



Pulsed Doppler Imaging of Ophthalmic and Central Retinal Arteries in Diabetics with and Without Retinopathy and Controls

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Abstract

Aims and Objective: *The aim of this study is to evaluate hemodynamic changes of ophthalmic artery and central retinal artery in diabetic patients with and without diabetic retinopathy by comparing it with normal individuals and to find the use of pulsed Doppler imaging in differentiating diabetic patients with retinopathy from those without retinopathy*

Materials and Methods: *Sixty patients, divided into three groups twenty each as non-diabetic controls, diabetes without retinopathy and diabetics with retinopathy. All the patients underwent pulsed doppler imaging through ultrasound modality. We qualitatively analysed the values of velocities and RI in ocular vessels.*

Results: *There was a statistically significant ($p < 0.001$) decrease in both the peak systolic velocity (PSV 0.10 m/s) and end diastolic velocity (EDV 0.02 m/s) of the central retinal artery in the diabetic patients with retinopathy compared to the diabetic patients without retinopathy (PSV 0.12 m/s, EDV 0.03 m/s) and the control group (PSV 0.14 m/s, EDV 0.04 m/s). The peak systolic velocity and resistance index of the ophthalmic artery was significantly increased in both groups of diabetic patients with retinopathy (PSV-0.35, RI-0.80) and without retinopathy (PSV-0.34, RI-0.77) compared to controls (PSV-0.31, RI-0.71)*

Conclusion: *Pulsed Doppler imaging is a useful modality to assess the risk of developing proliferative diabetic retinopathy which can lead on to visual loss. There was significant decrease in blood flow velocity of CRA of diabetic patients and it was much more reduced on comparing it with diabetic patients with retinopathy. The RI values of ophthalmic artery were also found to be increased in diabetic patients. Although the assessment of orbital blood flow in retinopathy requires further investigations, based on the results of our study we suggest pulsed Doppler imaging for its ability to provide information about hemodynamic changes and for the diagnosis of diabetic retinopathy as a supportive modality.*

Introduction

One of the vascular disorders that affect the retinal microvasculature is Diabetic retinopathy. It is estimated that some form of diabetes affects 8.3 percent of the world's population, almost half of

are associated with some degree of diabetic retinopathy at any given time^[1]. Both type I and type II diabetes mellitus patients show occurrence of diabetic retinopathy according to early epidemiological studies on long standing upto 15

years. It has been known that nearly 80% of type one and 85% of type two diabetic patients develop diabetic retinopathy^[2,3]. The world health organization (WHO) has reported India has been showing epidemic increase in type II diabetes mellitus^[4], and it is one of the fast progressing cause of visual disability is diabetic retinopathy. The severity of hyperglycaemia is considered as the key risk factor for developing retinopathy. Along with this duration of diabetes is known as the next possible risk factor. The introduction of orbital colour Doppler imaging (CDI) in 1989 by Erickson et al. presented the opportunity for assessment of orbital blood vessels and to see the vessel changes. Doppler imaging is a non-invasive method to assess the blood flow velocities and resistive index qualitatively and quantitatively through ultrasound. Orbital vessels may easily be identified because the Doppler shift is encoded in colour and is superimposed on the two dimensional, gray-scale ultrasound image. Thus, even vessels below resolution of a gray-scale image can be visualized. In this way, the circulation of the ophthalmic artery (OA) and central retinal artery (CRA) may be investigated. With very few studies performed on this topic outside India to our knowledge, in our study we aim in better characterization of orbital circulation in diabetic patients with and without retinopathy and compare it with normal subjects.

In India, diabetic retinopathy is liable to pose a public health burden due to its possibility of occurrence among the large number of diabetic subjects. As visual loss is being the end stage severe condition occurring in long standing cases, we look to provide a better modality to evaluate the progressive changes and help the patients with adequate anti-diabetic treatment to prevent further vascular damage and improve their quality of life with timely intervention

Aims & Objectives

1. The aim of this study is to evaluate hemodynamic changes of ophthalmic artery and central retinal artery in diabetic

patients with and without diabetic retinopathy by comparing it with normal individuals

2. To find the use of Pulsed Doppler imaging in differentiating diabetic patients with retinopathy from those without retinopathy

Materials and Methods

This was a prospective study, which was conducted at the Mahatma Gandhi Medical College and Research Institute Hospital, a rural tertiary care hospital with an annual volume of above 1,00,000 patients over one year period. The Institutional Medical Ethics Committee approved this study. All the known cases of diabetes with and without signs of diabetic retinopathy and those without diabetes (controls) were referred for Pulsed Doppler imaging from ophthalmology and those willing to give consent were included in this study. MINDRAY DC-8 ultrasound machine was used throughout the study with 7.5 MHz and 3.5MHz probes for examining CRA and OA respectively.

A TOTAL OF 60 Patients were involved in this study (MALE-31, FEMALE-29). An informed consent was obtained from every patient. Normal adult patients >18 years of age of both males and females having normal blood glucose and normal blood pressure levels volunteering for the study and diabetic patients with duration of disease from 2-15 years, those with and without manifestations of diabetic retinopathy clinically were included in the study.

Those not willing to give consent and those with history of smoking and other conditions such as congenital orbit pathology, trauma, infections or inflammatory lesions, benign or malignant lesions in orbit and cerebrovascular insult or CVA, hypertension/ dyslipidaemia, glaucoma and any intraocular surgery were excluded.

Around 20 adult patients as known case of diabetes mellitus with fundoscopic examination showing features of diabetic retinopathy, 20 patients with diabetes mellitus without diabetic retinopathy and 20 normal volunteers were used.

The diabetic subjects were prospectively from the ophthalmology department in our institute.

Initially, after obtaining consent from the patient, they were divided into three separate sub-groups controls, diabetics without diabetic retinopathy and diabetics with diabetic retinopathy. The diabetic subjects were categorized following dilated funduscopy using the biomicroscopic indirect ophthalmoscope by a single experienced medical ophthalmologist. Doppler imaging was performed on ophthalmic artery (OA) and central retinal artery (CRA) by using the Mindray machine with 7.5 and 3.5 MHz probe. Patients were examined in the supine position, with their heads inclined at a 30° angle. The transducer was covered in gel and gently placed externally upon the eyelid, avoiding excessive pressure. The flow velocity was measured in the vessels using a wall filter of 100 Hz and sample of 0.12 mm. Doppler insonation angle was adjusted between 0 and 40°. After the waveforms were obtained, measurements of peak systolic velocity (PSV, m/sec), end diastolic velocity (EDV, m/sec) and the resistance index (RI) were calculated by automatic algorithm of the machine. Both eyes are examined, though single eye can be affected in few patients for comparison and screening. The parameters are peak systolic velocity, end diastolic velocity and resistive index in Central

retinal artery and ophthalmic artery using Pulsed Doppler imaging.

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean \pm SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The Statistical software SPSS 15.0 was used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Results

Among the 60 patients, 36 patients were around the age 50-60 years. The PSV and EDV of the central retinal artery was found to be significantly lower in diabetic patients compared to controls regardless of retinopathy and a significant decrease in EDV and PSV of diabetic patients with retinopathy compared to diabetics without retinopathy was also found. The RI in the patients without diabetic retinopathy was significantly greater than that of normal subjects ($P < 0.001$) and the RI in the patients with diabetic retinopathy (0.81 ± 0.04) was significantly greater ($P < 0.001$) than that of normal subjects (0.72 ± 0.05) and of patients without diabetic retinopathy (0.75 ± 0.05). (Table 1)

Table 1: Comparison of Central Retinal Artery (CRA) parameters in three groups of patients studied

| Retinal artery parameters | Control Group | Diabetic patients without retinopathy | Diabetic patients with diabetic retinopathy | Total | P value |
|---------------------------|-----------------|---------------------------------------|---|-----------------|----------|
| PSV (m/sec) | 0.14 \pm 0.01 | 0.12 \pm 0.02 | 0.10 \pm 0.02 | 0.12 \pm 0.02 | <0.001** |
| EDV(m/sec) | 0.04 \pm 0.01 | 0.03 \pm 0.01 | 0.02 \pm 0.01 | 0.03 \pm 0.01 | <0.001** |
| RI | 0.72 \pm 0.05 | 0.75 \pm 0.05 | 0.81 \pm 0.04 | 0.76 \pm 0.06 | <0.001** |

On comparing among the different groups, significant correlation was noted. (Table 2)

Table 2: Pair wise Comparison of Retinal artery parameters in three groups of patients studied

| Retinal artery parameters | A vs B | | A vs C | | B vs C | |
|---------------------------|------------|----------|------------|----------|------------|----------|
| | Difference | P value | Difference | P value | Difference | P value |
| PSV(m/sec) | 0.1758 | <0.001** | 0.0375 | <0.001** | 0.0200 | <0.001** |
| EDV(m/sec) | 0.0083 | <0.001** | 0.018 | <0.001** | 0.0097 | <0.001** |
| RI | 0.028 | 0.020* | 0.089 | <0.001** | 0.062 | <0.001** |

A: Control group;

B: Diabetic patients without retinopathy;

C: Diabetic patients with retinopathy

In ophthalmic artery, the PSV values were significantly increased in diabetic patients compared to the normal group. EDV values did not show significant difference among three groups. The RI values of diabetic retinopathy

Table 3: Comparison of ophthalmic artery in three groups studied

| | Control Group | Diabetic patients without retinopathy | Diabetic patients with retinopathy | Total | P value |
|------------|---------------|---------------------------------------|------------------------------------|-----------|----------|
| PSV(m/sec) | 0.31±0.03 | 0.34±0.02 | 0.35±0.01 | 0.34±0.03 | <0.001** |
| EDV(m/sec) | 0.09±0.01 | 0.08±0.01 | 0.08±0.08 | 0.08±0.05 | 0.634 |
| RI | 0.71±0.03 | 0.77±0.02 | 0.80±0.02 | 0.76±0.05 | <0.001** |

On comparing among the three different groups, significant correlation was noted in all the three groups in the PSV and RI values. (Table 4)

Table 4: Pair wise Comparison of OPTHALMICARTERY in three groups of patients studied

| OPHTHALMICARTERY | A vs B | | A vs C | | B vs C | |
|------------------|------------|----------|------------|----------|------------|----------|
| | Difference | P value | Difference | P value | Difference | P value |
| PSV(m/sec) | 0.028 | <0.001** | 0.041 | <0.001** | 0.013 | 0.011** |
| EDV(m/sec) | 0.011 | 0.606 | 0.005 | 0.882 | 0.005 | 0.882 |
| RI | 0.055 | <0.001** | 0.090 | <0.001** | 0.036 | <0.001** |

A: Control group; B: Diabetic patients without retinopathy; C: Diabetic patients with retinopathy

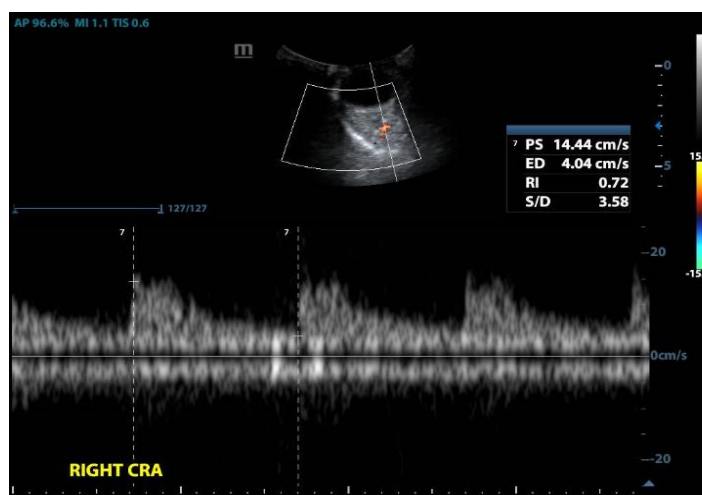


Fig 17 : Right Central Retinal Artery in Controls

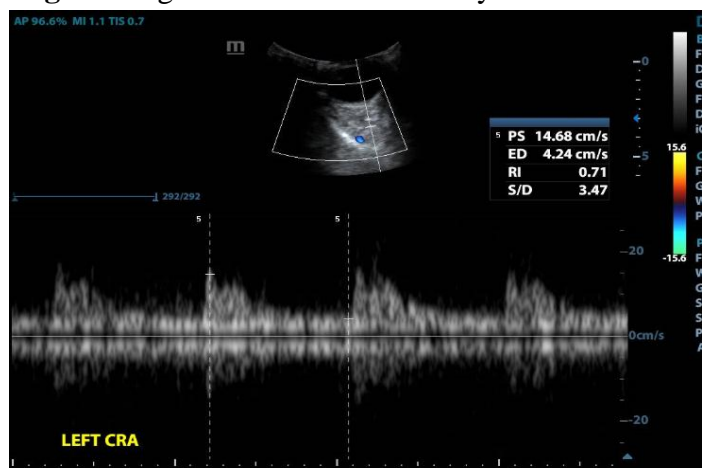


Fig 18 : Left Central Retinal Artery in Controls

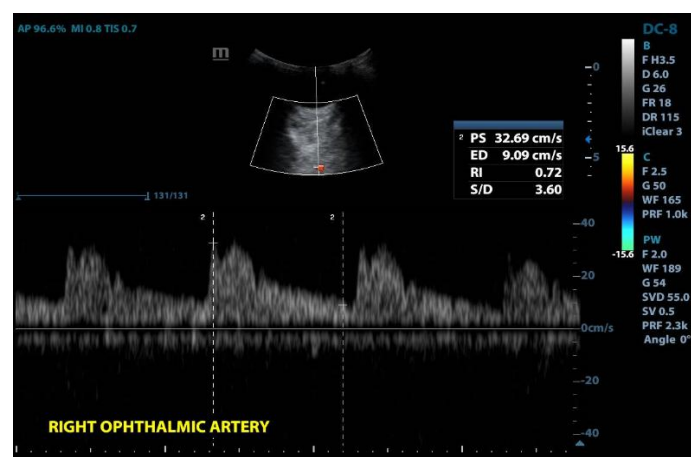


Fig 19 : Right Ophthalmic Artery in Controls

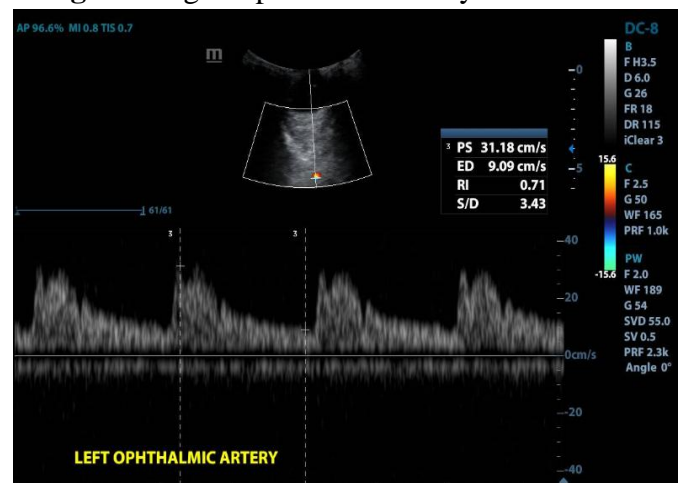


Fig 20 : Left Ophthalmic Artery in Controls



Fig 21 : Left Central Retinal Artery in Diabetics with no Retinopathy

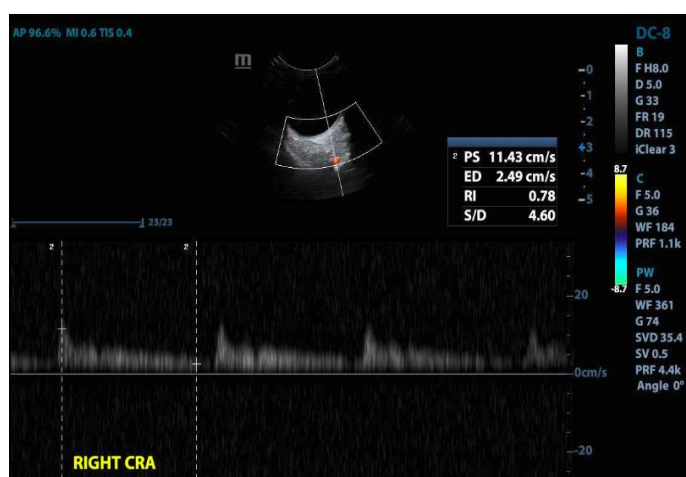


Fig 22 : Right Central Retinal Artery in Diabetics with Retinopathy

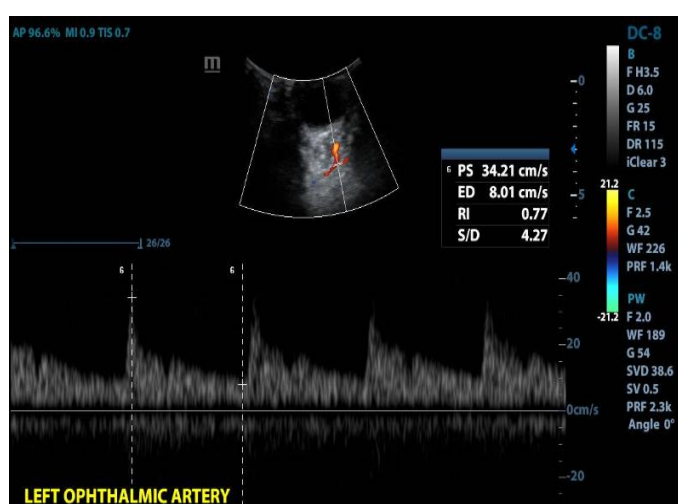


Fig 23: Left Ophthalmic Artery in Diabetics with no Retinopathy

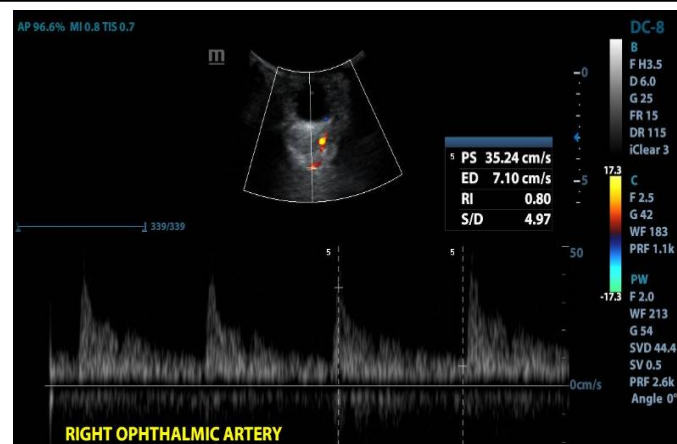


Fig 24: Right Ophthalmic Artery in Diabetics with Retinopathy

Discussion

Pulsed Doppler imaging has established itself a useful tool for evaluation of ocular hemodynamics in real time and physiological conditions. This modality is useful when standard procedures of diagnosis (fundus examination and fluorescein angiography) are difficult when there is cataract or vitreous haemorrhage. The other diagnostic methods which are used to measure the retinal circulation are blue light entoptic phenomenon, laser Doppler velocimetry and photo angiography. In our study we have compared diabetic patients with controls and found there was higher resistive index in ophthalmic artery and decreased velocities in central retinal artery among the diabetic patients. And the velocities were even decreased in CRA when we compared the diabetic retinopathy patients with no retinopathy diabetics. The resistive index of ophthalmic artery and velocity values of central retinal artery is strongly significant on comparing the patients with and without diabetic retinopathy with the control group. From the study, it was found that the arterial velocity in CRA decreases as severity of the disease increases. The results in this study matches to the study which was done by Goebel et al. (1995), in which he found the PSV and EDV of CRA to be significantly lower in diabetic retinopathy patients compared to the controls^[5]. The patients who had PDR had decreased PSV compared to the BDR patients used in that study. However the velocity changes in ophthalmic

artery and short posterior ciliary artery did not show significant changes and RI was not used as a parameter. There was a similar study by mendivil et al. (1995), which performed a study with 25 diabetes mellitus patients with PDR comparing them to 30 patients without diabetes. He found significant decrease in velocities of CRA and also in the velocities of ophthalmic artery. However non-proliferative retinopathy patients were not included in his study^[6]. But in our study, we had significant increase in peak systolic velocity and no significant change in end diastolic velocity of ophthalmic arteries in diabetic groups when compared to the normal patients. An increase in the PSV coincides with rise of systolic blood pressure which was studied by Williamson et al. in 1995, however, in our study we did not confirm the results to this correlation in group analysis and there was not any significance in systolic blood pressure of our patients. Resistive index parameter was not used by the above mentioned studies on Colour Doppler imaging. Similar to our study, increased value of RI in ophthalmic artery was high lightened by Jane R. MacKinnon et al.2000 and the probable reason could be due to increase in PSV and decrease in EDV, but this is suggested as vascular changes in retinal and choroidal vasculature^[7]. It is estimated that retina receives only less than 10% of blood flow of the total ocular blood supply (Hart 1992), the remainder being directed to the choroid via the ciliary circulation. CDI has also provided some interesting information of changes in ocular blood flow velocities in patients after retinal laser treatment. Mendivil and Cuartero (1996) have reported on the CDI findings of diabetics with PDR after scatter laser photocoagulation^[8]. Panretinal photocoagulation resulted in a reduction in the PSV of the OA compared to values before laser treatment. These results were obtained 6 months following treatment and did not change during 2 years of follow-up. Evans et al. (1997) also used CDI to investigate retrobulbar vascular reactivity in early diabetic retinopathy. In his study CDI of the ophthalmic artery and CRA

was performed on 11 diabetic patients with no diabetic retinopathy and compared to 11 non-diabetic controls. While under conditions of isocapnic hyperoxia, diabetic patients exhibited a significantly lower resistance index in both the ophthalmic artery and CRA compared to controls. Hypoxia also induced an increased EDV in the CRA and decreased PSV in the ophthalmic artery compared to normal subjects. There is conflicting evidence, whether blood flow velocity increases or decreases in diabetic retinopathy. Different techniques and sites of measurement have provided varying results.

Using laser Doppler velocimetry Patel et al. (1992) showed an increased blood flow velocity in temporal retinal veins in diabetics with untreated retinopathy compared to non-diabetics and diabetic patients with no retinopathy. In contrast, Feke et al. (1994) studied blood speeds were on average 33% lower using laser Doppler measurements from the temporal retinal arteries in diabetics with NDR or BDR. The finding of decreasing velocities in CRA of diabetics, which becomes progressively lower as severity of retinopathy increases is likely to have a significant effect on retinal perfusion and function. Harris et al. (1996) showed that hyperoxia improves contrast sensitivity in patients with retinopathy in early stages, indicating possibility of a link between tissue hypoxia and visual function in diabetics. As it is not possible to accurately measure the diameter of the vessels being studied with this technique, blood flow cannot be quantitatively calculated and the closer relationship between blood velocity and volume flow in the vessels which is studied is unknown.

In Our findings, the reduced velocities in the CRA of diabetics should be interpreted with caution. As vascular studies involving diabetics with vasoactive medication may become a confounding variable. As it is not possible to quantitatively measure blood flow in the ocular vasculature accurately, the pathogenesis of diabetic retinopathy is still unclear.

Limitations

A single observer for measurement of the Doppler indices to assess the hemodynamic changes, hence the measurement values could vary from user to user or even by the same user over time. The inclusion of posterior ciliary artery in assessing the hemodynamic changes would have been a supportive result. Much more specific age group of patients could have been helpful in finding the changes occurring at specific age. We have also ruled out the conditions like glaucoma and hypertension, those with history of smoking and previous history of intraocular surgery which are factors in causing ocular vasculopathy. Finding the hemodynamic changes between diabetic retinopathy patients among the different grades could have helped in finding the progression of vasculopathy.

Conclusion

Pulsed Doppler imaging is a useful modality to assess the risk of developing proliferative diabetic retinopathy which can lead on to visual loss. In pulsed Doppler imaging there was significant decrease in blood flow velocity of CRA of diabetic patients and it was much more reduced on comparing it with diabetic patients with retinopathy. The RI values of ophthalmic artery were also found to be increased in diabetic patients. Although the assessment of orbital blood flow in retinopathy requires further investigations, based on the results of our study we suggest pulsed Doppler imaging has the ability to provide information about hemodynamic changes and for the diagnosis diabetic retinopathy patients it can be used as a supportive modality.

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