# A Color Doppler Imaging Study of Ocular Haemodynamic Parameters in Normal Tension Glaucoma

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**Abstract**

***Context:*** *Normal tension glaucoma (NTG) is a multifactorial optic neuropathy characterized by progressive retinal ganglion cell death and glaucomatous visual field loss, even though the intraocular pressure (IOP) does not exceed the normal range.*

***Aim:*** *To evaluate the retrobulbar hemodynamic parameters in NTG patients by Color Doppler Imaging (CDI).*

***Settings and Design:*** *It was a hospital based cross-sectional institutional study carried out in the Medical College Out Patient Department (OPD).*

***Materials and Methods:*** *Twenty patients with untreated NTG (mean age 53.27 ± 11.11 years) and 23 healthy volunteers (mean age 49.39 ± 9.56 years) were included in a prospective cross-sectional institutional study. Peak systolic velocity (PSV), end-diastolic velocity (EDV) and resistivity index (RI = (PSV–EDV)/PSV) of the ophthalmic artery (OA), central retinal artery (CRA) and short posterior ciliary arteries (SPCA) were measured by means of CDI.*

***Statistical Analysis:*** *Mean, standard deviation (SD) and Independent t- test was applied.*

***Results:*** *Patients with NTG showed significantly decreased PSV (P<0.001) and EDV (P<0.001) of the OA, significantly decreased PSV (P= 0.017) and EDV (P = 0.046) of the CRA, and significant decrease in EDV (P = 0.018) of SPCA. All the three vessels showed significantly increased RI; OA (P = 0.036), CRA (P = 0.008) and SPCA (P = 0.033).*

***Conclusions:*** *We found decreased flow and increased resistivity index in the ocular vasculature in NTG and CDI may provide an effective and non-invasive method to evaluate vascular component in glaucoma.*

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***Keywords:*** *Color Doppler Imaging (CDI), Normal Tension Glaucoma (NTG), End Diastolic Velocity (EDV), Peak Systolic Velocity (PSV), Resistivity index (RI), Retrobulbar blood flow, Ocular Haemodynamic Parameters*

## Introduction

Ocular haemodynamics have been shown to be a major factor in the pathogenesis of glaucomatous optic neuropathy.[1-3] In addition, systemic vascular risk factors and vascular dysregulation have also been identified to contribute to glaucomatous etiology and may result in impaired ocular blood flow.[4-8] Despite the fact that the IOP in NTG patients is within the normal range, the glaucomatous optic neuropathy may keep getting worse progressively and irreversibly with time.[5,6] The disturbance in ocular blood flow is one of the significant risk factor in pathogenesis of NTG.[4-6] The vascular failure including vasospasms, small vessel disease, or autoregulatory dysfunction will lead to perfusion deficits of the optic nerve head, retina, and choroid and furthermore develop to the glaucomatous optic neuropathy in NTG compared to healthy subjects.[9] Earlier studies have also showed that the impaired vascular autoregulation was more pronounced in NTG than in high tension glaucoma (HTG), especially in NTG patients with progressive optic neuropathy than those with relatively stable status.[10,11]

New technologies for ocular blood flow evaluation have been introduced to clinical ophthalmology, and Color Doppler imaging (CDI) has its particular advantages because of its non-invasiveness and the reliability of its results.[12] This ultrasonic technique combines synchronous B-ultrasonic wave imaging with color which represents the movement of blood flow based on Doppler frequency shifts. Color Doppler imaging has been widely used in glaucoma to study pathogenetic aspects of the disease and the vascular effects of its treatment.[13-15] Color Doppler Imaging is an established method for qualitative assessment of blood flow in retrobulbar vessels (Ophthalmic artery, Central Retinal and Short Posterior Ciliary Artery). The fact that the optic nerve head perfusion is directly related to retrobulbar circulation, that is directly accessible to ultrasound study makes Color Doppler imaging a potential tool for the evaluation of early changes in vascular flow related to glaucoma.[13]

This study has been conducted to evaluate the retrobulbar hemodynamic parameters in NTG patients by Color Doppler imaging (CDI).

## Subjects and Methods

All study procedures adhered to the Declaration of Helsinki for research involving human subjects and informed consent was obtained from all participants. Data accumulation was carried out with Institutional Review Board approval. This was a hospital based cross-sectional study carried out in a Medical College Out Patient Department (OPD) for a period of one year i.e. from July 2014 to June 2015. A total of 20 patients with untreated NTG and 23 healthy

volunteers (controls) were randomly selected for the study. Inclusion criteria for the NTG group were IOP < 20 mmHg, gonioscopically open angles with characteristic glaucomatous optic disc appearance and visual field defects. Patients with lenticular and other media opacities, uveitis, myopia or hyperopia of more or equal to 5 diopters, retinal disorders other than glaucoma and those with systemic diseases or on systemic drugs for example diabetes, systemic hypertension, any cardiovascular disease, any neurological problem were excluded from the study. All patients with NTG and controls underwent a detailed ophthalmological examination, visual field testing, and CDI analysis of the retrobulbar blood vessels.

Visual field examinations were performed with the Humphrey Field Analyzer using the achromatic 24–2 full threshold or Swedish Interactive Threshold Algorithm (SITA) program. An ISTYLE (TOSHIBA Company) machine with 6-12 mHz linear high frequency probe was used for Color Doppler Imaging in the Medical College Radiodiagnosis Department. The examination was performed by a single experienced sonographer, who was unaware of subject's clinical status. The test was performed with undilated pupil. Patient was asked to lie supine with the eye closed and gaze directed to the ceiling. The ultrasound transducer was applied with sterile ophthalmic methylcellulose as a coupling agent, through the closed upper lid. The examiner's hand rested on the orbital margin to minimise the pressure over globe. Each eye was initially examined with B-scan in both transverse and sagittal planes.

This non-invasive method is based on the back-scattering of ultrasound by the formed elements in the blood vessels. Doppler effect results in frequency shifts, the measurement of which helps to assess blood velocity. In orbital CDI blood flow towards the transducer (usually arterial) is encoded as red and flow away from the transducer (usually venous) is encoded as blue. The anatomy of the eye followed by that of the optic nerve head were identified using the grey scale images in the B-scan mode. Color Doppler was used to visualize the flow within the vessels and allowed for identification of the appropriate vessels. Care was taken to place the sample volume in the centre of the vessel and to set the angle parallel to the vessel to account for the Doppler angle. Pulsed Doppler with spectral analysis is used in conjunction with the colour Doppler image for accurate quantification of the flow characteristics of vessels.

The sample volume depth was set at about 40 mm when imaging the ophthalmic artery (OA). The Doppler sample gate (≤2 mm) was then placed at the centre of the detected vessel to image the spectral pattern. The parameters of OA flow was measured nasally and superior to optic nerve soon after it crosses the optic nerve.[12] The flow velocity wave form of the ophthalmic artery (OA) is similar to that of the internal carotid artery, showing a high maximum peak systolic flow and low diastolic flow velocity. A dicrotic notch because of aortic valve closure is usually present and a window indicate relatively uniform blood velocity (Figure 1).

The central retinal artery (CRA) leaves the second part of the OA and enters the inferior surface of the optic nerve about 12 mm behind the globe.[12] It possess straighter course in optic nerve and lie in close proximity to the central retinal vein. With orbital CDI the CRA and CRV are easily identified within the optic nerve and their colour images are immediately adjacent to each other with artery on the nasal side and the vein to the temporal side. CRA waveform shows pulsatile arterial flow with a steep systolic peak suggesting a high-resistance distal vascular bed (Figure 2).

The nasal and temporal short posterior ciliary arteries (NPCA and TPCA) are located on each side of the optic nerve and need to be measured at a position that is close to the optic nerve.[12] It should also be as anterior as possible to avoid receiving noise from the choroid. Color Doppler imaging could not distinguish individual short posterior ciliary vessels. Therefore, the obtained waveform represented the mass effect produced by bundle of vessels rather than from individual ciliary vessels. The waveform in these vessels are almost similar to CRA but often with a sharper PSV (Figure 3).

The Peak Systolic Velocity (PSV) and End Diastolic Velocity (EDV) values were obtained by taking the velocity reading at the peak of the spectral wave pattern and that at the wavetrough, respectively. Three readings of each artery were obtained and the average was taken, this was to minimize intra observer error. Resistivity index (RI) was calculated as (PSV − EDV)/ PSV. Before measurement of retrobulbar haemodynamics, systolic and diastolic blood pressures as well as the heart rate were measured after rest of 5 min in the supine position. Intraocular pressure (IOP) was measured in a sitting position using Goldmann applanation tonometry before CDI.

A written informed consent was taken from each participant after explaining them about the nature & consequence of study. Privacy & confidentiality was assured. The study protocol was approved by the institutional ethics committee of the Medical College.

## Statistical Analysis

Data was entered and analyzed using SPSS software ver 20. Data normalcy was checked using Shapiro-Wilks test. Descriptive analysis in the form of mean and SD was done. Inferential analysis in the form independent t-test was used to compare the haemodynamic parameters of retrobulbar flow between NTG and controls. P value less than 0.05 was considered statistically significant.

## Results

Table 1 shows the baseline characteristics of study population. The study population comprised of 26 males (NTG-12, control-14) & 17 females (NTG-08, control-09) (p = 0.954). The mean age of NTG group was 53.27±11.11 years while that of control group was 49.39±9.56 years (p=0.301). The mean IOP of NTG patients (17.36±1.36 mmHg) was comparable to controls (17.04±1.26 mmHg) (p = 0.504). There were no significant difference in the vitals of the NTG and controls as shown in the Table 1.

Patients with NTG showed significantly decreased PSV in OA and CRA, significantly decreased EDV in OA, CRA and SPCA and significantly increased RI in all the three vessels (OA, CRA and SPCA) as shown in Table 2.

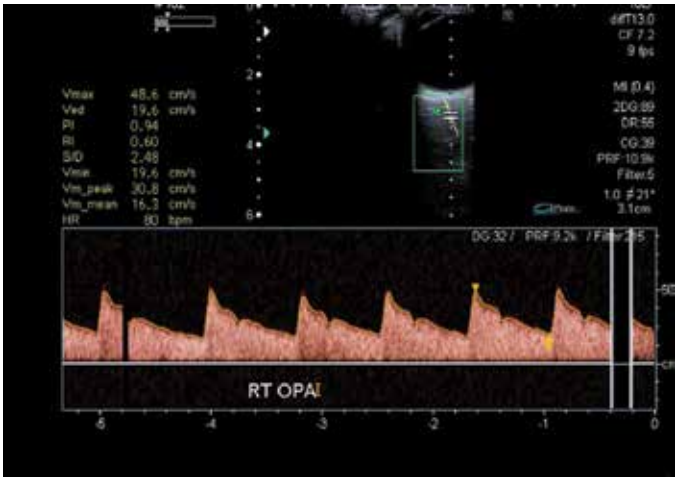


**Figure 1:** *Color Doppler Imaging of Ophthalmic Artery and characteristic waveform*

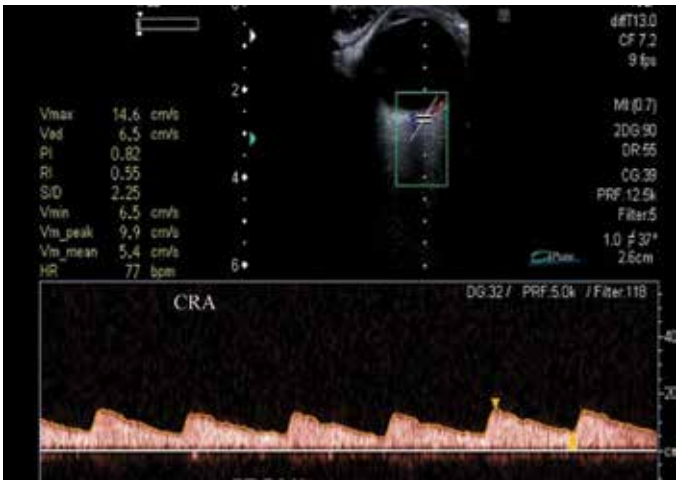


**Figure 2:** *Color Doppler Imaging of Central Retinal Artery and characteristic waveform*

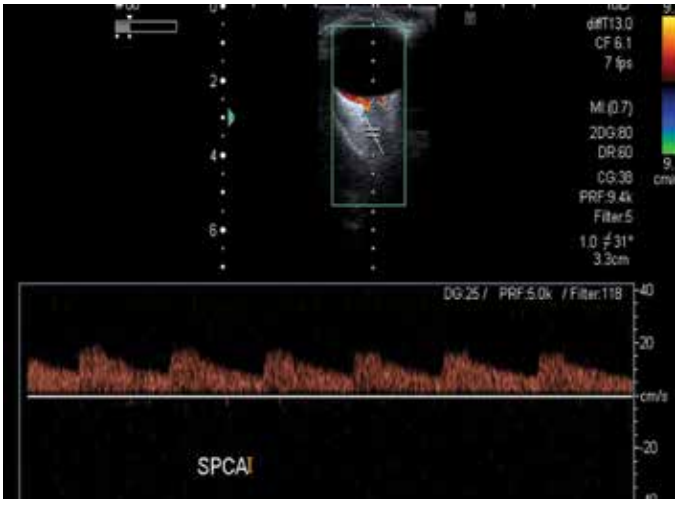


**Figure 3:** *Color Doppler Imaging of Short Posterior Ciliary Artery and characteristic waveform*

**Table 1: Baseline characteristics of study population**

| Parameters | Controls (n=23) | NTG (n=20) | P value |
|---|---|---|---|
| Sex (male/female) | 14/09 | 12/08 | 0.954 |
| | MEAN ± SD | MEAN ± SD | |
| Age (years) | 49.39±9.56 | 53.27±11.11 | 0.301 |
| IOP (mmHg) | 17.04±1.26 | 17.36±1.36 | 0.504 |
| PR (beats/min) | 79.65±5.89 | 78.90±4.04 | 0.709 |
| SBP (mmHg) | 128.96±5.18 | 133.09±6.02 | 0.067 |
| DBP (mmHg) | 80.35±3.98 | 83.64±5.78 | 0.061 |
| AXL (mm) | 22.99±0.70 | 23.22±0.92 | 0.444 |
| ACD (mm) | 3.48±0.53 | 3.79±0.51 | 0.112 |

*IOP-intraocular pressure, PR- pulse rate, SBP- systolic blood pressure, DBP- diastolic blood pressure, AXL- axial length, ACD- anterior chamber depth.*

**Table 2: Comparison of ocular haemodynamic parameters of controls and Normal Tension Glaucoma patients**

| Parameters | Controls (n=23) MEAN ± SD | NTG(n=20) MEAN ± SD | P value |
|---|---|---|---|
| OA-PSV | 38.79±9.07 | 20.05±6.89 | <0.001 |
| OA-EDV | 13.70±6.26 | 5.19±1.36 | <0.001 |
| OA-RI | 0.64±0.11 | 0.72±0.67 | 0.036 |
| CRA-PSV | 11.37±2.68 | 9.08±1.97 | 0.017 |
| CRA-EDV | 4.05±1.49 | 3.03±1.40 | 0.046 |
| CRA-RI | 0.63±0.12 | 0.88±0.37 | 0.008 |
| SPCA-PSV | 12.28±2.22 | 11.28±2.43 | 0.240 |
| SPCA-EDV | 5.05±1.69 | 3.66±1.07 | 0.018 |
| SPCA-RI | 0.58±0.11 | 0.67±0.94 | 0.033 |

*PSV = Peak Systolic Velocity, EDV = End Diastolic Velocity, RI =Resistive Index*

## Discussion

The problem in the optic nerve circulation resulting from localized organic changes in the blood vessels of the nerve with or without a low perfusion pressure has been implicated as one of the likely mechanisms in the pathogenesis of glaucomatous damage.[5] The OA, CRA and SPCA are vessels in providing evidence of the influence of vascular factors in pathogenesis of glaucomatous optic neuropathy. Color Doppler Imaging is a reproducible technique for evaluation of ocular vessels.[14] The blood flow velocities in these vessels in glaucomatous and non-glaucomatous eyes were the focus of this study.

The present study confirmed reduced PSV in OA and CRA, reduced EDV in OA, CRA and SPCA and significantly increased RI in all the three vessels ( OA, CRA and SPCA). Result of this study was comparable to previous study. It is generally considered that the OA is the main source of blood supply to the optic nerve; the SPCAs are the main source for optic nerve head (ONH) perfusion with small contributions from the pial vessels and CRA, and the blood supply of retina mainly from the CRA[15]; CRA and all SPCA are branches of the OA. Therefore, the hemodynamic parameters of the OA, CRA and SPCA can show the blood supply conditions of the ONH and retina.

Rojanapongpun et al showed that when compared to normal subjects NTG patients showed a significant reduction in

mean PSV and mean EDV of OA.[16] The mean PSV in NTG was 35.35±1.20 cm/sec when compared to normal 43.86±1.32 cm/s, this difference was statistically significant. The mean EDV in normal and NTG patients were 11.92±0.44 cm/s and 8.96±0.41 cm/sec respectively. Zahida et al found significantly decreased EDV in NTG patients when compared to normal in OA and CRA. RI was significantly increased in OA and CRA of NTG patients when compared to normal.[17] Klingmuller et al found statistically significant decrease in PSV and EDV of SPCA when compared to normal and significantly higher RI in SPCA when compared to normal.[18] Plange et al found significantly decreased PSV and EDV of the CRA, significantly decreased EDV of the SPCA, and significantly increased RI of the temporal SPCAs compared to healthy controls.[19] Mamikonian et al was also found that NTG is associated with a more significant decrease of ocular blood flow volume and found a statistically reliable correlation between volumetric and velocity parameters of ocular blood flow in NTG.[20] Abegão et al found lower retrobulbar blood flow in NTG patients.[21]

## Conclusions

This CDI study results showed decreased flow and increased resistivity index in ocular vasculature in NTG as compared to non-glaucomatous eyes suggesting the importance of ocular blood flow analysis in NTG and necessity to know not only the IOP, but also the ocular blood flow. CDI can be an effective and non-invasive tool to evaluate ocular blood flow.

## Limitations

The limitation of this study was less number of patients. This study being a cross-sectional study on newly diagnosed NTG group yet to commence anti-glaucoma medications could not assess the effect of lowering IOP on the blood flow parameters studied. The third limitation was that a highly trained personnel was needed to obtain reproducible data. Another limitation was that CDI measures the vessels that supply tissue but not the flow within the retinal tissue or at the level of the ganglion retinal cells.

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