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Original Research Article

Normal Tension Glaucoma versus Primary Open-Angle Glaucoma: A Comparative Study

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Abstract

Aim: The study was conducted to determine the functional and structural differences between NTG and POAG, to assess the rate of conversion of NTG into POAG and its early intervention.

Material & Methods: A comparative study including 200 patients attending the Department of Regional Institute of Ophthalmology screened during the period of 2 years.

Results: Mean age was found to be 57.73 years in NTG and 56.04 in POAG. NTG was more common in females (60%), whereas POAG was more common in males (72%). Systemic involvement was more common in NTG (70%). There was no significant difference in CDR between two groups. Temporal (30%) and inferior (40%) NRR thinning was more common in NTG, whereas bipolar thinning (56%) was more common in POAG. Retinal Nerve Fiber Layer (RNFL) was significantly thinner in POAG in all four quadrants. There were no significant changes in MD and PSD values of Visual fields (VF) between NTG and POAG. NTG showed localized field defects which were closer to centre of fixation, while it was diffuse and denser in POAG. No significant changes were observed in VF on follow up.

Conclusion: These differences between NTG and POAG suggest that the pathogenesis of NTG includes IOP and IOP independent risk factors, while IOP is the main risk factor in POAG. The parameters assessed determine the risk and progression of NTG to POAG.

Keywords: Intraocular Pressure (IOP), Primary Open-Angle Glaucoma (POAG), Normal Tension Glaucoma (NTG).

Introduction

Glaucoma is progressive optic neuropathy that causes characteristic changes of the optic nerve and visual field in relation to intraocular pressure (IOP). [1] For many years, it has been common practice to separate primary open-angle glaucoma (POAG) into two distinct clinical entities on the basis of intraocular pressure (IOP), with glaucomatous optic neuropathy(GON), the only difference between normal tension glaucoma (NTG) and primary (or chronic) open-angle glaucoma (POAG) is that the former patients have intraocular pressures (IOP) that are consistently at or below 21 mmHg, while the latter have pressures above this level. [2] NTG may be simply a form of open angle glaucoma in which one of the signs (IOP) is absent. [3] In established NTG, visual field defects are typically glaucomatous in nature but as in POAG, early visual field loss can be subtle and difficult to differentiate from normal variations in visual thresholds. During recent years, however, additional risk factors, such as ocular and systemic circulation abnormalities, have been linked to the cause and progression of both POAG and NTG and IOP reduction has been shown to have a positive effect on disease progression in both conditions. [4]

The aetiology of NTG is likely to be multifactorial, as is probably the case with POAG. [5] In POAG, axonal damage at the optic nerve could be secondary to the effect of elevated intraocular pressure ('baro-trauma' at the pre-laminar portion of the disc) but it is also possible that ischaemia, hypoxia, disruption of axoplasmic transport or a genetically determined accelerated apoptosis is responsible for the optic neuropathy characteristic of glaucoma. More than one mechanism may

contribute to the pathology in some individuals. In NTG, IOP is considered to be a risk factor of lesser significance than in POAG and other factors take on greater significance. Various vascular and cardiovascular disorders are recognised as being risk factors for NTG. [6,7,8] They include systemic hypotension, arterial hypertension, previous haemodynamic crisis, increased blood viscosity, diabetes, migraine and other vasospastic disorders. Each of these risk factors tends to support a vascular cause, or at least a vascular component in the cause of' glaucoma, where optic nerve perfusion may be affected by longstanding systemic hypertension, or sustained or acute hypotension.

Optical coherence tomography angiography (OCTA) enables visualization of the fine microvasculatures of multiple retinal layers, and many OCTA studies have reported impairment of the retinal microvasculature in patients with glaucoma. Hou et al. [9] reported that OCTA-based superficial macular vessel density (VD) was significantly lower in primary open-angle glaucoma (POAG) eyes than in healthy ones. Scripsema et al. [10] found that the OCTA-measured annular perfused capillary density in normal-tension glaucoma (NTG) patients was significantly lower than that in normal controls. Although microvasculature impairment is evident in both NTG and POAG, the extents may differ because the pathological mechanisms of the two diseases may be different. Several studies have reported impairment of the retinal microvasculature in both eyes with NTG and POAG; however, studies comparing detailed microvasculature pathologies are lacking. Hence the aim of study was to determining the differences in functional and structural deficits in NTG and POA and rate of progression of NTG into POAG.

Material & Methods

A comparative study including 200 patients attending the Department of Regional Institute of ophthalmology, IGIMS, Patna, Bihar, India screened during the period of 2 years.

Inclusion criteria

1. Patients during Gonioscopy showing open angles,
2. Optic nerve cupping,
3. Corresponding visual field defects were taken into study.

Exclusion criteria

1. Ocular hypertensives,
2. Patients with Primary angle closure glaucoma, Secondary glaucoma and Corneal disorders,
3. Posterior-segment pathologies and non-glaucomatous optic neuropathy were excluded from the study.

Diurnal IOP was recorded and subjects divided into two groups based on the readings.

- GROUP I- Patients with <21mmHg IOP (50) were put in NTG group.
- GROUP II- Patients with >21mmHg (50) were grouped into POAG group.

Methodology

Detailed history was taken from all the patients and ocular examination of both eyes was done, which included visual acuity with Snellen's chart, Slit-lamp biomicroscopy, IOP was measured using Goldmann applanation tonometer, Indirect Gonioscopy using Goldmann three mirror lens, optic disc evaluation was done with slit-lamp biomicroscopy using by 78 D, Time domain OCT (Zeiss Cirrus HD OCT) done to asses RNFL parameters, Pachymetry was done and Visual fields assessment were done using Zeiss Humphrey field-analyser. Each patient was followed-up till 34 months.

Statistical Analysis

Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 are used for the analysis of the data. Student t test, Chi-square test / Fisher Exact test were used to study the significance of study parameters. Leven's test was performed to assess the homogeneity of Variance. P-value of 0.05 was considered as significant.

Results

Table 1: Demographic comparison of patients and Mean disc CDR comparison between the two groups

Variables	Group I (NTG)	Group II (POAG)	P Value
Gender			
Male	60 (60)	71 (72)	0.001
Female	40 (40)	28 (28)	
Mean	57.73 Yrs	56.04 Yrs	0.002
Systemic involvement			
Yes	70 (70)	50 (50)	0.012
No	30 (30)	50 (50)	
Mean Disc CDR			
Right	0.65±0.15	0.72±0.08	0.450
Left	0.70±0.10	0.77±0.13	

Mean age was found to be 57.73 years in NTG and 56.04 in POAG. NTG was more common in females (60%), whereas POAG was more common in males (72%). Systemic involvement was more common in NTG (70%). There was no significant difference in CDR between two groups.

Table 2: Disc NRR distribution of patients in two groups of patients studied

	NTG			POAG	
Disc NRR	**Right Eye**	**Left Eye**	**Disc NRR**	**Right Eye**	**Left Eye**
WNL	14(14%)	6(6%)	WNL	2(2%)	2(2%)
Temporal thinning	30(30%)	32(32%)	Temporal thinning	24(24%)	8(8%)
Bipolar thinning	10(10%)	14(14%)	Bipolar thinning	40(40%)	56(56%)
IR Thinning	36(36%)	40(40%)	IR Thinning	6(6%)	0(0%)
Superior thinning	2(2%)	4(4%)	Superior thinning	28(28%)	26(26%)
Superior notch	6(6%)	2(2%)	Superior notch	0(0%)	0(0%)
All rims thinned	2(2%)	2(2%)	All rims thinned	0(0%)	0(0%)
Inferior thinning	0(0%)	0(0%)	Inferior thinning	0(0%)	6(6%)

Temporal (30%) and inferior (40%) NRR thinning was more common in NTG, whereas bipolar thinning (56%) was more common in POAG. Retinal Nerve Fiber Layer (RNFL) was significantly thinner in POAG in all four quadrants.

Table 3: Distribution of RNFL thickness on OCT

RNFL	NTG	POAG	P Value
Superior Quadrant	83.67±15.5	55.35±7.33	<0.001
Inferior quadrant	86.04±12.48	58.62±8.16	<0.001
Nasal quadrant	64.36±13.47	48.02±6.74	<0.001
Temporal quadrant	56.24±5.25	46.04±6.84	<0.001
Average thickness	66.44±6.34	55.65±6.34	<0.001

There were no significant changes in MD and PSD values of Visual fields (VF) between NTG and POAG. NTG showed localized field defects which were closer to centre of fixation, while it was diffuse and denser in POAG.

Table 4: Visual fields- distribution of patients in two groups of patients

Visual fields	NTG	POAG	P Value
Right eye			
MD (Db)	-16.14±7.43	-18.22±8.02	0.242
Mean PSD	8.32±3.14	12.48±3.20	0.002
Left eye			
MD (Db)	-16.24±6.84	-17.43±6.44	0.314
Mean PSD	9.51±2.88	2.08±3.67	0.005

No significant changes were observed in VF on follow up.

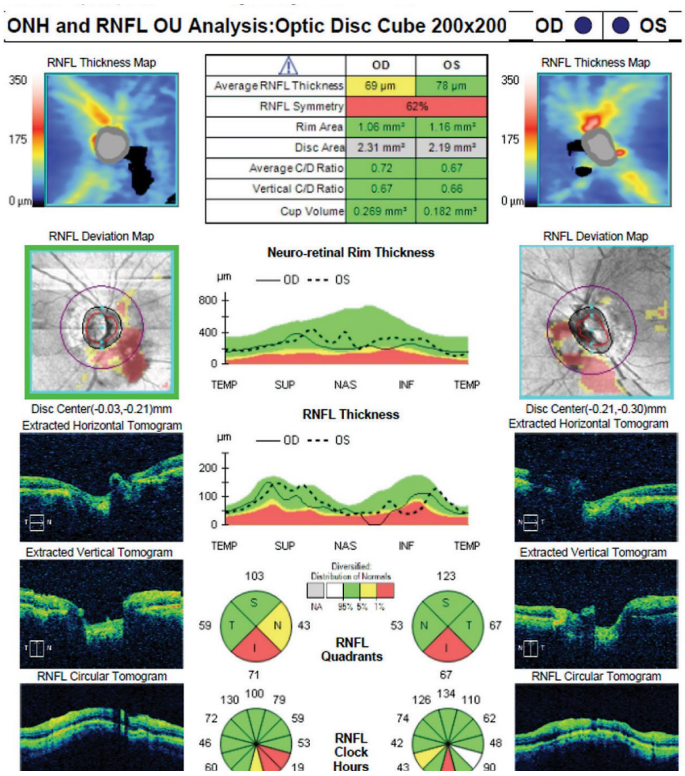

Figure 1: RNFL OCT showing bilateral inferior rim thinning

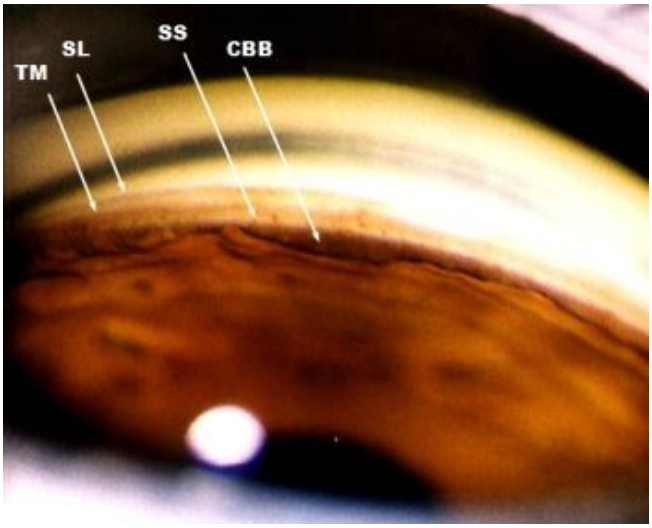

Figure 2: Gonisoscopic picture of open angle. All four structures are visible. (SL – Schwalbe's line, TM – trabecular meshwork, SS – Scleral spur, CBB – ciliary body band)

Discussion

Glaucoma is a chronic progressive optic neuropathy with characteristic optic nerve head changes and visual field defects for which increased IOP is an important risk factor. Although factors other than IOP are involved in glaucoma, IOP is important because it is the only risk factor which can be pharma co modulated to date. Cartwright and Anderson in their study on patients with NTG with asymmetric IOP showed that glaucomatous damage was greater in the eye with higher IOP. [11] Visual field loss of patients whose IOP is lowered pharmacologically is usually slowed. [12] Most glaucoma patients appear to have abnormal sensitivity to IOP that may be offset if IOP is lowered to mid normal or low normal range and perhaps 90% or more may benefit from sufficiently low IOP. Measurement of accurate IOP is important not only for classification but for clinical management of glaucoma patients. It is important therefore to ensure that IOP readings are taken using highly accurate method. Goldman Applanation Tonometry (GAT) has been considered to be the gold standard for measurement of IOP. Ehlers et al have shown that central corneal thickness affects the accuracy of applanation

tonometry. Reduced corneal thickness of 0.45mm causes an underestimation of IOP by up to 4.7mmHg, whereas an increased CCT of 0.59mm could cause an overestimation of 5.2mmHg. [13] Therefore in individuals with thick cornea, IOP measurement by GAT may show falsely high readings and for thin cornea low readings.

Mean age was found to be 57.73 years in NTG and 56.04 in POAG. NTG was more common in females (60%), whereas POAG was more common in males (72%). Systemic involvement was more common in NTG (70%). There was no significant difference in CDR between two groups. Copt RP et al in their study found no significant difference in CCT between controls (552 +/- 35 microns) and patients with POAG (543 +/- 35 microns), but the CCT in the group with NTG (521 +/- 31 microns) was significantly lower than that in the control group or the group with POAG ($P < .001$), and the CCT in the group with OHT (583 +/- 34 microns) was significantly higher than in controls or patients with POAG ($P < .001$) and concluded that underestimation of IOP in patients with POAG who have thin corneas may lead to a misdiagnosis of NTG, while overestimation of the IOP in normal subjects who have thick corneas may lead to a misdiagnosis of OHT. [14]

Thomas R and associates in their study of effect of CCT on applanation reported that there was a statistically significant difference in the mean CCT of the ocular hypertensive's (0.574 +/- 0.033 mm) as compared to the glaucoma (0.534 +/- 0.030 mm) and normal's (0.537 +/- 0.034 mm). Measurement of central corneal thickness is advisable when the clinical findings do not correlate with the applanation IOP. [15] Ventura et al measured CCT in NTG, POAG, OHT and pseudoexfoliatives using optical low coherence reflectometry which is a more precise method than ultrasound pachymeter and confirmed that a significant number of patients with OHT have normal IOP after appropriate adjustments. [16]

Shah S, Chatterji A, Mathai M et al found corneal thickness as a confounding factor in classification of glaucoma patients and reported that patients with thick corneas and high IOP's may not be followed as Glaucoma suspects. [17] Shah S, Spedding C et al assessed the diurnal variations in CCT of Glaucoma suspects and found no significant variation in CCT and concluded that a single measurement of CCT is sufficient when assessing patients with suspected glaucoma. [18] Singh RP and associates measured a CCT of 538 ± 51 microns in NTG patients, 570 ± 32 microns in OHT patients, 547 ± 34 microns in POAG patients and 554 ± 32 microns in normal's showing a significant difference and when CCT is markedly different from normal, the clinician may need to consider this in the diagnosis and management. [19] Temporal (30%) and inferior (40%) NRR thinning was more common in NTG, whereas bipolar thinning (56%) was more common in POAG. Retinal Nerve Fiber Layer (RNFL) was significantly thinner in POAG in all four quadrants. There were no significant changes in MD and PSD values of Visual fields (VF) between NTG and POAG. NTG showed localized field defects which were closer to centre of fixation, while it was diffuse and denser in POAG. No significant changes were observed in VF on follow up.

Conclusion

These differences between NTG and POAG suggest that the pathogenesis of NTG includes IOP and IOP independent risk factors, while IOP is the main risk factor in POAG. The parameters assessed determine the risk and progression of NTG to POAG. This study confirmed that central corneal thickness is significantly lower in normal tension glaucoma patients compared to controls and primary open angle glaucoma patients whereas ocular hypertension patients have significantly higher central corneal thickness than controls and primary open angle glaucoma patients. No significant difference is found between primary open angle patients and controls.

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