic retinopathy.[13,14]

Some studies reported prevalence rates of 15% and 38% among clinic attending diabetics patients in Sub Saharan Africa.[15,16] Before now, diabetic retinopathy was reported to be rare in Nigerians.[17] Recent studies however have shown that the occurrence of diabetic retinopathy in Nigeria is on the increase, and that it accounts for 16.7% of all retinal diseases.[18] Ashaye et al reported a prevalence of 42.1% patients with diabetic retinopathy in a hospital in south-west Nigeria, while Kyari et al estimated that about 10% of people with diabetes aged over 40 years in Nigeria may have sight-threatening diabetic retinopathy.[3,18]

Several methods have been used to assess diabetic retinopathy, including ophthalmoscopic evaluation of the ocular fundus, examination through a slit lamp with the application of lenses and retinal photography. Other supplemental examination methods that have been employed include: fluorescein angiography and optical coherence tomography of the retina.[19] Some of these investigative techniques are invasive and not readily available in our environment but the complementary role of evaluating blood flow and physical characteristics of ocular vessels by new techniques such as Doppler imaging may help in early diagnosis and monitoring of this complication of diabetes mellitus.[19]

Colour Doppler imaging has been used in ophthalmology as a safe, non-invasive method for evaluating hemodynamic alteration in the orbital blood vessels for 20 years.[20] It allows two-dimensional structural imaging together with evaluation of blood flow in fine vessels such as ophthalmic artery. Peak systolic velocity (PSV) and end diastolic velocity (EDV) can be measured. In addition, resistivity index (RI), a measure of peripheral vascular resistance can be calculated for retrobulbar vessels.

The Doppler parameters used for characterizing flow in ophthalmic artery include the resistivity index, pulsatility index, peak systolic velocity and end diastolic velocity (RI, PI, PSV and EDV).[21] The PI and RI measure the resistance to blood flow in a blood vessel. The RI, however, measures blood flow resistance in the microvascular bed distal to the point of measurement.

The RI and PI are preferred to the PSV and EDV in the study of ophthalmic artery as both parameters are independent of the angle of insonation, unlike the PSV and EDV. There is also more variability between the PSV and the EDV for both eyes unlike the good correlation for PI and RI values obtained from both eyes.[21] RI values vary from 0 to 1, with higher scores indicating greater vascular resistance.[21]

The aim of this study was to evaluate blood flow features in the ophthalmic artery that may be present in diabetic retinopathy, to assess the usefulness of Doppler sonography for differentiating diabetic patients with diabetic retinopathy from those without diabetic retinopathy and to determine predictive value of the ophthalmic arteries Doppler indices in diabetic retinopathy prognostication and monitoring in a Nigerian teaching hospital.

METHODS

This comparative cross-sectional study was carried out in the Department of Ophthalmology, Lagos University Teaching Hospital, Lagos, South-west Nigeria. It is a tertiary level hospital located in the heart of the Lagos metropolis. The study was carried out over 7 months, from April 2017 to October 2017 after approval was granted by the Research and Ethical Committee of Lagos University Teaching Hospital.

Patients who were within the fasting plasma glucose reference range of 90-130 mg/dl for diabetics and 70-100 mg/dl for non-diabetic controls according to American diabetes association were recruited for the study. Only type 2 diabetic patients were recruited for the study. All diabetic patients did HbA1c test. All the diabetic patients for this study underwent indirect fundoscopy using an ophthalmoscope by a consultant ophthalmologist. The diagnosis and severity of diabetic retinopathy were determined according to the early treatment diabetic retinopathy study classification of diabetic retinopathy (ETDRS).[22]

Non-diabetic controls were recruited from hospital staff and voluntary workers. The weight, height and body mass index value of all patients were noted. Only subjects whose systolic pressure was below 140 mmHg and diastolic pressure below 90 mmHg were recruited for the study.

Three population groups were used for this study. The study population A involved diabetic patients with retinopathy attending the ophthalmology clinic of the Lagos University Teaching Hospital. Sixty-five (65) of whom gave their consent having met inclusion criteria and were recruited. The sub-study population B involved sixty-five (65) diabetic patients without retinopathy. The sub-study population C involved sixty-five (65) non-diabetic volunteers after their fasting blood sugar test had been done and were drawn from the Lagos University Teaching Hospital members of staff, health workers and patient relations who had met inclusion criteria. Informed consent was obtained for every participant.

Inclusion criteria (diabetic patients with retinopathy) were consenting diabetic men and women between the ages of 20 and 79 years and diagnosis of diabetic retinopathy on dilated fundoscopy made by the ophthalmologist on ocular examination.

Inclusion criteria (diabetic patients without retinopathy) were consenting diabetic men and women between the ages of 20 and 79 years and diagnosis of no diabetic retinopathy on dilated fundoscopy made by the ophthalmologist on ocular examination.

Inclusion criteria (controls) were consenting non-diabetic men and women between the ages of 20 and 79 years, normal fasting blood glucose test result and diagnosis of no retinopathy on dilated fundoscopy made by the ophthalmologist on ocular examination.

Exclusion criteria (for all 3 groups) were non-consenting individuals, patients with a history of non-diabetic vascular ocular disease (central artery or vein occlusion, ocular ischemic syndrome), patients on ocular medication, previous ocular surgery, glaucoma, hypertensives, previous history of ocular trauma and retinal pathologies leading to asymmetric retinopathy. Pregnant and breastfeeding women were also excluded from the study.

Sample size determination

Estimation of the sample size of this study was derived using the formula to calculate sample size for a comparison study of population means of continuous outcome.[23]

$$n = \frac{(Z + Z\beta)^2 \times (\sigma_1^2 + \sigma_2^2)}{(\mu_1 - \mu_2)^2}$$

Where n=the desired sample size for each group, z=standard normal deviation at 95% confidence interval=1.96 (a constant), Zβ=standard deviation of type 11 error at 10%=1.28 (a constant), μ_1=mean RI value of diabetic group with retinopathy=0.853 (population 1), μ_2=mean RI value of control group=0.824 (population 3), σ_1=standard deviation of the diabetic group with retinopathy=0.047 (population 1), σ_2=standard deviation of the control group=0.05 (population 3). Specifications for μ_1, μ_2, σ_1, and σ_2 were based on information from a previous study.[30] 10% attrition was added to account for incorrect data entry or data loss. 65 diabetic patients with retinopathy were used for the study and this made population A. 65 diabetic patients without retinopathy were used for the study and this made-up population B.

65 non-diabetic control patients were used for the study and this made up population C.

Procedure

This was clearly explained to the participants. They were made to understand that the investigation is safe, and any findings seen will be explained to them by their referring physician. After obtaining informed consent, each participant was placed in the supine position with the patient's head closer to the ultrasound machine. A resting period of at least 3 min was observed with the head lifted about 30°. The subject was told to keep both eyes closed and immobile as possible, looking in front of them. An adequate amount of standard water-soluble ultrasound transmission gel was applied to the patient's closed eyelid to avoid creating pressure derived artifacts. Both eyes were scanned. The patient was asked to look straight ahead with eyes closed, but without clenching the eyelids. The globe was scanned with the transducer in both sagittal and transverse planes. The depth was adjusted so that the image of the eye filled the screen. The gain was adjusted to achieve acceptable imaging. The normal eye appeared as a circular hypoechoic structure. The optic nerve was seen posterior as a hypoechoic linear region radiating away from globe. The ophthalmic artery was identified at the nasal and superior part of the optic nerve shadow just lateral to the visible hypoechoic stripe representing the nerve, nearly 12 to 15 mm from the posterior wall of the sclera. This was to allow for less angle correction (less than 200) and to ensure that the strongest values were recorded for the vessel. The colour Doppler and power Doppler knobs were activated with adequate gating and angle alignment was done to minimize errors in the measured velocities. Measurements of peak systolic velocity, end

diastolic velocity, RI and PI parameters were obtained. Both ophthalmic arteries were insonated, the right before the left.

Method of data analysis

The data collected was analyzed using standard statistical package for social science (SPSS®) for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA) and Microsoft excel 2010 edition. Data was analysed and descriptive summary, expressed as mean±standard deviation (SD). Test statistics were carried out using one-way analysis of variance (ANOVA). Comparisons between characteristics and control group with diabetes were obtained using t-test. Comparisons among Doppler parameters (PSV, EDV, RI and PI) for the three groups were obtained using ANOVA. Bonferroni post-hoc test of the results was also carried out to confirm which group or groups were responsible for the differences obtained in the results.

The Pearson correlation coefficient assessed the associations or relationships among HbA1c, duration of diabetes (DM), blood pressure and the Doppler parameters. Statistical level of significance of $p<0.05$ was chosen.

RESULTS

A total number of 195 age and sex-matched subjects who met the inclusion criteria were recruited for this study comprising of 65 diabetic patients with retinopathy, 65 diabetic patients without retinopathy and 65 non-diabetic patients (control group). The patients were type 2 diabetics. The mean ages of all the subjects were 51.52±8.90 years. 99 (50.7%) males and 96 (49.2%) females in total were recruited for this study. Each of the three groups had 33 (50.7%) men and 32 (49.2%) women, respectively. The mean body mass index of all the subjects was 26.48±4.32 and all the three groups had similar body mass indices value.

The mean fasting plasma glucose level for the three groups was 108.30±34.60. The mean fasting plasma glucose level for diabetic patients with retinopathy was 125.77±31.19 which was the highest of the three groups. This was followed by the diabetic group without retinopathy being 117.90±37.45. The mean fasting plasma glucose level for the non-diabetic control group was

81.17±10.08 and this was lowest value of the three groups.

All the three groups had similar blood pressure values.

Only the fasting plasma glucose was statistically significant between the three groups. There was no statistically significant difference between the ages of the three groups due to age matching. No statistically significant difference was seen between the body mass index, systolic blood pressure and diastolic blood pressure of the three groups as shown in Table 1.

Only the fasting plasma glucose was statistically significant between the 65 diabetic patients without retinopathy and 65 non-diabetic control patients as shown in Table 2.

There were no statistically significant difference between the age, body mass index, systolic blood pressure and diastolic blood pressure of the two groups. A similar observation was seen between the 65 diabetic patients with retinopathy and 65 non-diabetic control patients as depicted in Table 3.

There was no statistically significant difference between fasting plasma glucose between the two diabetic groups as seen in Table 4.

The mean HbA1c value for the two diabetic groups was 7.02±1.95. The mean diabetic duration was 7.55±6.05. The duration of diabetes was statistically significant. However, there was no statistics significance in the HbA1c value between the two diabetic groups as shown in Table 5.

There were no statistically significant differences between the PSV of ophthalmic artery of right and left eyes in the three groups. EDV in the diabetic patients, regardless of the presence or absence of retinopathy, were significantly lower than those of control group. EDV in diabetic patients with retinopathy was significantly lower than those of diabetic patients without retinopathy. The RI was significantly higher in both eyes of diabetic patients with retinopathy and diabetic patients without retinopathy compared to control group. Also, the PI was significantly higher in both eyes of diabetic patients with retinopathy and diabetic patients without retinopathy compared to control group as depicted in Table 6.

The difference in mean EDV was statistically significant in both eyes between control and diabetic without retinopathy, control and diabetic with retinopathy and diabetics without retinopathy and diabetics with retinopathy. This is shown in Table 7 after Bonferroni adjustment. The difference in mean RI was statistically significant in both eyes between control and diabetics with retinopathy. The mean PI was statistically significant in both eyes between control and diabetics with retinopathy and diabetics with and without retinopathy. The PSV was not significant in any of the groups.

The diabetic patients with retinopathy had the highest RI value in both eyes (0.9 right eye, 0.8 left eye). This was followed by the diabetic patients without retinopathy (0.8 right eye, 0.76 left eye). The healthy control group had the least RI values (0.71 right eye, 0.73 left eye) as shown in Figure 1.

The relationship between HbA1c, duration of diabetes, and hemodynamic parameters was tested using Pearson's correlation. The analysis showed significant negative correlations between HbA1c levels and the EDV values of both eyes ($p<0.05$ both eyes). There was significant

positive correlation between the HbA1c levels and PI values of both eyes (p<0.001 both eyes). Only the RI value of the left eye showed significant positive correlation (p<0.001) as shown in Table 8. There was no statistically significant correlation between duration of diabetes and any of the Doppler parameters.

The relationship between blood pressure (systolic and diastolic) and the Doppler parameters was tested using Pearson's correlation as seen in Table 9. Only the RI value of the left eye showed significant positive correlation with the systolic blood pressure (RI= 0.189, p<0.05). There was no statistically significant correlation between diastolic blood pressure and any of the Doppler parameters.

Incidental occular pathologies

Incidental occular pathologies were seen in this study. Four (6.1%) diabetic patients with retinopathy had tractional retinal detachment. One (1.5%) diabetic patient with retinopathy had cataract. One (1.5%) diabetic patient without retinopathy had cataract. Four (6.2%) diabetic patients with retinopathy have vitreous hemorrhage as shown in Table 10.

Table 1: Characteristics of participants with and without diabetic retinopathy and the control group.

Characteristics	Control group (mean±SD)	Diabetes (no retinopathy) group (mean±SD)	Diabetes (with retinopathy) group (mean±SD)	Total (mean±SD)	P value
Number (%)	65 (33.33)	65 (33.33)	65 (33.33)	195 (100)	-
Sex(male/female)	65 (33/32)	65 (33/32)	65 (33/32)	195 (99/96)	-
Age	50.95±6.00	51.69±7.25	51.91±6.83	51.52±8.90	0.698
Body mass index (BMI) kg/m^2	26.02±5.38	26.52±3.09	26.90±4.02	26.48±4.32	0.512
Fasting plasma glucose (mg/dl)	81.17±10.08	117.90±37.45	125.77±31.19	108.30±34.60	<0.001
Systolic blood pressure (SBP) (mm Hg)	124.43±12.16	126.54±8.81	127.85±8.80	126.27±10.09	0.150
Diastolic blood pressure (DBP) (mm Hg)	77.09±7.00	76.66±6.04	75.18±7.67	76.31±6.95	0.261

Table 2: Characteristics of diabetic participants without retinopathy and control group.

Characteristics	Control group (mean±SD)	Diabetes (no retinopathy) group (mean±SD)	Total (mean±SD)	P value
Number (%)	65 (50)	65 (50)	130 (100)	-
Sex (male/female)	65 (33/32)	65 (33/32)	130 (66/64)	-
Age	50.95±6.00	51.69±7.25	51.32±6.64	0.528
Body mass index (BMI) kg/m^2	26.02±5.38	26.52±3.09	26.27±4.37	0.516
Fasting plasma glucose (mg/dl)	81.17±10.08	117.90±37.45	99.53±32.95	<0.001
Systolic blood pressure (SBP) (mm Hg)	124.43±12.16	126.54±8.81	125.48±10.70	0.260
Diastolic blood pressure (DBP) (mm Hg)	77.09±7.00	76.66±6.04	76.87±6.51	0.708

Table 3: Characteristics of diabetic participants with retinopathy and control group.

Characteristics	Control group (mean±SD)	Diabetes (with retinopathy) group (mean±SD)	Total (mean±SD)	P value
Number (%)	65 (50)	65 (50)	130 (100)	-
Sex (male/female)	65 (33/32)	65 (33/32)	130 (66/64)	-
Age	50.95±6.00	51.91±6.83	51.43±6.42	0.399
Body mass index (BMI) kg/m^2	26.02±5.38	26.90±4.20	26.46±4.82	0.302
Fasting plasma glucose (mg/dl)	81.17±10.08	125.77±31.19	103.47±32.16	<0.001
Systolic blood pressure (SBP) (mm Hg)	124.43±12.16	127.85±8.79	126.14±10.71	0.069
Diastolic blood pressure (DBP) (mm Hg)	77.09±7.00	75.18±7.67	76.13±7.38	0.141

Table 4: Characteristics of diabetic participants without retinopathy and diabetic patients with retinopathy.

Characteristics	Diabetes (no retinopathy) group (mean±SD)	Diabetes (with retinopathy) group (mean±SD)	Total (mean±SD)	P value
Number (%)	65 (50)	65 (50)	130 (100)	-
Sex (male/female)	65 (33/32)	65 (33/32)	130 (66/64)	-
Age	51.69±7.25	51.91±6.83	51.80±7.02	0.862
Body mass index (BMI) kg/m^2	26.52±3.09	26.90±4.20	26.71±3.68	0.562
Fasting plasma glucose (mg/dl)	117.90±37.45	125.77±31.19	121.84±34.56	0.195
Systolic blood pressure (SBP) (mm Hg)	126.54±8.81	127.85±8.79	127.19±8.79	0.398
Diastolic blood pressure (DBP) (mm Hg)	76.66±6.04	75.18±7.67	75.31±6.92	0.225

Table 5: Characteristics of diabetic participants.

Characteristics	Diabetes (no retinopathy) group (mean±SD)	Diabetes (with retinopathy) group (mean±SD)	Total (mean±SD)	P value
Number (%)	65 (50)	65 (50)	130 (100)	
HbA1c(%)	6.44 ± 1.55	7.60 ± 2.14	7.02 ± 1.95	0.801
Duration of diabetes	6.23 ± 4.65	8.86 ± 6.99	7.55 ± 6.05	0.013

Table 6: Comparing the mean difference between the Doppler parameters of control, diabetic patients without retinopathy and diabetic patients with retinopathy groups using ANOVA for the test analysis.

Characteristics	Diabetes (no retinopathy) group (mean±SD)	Diabetes (with retinopathy) group (mean±SD)	Total (mean±SD)	P value
Right eye				
Peak systolic velocity (cm/s)	33.15±10.31	31.23±8.79	32.74±9.64	0.488
End diastolic velocity (cm/s)	9.11±3.25	7.65±3.08	5.84±2.59	<0.001
Resistivity index	0.71±0.12	0.81±0.04	0.92±0.07	0.044
Pulsatility index	1.42±0.29	1.49±0.33	1.86±0.34	<0.001
Left eye				
Peak systolic velocity (cm/s)	33.04±11.29	30.01±7.89	31.97±8.70	0.179
End diastolic velocity (cm/s)	8.94±3.56	7.26±3.11	5.75±2.39	<0.001
Resistivity index	0.73±0.06	0.76±0.06	0.82±0.05	<0.001
Pulsatility index	1.46 ± 0.27	1.50 ± 0.27	1.61 ± 0.38	<0.001

Table 7: Comparing the mean difference between groups using post hoc Bonferroni adjustment procedure.

Variables	Control and diabetes (no retinopathy) (p value)	Control and diabetic retinopathy (p value)	Diabetes (no retinopathy) and diabetic retinopathy (p value)	P value
Right eye				
Peak systolic velocity (cm/s)	0.768	0.999	0.999	0.488
End diastolic velocity (cm/s)	<0.05	<0.001	<0.05	<0.001
Resistivity index	0.712	<0.05	0.555	0.044
Pulsatility index	0.624	<0.001	<0.001	<0.001
Left eye				
Peak systolic velocity (cm/s)	0.203	0.999	0.707	0.179
End diastolic velocity (cm/s)	<0.05	<0.001	<0.016	<0.001
Resistivity index	<0.05	<0.001	<0.001	<0.001
Pulsatility index	0.999	<0.001	<0.001	<0.001

Table 8: Pearson correlation coefficient between HbA1c, duration of diabetes and the Doppler parameters.

Variables	HbA1c (Pearson correlation coefficient) (r)	P value	Duration of diabetes (Pearson correlation coefficient) (r)	P value
Right eye				
Peak systolic velocity (cm/s)	-0.091	0.306	-0.015	0.867
End diastolic velocity (cm/s)	-0.275*	<0.05	-0.061	0.488
Resistivity index	0.590	<0.508	0.015	0.861
Pulsatility index	0.350**	<0.001	0.021	0.812
Left eye				
Peak systolic velocity (cm/s)	-0.022	0.808	-0.046	0.605
End diastolic velocity (cm/s)	-0.261	<0.05	-0.078	0.377
Resistivity index	0.348**	<0.001	0.015	0.862
Pulsatility index	0.284**	<0.001	0.023	0.798

Table 9: Pearson correlation coefficient between blood pressure (systolic and diastolic) and the Doppler parameters.

Variables	Systolic blood pressure (Pearson correlation coefficient) (r)	P value	Diastolic blood pressure (Pearson correlation coefficient) (r)	P value
Right eye				
Peak systolic velocity (cm/s)	0.034	0.702	0.055	0.531
End diastolic velocity (cm/s)	-0.064	0.469	0.097	0.272
Resistivity index	0.049	0.577	-0.050	0.576
Pulsatility index	0.052	0.556	-0.047	0.598
Left eye				
Peak systolic velocity (cm/s)	0.083	0.345	-0.094	0.605
End diastolic velocity (cm/s)	-0.072	0.416	-0.034	0.285
Resistivity index	0.189*	<0.05	0.007	0.940
Pulsatility index	0.085	0.334	0.047	0.594

Table 10: Comparison of incidental ocular pathologies.

Ocular parameters	Control	Diabetes (no retinopathy)	Diabetes (with retinopathy)	Total (100)
Retinal detachment	None	None	4 (6.2)	4 (2.1)
Cataract	None	1 (1.5)	1 (1.5)	2 (1.0)
Vitreous hemorrhage	None	None	4 (6.2)	4 (2.1)
Total	65 (100)	65 (100)	65 (100)	195 (100)

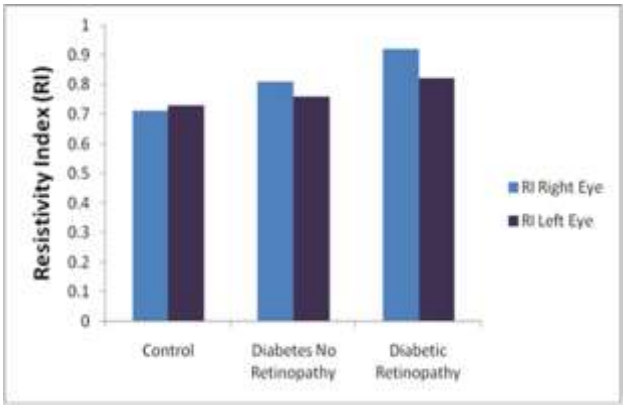

Figure 1: The relationship between the resistivity index values amongst the three groups.

DISCUSSION

The pathophysiological mechanism of diabetic retinopathy remains a challenge for medical research. Although the exact pathogenesis of the disease is yet unknown, there are several theories about the processes that affect the ocular blood flow in diabetic retinopathy. Most studies claim that the central abnormality in diabetic retinopathy is microangiopathy, which causes macular edema and retinal ischemia. The microangiopathy is multifactorial and appears to be a consequence of hyperglycemic and hypoxic damages.[24,25]

The findings of this study are consistent with those of Arai et al who found no differences in the PSV values of the ophthalmic artery amongst the three groups however,

found that EDV values of the ophthalmic artery in the diabetic patients with retinopathy were significantly lower than those of diabetic patients without retinopathy and controls.[26]

Compared with healthy controls, diabetic patients with retinopathy had significantly higher RI values in the ophthalmic artery. The findings of an increased RI in diabetic patients with retinopathy is similar to that reported by previous researchers.[26,27] Arai et al found that the RI values in diabetic patients with retinopathy were significantly greater than those of normal subjects and diabetic patients without retinopathy.[26]

They concluded that measurements of the RI in the ophthalmic arteries are better parameters than the velocities of the blood flow in these vessels for evaluating the severity of diabetic retinopathy. Our finding of an increased RI in the ophthalmic artery is similar to that reported by MacKinnon et al.[27] Dimitrova et al measured ophthalmic artery parameters using colour Doppler imaging in 35 diabetic patients with retinopathy, 38 diabetic patients without retinopathy and 22 healthy controls.[28] They found decreased EDV values and increased RI values in diabetic patients with retinopathy than in diabetic patients without retinopathy and healthy controls. These findings are consistent with our results.

Our finding of increased PI value in diabetic patients with retinopathy compared with diabetic patients without retinopathy and healthy controls is also consistent with some studies. Karami et al evaluated 123 individuals including 25 healthy controls, 74 diabetic patients without retinopathy and 24 diabetic patients with retinopathy and observed PI values of ophthalmic artery in diabetic patients with retinopathy individuals were significantly higher than diabetic patients without retinopathy and healthy controls.[29]

Ino-ue et al found increased PI values in diabetic patients with retinopathy when compared to controls.[30] It has been that higher PI values of the ophthalmic arteries may indicate an increase in the peripheral vascular resistance secondary to the arterio- and atherosclerosis process involving the orbital arteries in diabetic patients.[31]

Gracner assessed the parameters in the ophthalmic artery on various stages of diabetic lesion development and demonstrated a significant increase in PSV values in the ophthalmic artery.[32] His sample size was 44 diabetic patients with pre-proliferative lesions and 22 healthy controls. There was also no statistical significance in the RI value between the two groups. His results contrast with our results. Our research showed no statistical significance in the PSV value between diabetic patients with retinopathy and healthy controls after Bonferroni post hoc comparison. Our research also showed increased RI value in diabetic patients with retinopathy than healthy controls. These differences may be due to different demographic variables and sample.

Kraśnicki et al assessed PSV and EDV in the vessels of the eyeball in patients with type II diabetes without retinopathy and type II diabetes patients with retinopathy.[33] The authors observed considerably lower PSV and EDV values in the ophthalmic artery (OA) in all patients compared to healthy controls. The RI did not change in a statistically significant way. These findings are in contrast with our study. Our research showed no statistical significance in the PSV values of the ophthalmic artery in the three groups. However, we observed a decrease in EDV values and an increase in RI of ophthalmic artery in diabetic patients with retinopathy compared with diabetic patients without retinopathy and healthy controls.

Previous studies show that decreased EDV and increased RI in diabetic patients with retinopathy are considered to represent an increase in the peripheral vascular resistivity.[34] Pathological findings found in diabetic retinopathy and diabetes that are known to increase the peripheral vascular resistivity (capillary rarefaction, atherosclerotic changes, leucocyte adhesion, increased blood viscosity) were shown to support this circulatory finding.[35] The increased vascular resistivity may further compromise the ocular tissue oxygenation and nourishment and may contribute to the occurrence of neovascularisation.

The prevalence of diabetic retinopathy increases with prolonged duration of diabetes. This association was confirmed from our study (p=0.0130) and other studies and it was probably related to the magnitude, prolonged exposure, or due to hyperglycaemia.[36,37] Our study saw incidental ocular finding of cataract in two diabetic patients and none in control.

Klein et al demonstrated that patients with diabetes mellitus are 2–5 times more likely to develop cataracts than their non-diabetic counterparts.[38] Studies related to cataract formation in diabetic patients have shown that hyperglycemia is associated with loss of lens transparency in a cumulative manner.[39] Four diabetic patients with retinopathy had vitreous haemorrhage. Vitreous haemorrhage is the most common complication of diabetic retinopathy that causes decreased visual acuity.[40] Four diabetic patients with retinopathy had retinal detachment. The fibrovascular proliferation of tissue contracts and pulls the underlying retina due to vitreoretinal adhesions resulting in the development of tractional retinal detachment (TRD).[40] It is also worthy to note in this study, that the higher resistive index values in the left eye was statistically significant in all groups after Bonferroni adjustment post hoc comparison. This finding has not been previously reported as most studies used only a single eye.

Limitations

There is paucity of data for the use of two eyes in studies that involve diabetic retinopathy which limited final analysis. Another limitation was the use of indirect

ophthalmoscopy instead of retinal photography in the assessment of diabetic retinopathy. The use of fundal photography could have led to better detection of early retinopathy, resulting in elevated prevalence of retinopathy. Retinal photography was not used because it was unavailable in our hospital.

CONCLUSION

Doppler sonography has the potential to provide useful information about hemodynamic changes in patients with diabetic retinopathy. Diabetic retinopathy may be triggered by increased resistances in the peripheral ocular vascular bed, changes which may begin in the early stage of diabetes. The finding of increased RI and PI values in the ophthalmic artery in this study may indicate disturbances of retinal and choroidal circulation in patients with diabetic retinopathy and an increase in ocular peripheral vascular resistivity. These events may be among the early changes in diabetic retinopathy.

Recommendations

This study has demonstrated reduced EDV, increased RI and PI values in ophthalmic artery of diabetics with retinopathy and therefore shown that color Doppler is a useful method for screening patients with retinopathy. Color Doppler has the potential to provide helpful information related to altered orbital blood flow in diabetic patients even before the appearance of retinopathy. It is recommended that every newly diagnosed diabetic should be monitored with orbital colour Doppler ultrasound. This would help in identifying eyes at risk of developing sight threatening proliferative disease thereby improving quality of life.

Further studies with much larger groups of patients on both eyes are needed to understand better the role of retrobulbar hemodynamics in the pathogenesis of diabetic retinopathy. There is a need to assess the mechanism for the association, whether it is through change in retinal blood flow, change in perfusion pressure, change in intraluminal capillary pressure, poor glycemic control, chance, or a combination of these and other factors.

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