

Analysis of Ganglion Cell Complex in Various Stages of Primary Open Angle Glaucoma

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ABSTRACT

Introduction: Glaucoma is a major public health problem, causing visual impairment which hampers day to day work. The disability caused by glaucoma is irreversible. It is a 'silent killer' as most of the time, it is asymptomatic up to the very advanced stage and at the time of presentation to the ophthalmologist, the visual loss is often irrecoverable.

Materials and methods: 100 control & 100 primary open angle glaucoma POAG patients were analysed for Ganglion Cell Complex (GCC). In all the patients clinical examination included assessment of visual acuity, evaluation of refractive status, Intraocular pressure (IOP) measurement, slit-lamp bio microscopy with +90D lens, Gonioscopy, Visual field charting by Humphrey Field Analyser (HFA) and scanning with the Cirrus spectral domain – optical coherence tomography (SD-OCT).

Result: Of 100 patients of POAG and equal number of controls analysis revealed that overall Ganglion Cell Complex thickness in POAG cases ($60.40 \pm 19.1 \mu\text{m}$) was less than in controls ($114.70 \pm 18.8 \mu\text{m}$) and this difference is statistically significant ($p < 0.001$).

Conclusion: As the severity of glaucoma increases the overall average GCC thickness becomes progressively thinner. The Ganglion Cell Complex thickness is reduced in POAG.


Keywords: Glaucoma, Ganglion cell layer, OCT.

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INTRODUCTION

About 60 million persons are estimated to be affected by glaucoma. Of these, an estimated 11.2 million cases are from the Indian subcontinent.^{1,2} It is the world's second leading cause of irreversible blindness¹. Glaucomatous neuronal death is not limited to changes in the retinal ganglion cell axons, soma, and dendrites,³ neurons in the lateral geniculate nucleus⁴⁻⁶ and the visual cortex⁴ are also lost. Outcomes of both functional (psychophysical) testing⁴ and histological studies suggest that the pathological process does not discriminate among subsets of retinal ganglion cells. Glial cells also are affected, and it is possible that astrocytes, perhaps activated by raised intraocular pressure or by other mechanisms, alter the environment of the axons and produce a milieu that causes axonal degeneration or that prevents survival of the healthy retinal ganglion cells.^{5,6} Glaucomatous optic neuropathy causes progressive death of retinal ganglion cells and their axons. These structural changes precede visual field (VF) defects as measured by standard automated perimetry. The level of intraocular pressure is unquestionably related to the death of retinal ganglion cells and optic nerve fibers in some, if not all, patients with POAG. When pressure increases above physiological levels, the pressure gradient across the lamina cribrosa also increases. As a result, the lamina cribrosa and the retinal ganglion cell axons undergo deformation and mechanical stress.⁵

In POAG, retinal ganglion cell axon compression can impair trophic factor axonal transport, causing death of the cells by trophic insufficiency. Excessive stimulation of the glutamatergic system, specifically the N-methyl-D-aspartate subtypes, has also been proposed to contribute to death of retinal ganglion cells in glaucoma.⁶⁻⁸ The response to an initial optic nerve injury in glaucoma also can lead to secondary neurodegeneration among surviving retinal ganglion cells and their fibers.

Optical Coherence Tomography (OCT) can give very accurate parameters for optic nerve head assessment along with the retinal nerve fibre layer analysis⁶ With the help of optical coherence tomography OCT it is possible to detect the loss of ganglion cell complex (GCC). The ganglion cell complex has the maximum density at the macula. Roughly, one lac ganglion cells are found in the human retina and half of this number is centered on the fovea. This anatomic arrangement suggests that a macula scan with GCC analysis could be an early indicator for impending damage caused by POAG.⁷

Optical coherence tomography, a well-accepted tool for glaucoma diagnosis, Spectral domain OCT (SD-OCT) is a recent technique that enables the imaging of ocular structures with higher resolution and faster scan rate compared with the previous version of this technology.⁸

In addition to the changes that occur in optic nerve head (ONH)

and Retinal nerve fibre layer (RNFL), another region that has been proposed to manifest changes in glaucoma is the macula, because more than 50% of the ganglion cells in the retina are located at macula and the ganglion cell layer is more than one-cell-layer thick at the macula.^{19,20} This study was done to analyze the ganglion cell complex among the patients of POAG and to correlate it with the severity of the disease.

MATERIALS AND METHODS

This was a **cross** sectional study conducted at Tertiary Medical College in North India. This study was conducted in accordance with the tenets of the Declaration of Helsinki and was approved by an institutional review board. 100 control and 100 POAG patients were analysed for Ganglion Cell Complex. Patients with Advanced lens opacities ,prior ocular surgeries, H/O Laser treatments ,refraction – Spherical>5.0 D Cylinder>3.0D, Age related macular degeneration (ARMD), Diabetes Mellitus ,hypertension were excluded from the study.

An individual (age > 40 years) was included in the study as a case of POAG only if he / she met with at least two of the following three criterias: Elevated intraocular pressure (IOP) greater than 21mm Hg without treatment on at least two separate visits; Vertical asymmetry of cup disk ratio (CDR) > 0.2 between two eyes. High CDR > 0.6 . And the Control Group comprised of Individuals (age >40 years) having I.O.P within normal range (11-20 mm Hg) and no glaucoma.

In all the patients clinical examination included assessment of visual acuity by Snellen’s chart, evaluation of refractive status by Retinoscopy, IOP measurement by applanation tonometry, slit-lamp bio microscopy with +90D lens, Gonioscopy, Visual field charting by Humphrey Field Analyser (HFA).

All included subjects were scanned with the Cirrus SD-OCT (software version 4.0) Carl-Zeiss Meditec Inc., Dublin, CA) by a

single operator. Statistical analysis was done using Statistical Package for Social Sciences, version 20.0.

Table 1: Severity Grade of POAG (N=100) (Based on visual field by HFA: Hodapp’s grading)

Severity of POAG	No. of Cases (N=100)
Pre perimetric	12 (12.0%)
Mild	20 (20.0%)
Moderate	56 (56.0%)
Severe	12 (12.0%)
Total	100(100.0)

(Preperimetric POAG cases did not show any defect/abnormal finding in HFA)

RESULTS

To analyze the Ganglion Cell Complex among the patients of POAG we evaluated 100 patients of POAG and equal number of controls. Among cases there were 42 males, and 58 females, whereas among controls there were 44 males and 56 females. Majority of controls as well as patients were in the age group of 51-60 years (38 and 43 respectively). The age categories and Gender wise variation in the patients and control groups was not statistically significant.

The data distribution of Ganglion Cell Complex layer thickness analysis in POAG group is given in (Table 2). The severity of glaucoma increases the overall average GCC thickness becomes thinner further and further.

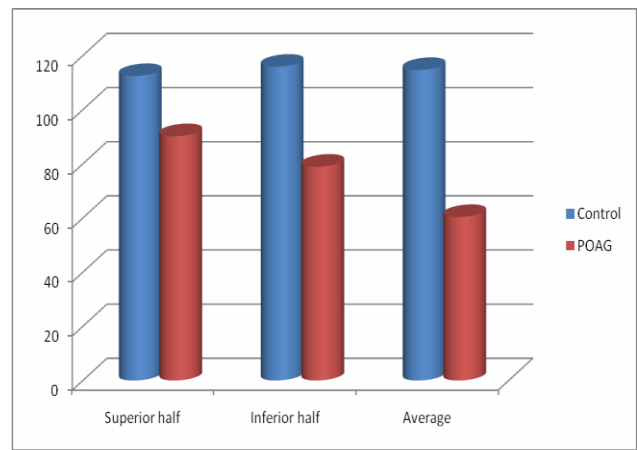
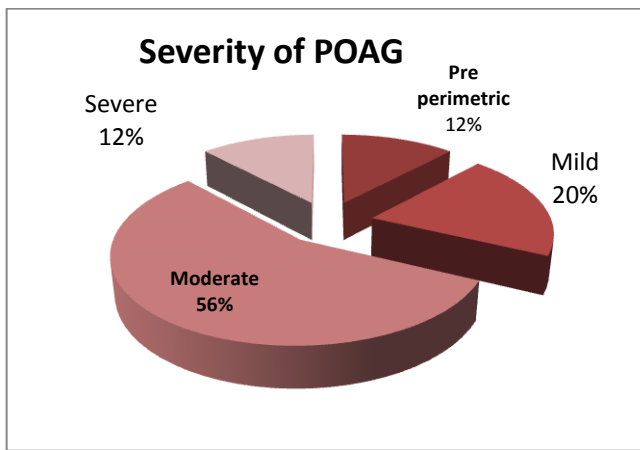
Comparison of Average Ganglion cell complex GCC thickness in control and cases POAG group is given Table 3. The analysis reveals that overall GCC thickness in POAG cases (60.40±19.1µm) was less than in controls (114.70±18.8µm) and this difference is statistically highly significant (p<0.001).

Table 2: Data Distribution; GCC Thickness by OCT in POAG Group (N=100)

MACULAR AREA	Severity grade of POAG	GCC THICKNESS (µm)			
		120±10	100±10	80±10	60±10
SUPERIOR	Preperimetric (n=12)	1(8.3%)	6 (50%)	4 (33.3%)	1 (8.3%)
	Mild (n=20)	4 (20%)	12 (60%)	2 (10%)	2 (10%)
	Moderate (n=56)	5 (8.9%)	12 (21.4%)	23 (41.1%)	16 (28.5%)
	Severe (n=12)	0 (0%)	1 (8.3%)	5 (41.6%)	6 (50%)
INFERIOR	Preperimetric (n=12)	2(16%)	6(50%)	3(25%)	1 (8.3%)
	Mild (n=20)	2 (10%)	9 (45%)	8 (40%)	1 (5%)
	Moderate (n=56)	5 (8.9%)	14 (25%)	30 (53.5%)	7 (12.5%)
	Severe (n=12)	0 (0%)	2 (16.7%)	4 (33.3%)	6 (50%)
AVERAGE	Preperimetric (n=12)	2(16%)	4 (33.3%)	5 (41.6%)	1 (8.3%)
	Mild (n=20)	1 (5%)	7 (35%)	7 (35%)	5 (25%)
	Moderate (n=56)	7 (12.5%)	11 (19.6%)	15 (26.7%)	23 (41.1%)
	Severe (n=12)	0 (0%)	1 (8.3%)	4 (33.3%)	7 (58.3%)

Table 3: Comparative evaluation GCC thickness (µm); Control v/s Case (POAG) group

MACULAR AREA	CONTROL (n=100)	POAG (n=100)	p value
Superior half	112.47±18.5	90.28±18.7	0.001
Inferior half	115.91±19.1	78.98±19.2	0.001
Average	114.70±18.8	60.40±19.1	0.001



DISCUSSION

In the present study we aimed to study the changes in ganglion cell complex in primary open angle glaucoma in relation to different grades of its severity and correlate GCC parameters with visual field indices.

The Intraocular pressure variation among POAG cases, ranged from <20 to > 50mm Hg with overall mean IOP 31.52 ± 9.2 mmHg. In about 32 (32%) cases the ocular pressure was between 40 - 50 mmHg which was the maximum for the age group.

Severity of Primary Open Angle Glaucoma (POAG) cases was assessed based on visual field analysis by HFA: using Hodapp’s grading system (Table 1). The patients were categorized as Mild 20 (20.0%) cases, Moderate 56 (56.0%) cases and Severe 12 (12.0%) cases.

The data distribution of Ganglion Cell Complex layer thickness analysis in POAG group is given in (Table 2). In superior quadrant majority patients in preperimetric group 6 (50%) and in mild group 12 (60%) cases were in the range 100±10µm, while moderate glaucoma 23 (41.1%) cases were in the range 80±10µm and severe 6 (50%) were in the range 60±10µm. In inferior macular quadrant the GCC thickness in majority preperimetric group, 6 (50%) cases and mild group 9 (45%) was in the range 100±10 µm. In moderate 30 (53.5%) cases GCC thickness was in the range of 80±10 µm and in severe 6 (50%) were in the range 60±10µm. The overall GCC thickness in majority preperimetric and mild glaucoma cases (41.6% and 35% respectively) was in range of 80±10 µm and was in lowest range of 60±10µm in maximum moderate and severe glaucoma cases (i.e 41.1% and 58.3% respectively). The above observation clearly suggests that as the severity of glaucoma increases the overall average GCC thickness becomes thinner further and further.

Comparison of Average Ganglion cell complex GCC thickness in control and cases POAG group is given Table 3. The analysis reveals that overall GCC thickness in POAG cases (60.40±19.1µm) in which less than in controls (114.70±18.8µm) and this difference is statistically highly significant (p<0.001). The comparison of GCC thickness between superior and inferior macular area shows that in the inferior macular area shows that in the inferior area GCC thinning is more marked.

The Ganglion Cell Complex was studied at macular area level and its thickness (µm) evaluated in relation to severity of POAG and compared with controls. The GCC thickness in relation to severity of POAG i.e normal with preperimetric is analysed. In controls the mean GCC thickness in the Superior part was 112.47±18.5µm, while in the preperimetric POAG cases in the corresponding area

it was 99.47±18.5µm. In the Inferior part the thickness in controls 115.91±19.1µm as against the mean thickness in the preperimetric POAG cases in the same region was 102.91±18.9µm. The difference between the thicknesses was statistically highly significant (p<0.001). Further the average normal GCC thickness in controls was 114.70±18.8µm against which the mean average GCC thickness in preperimetric glaucoma cases was 101.2±19.4µm. The difference between the two average thicknesses too was statistically significant.

Avadshesh Oli and D. Joshi²¹ (2015) studied the ganglion cell complex assessment on (cirrus HD OCT) aid in detection of early glaucoma and they observed that the GCC was 69.19 I in glaucoma patients and it was 71 I in pre-perimetric glaucoma and 99.6 I and 85.16 I in controls respectively. Receiver operating characteristic curve for GCC was 0.83. GCC can be used as a supplementary tool in picking up cases of pre-perimetric glaucoma as loss is significant in pre-perimetric glaucoma also.

GCC thickness evaluated in relation to increasing severity of POAG and compared with normal i.e in mild glaucoma; moderate glaucoma and severe glaucoma followed the similar pattern as seen in preperimetric glaucoma i.e irrespective of severity grade of glaucoma the average GCC thickness as well as individually in both superior and inferior macular areas it was less as compared to normal controls. The thinning of GCC complex and its difference from normal control group in all the severity grades of glaucoma is statistically significant (p<0.001).

We found that values of GCC were lower both in glaucoma and preperimetric glaucoma patients indicating the importance and superiority of GCC analysis in early diagnosis of glaucoma. Experimental animal models have shown that GCC loss correlates well with visual field defects.¹⁶ In glaucoma GCC is first to be affected so evaluation of GCC is early indicator of damage GCC can be used as a supplementary tool in picking up cases of preperimetric glaucoma as Ganglion Cell Complex loss is significant in pre-perimetric glaucoma.²²

Ganekal S²³ (2012) studied the ganglion cell complex scan in the early prediction of glaucoma and they concluded that the ability to diagnose glaucoma with macular GCC thickness is comparable to that with peripapillary RNFL thickness. Macular GCC thickness measurements may be a good alternative or a complementary measurement to RNFL thickness assessment in the clinical evaluation of glaucoma.

GCC had also shown to be good predictor of damage due to glaucoma.²⁴ Some of the studies have tried to differentiate the type of glaucoma based on the nature of GCC loss but other

studies have failed to establish such a difference.²⁵ Periodic GCC measurements can be utilized to detect progression of glaucoma in very nascent stage.²⁶ The ability of GCC as compared to RNFL to detect early glaucoma is found to be slightly better in some studies.²⁷ Addition of GCC data to RNFL data has been found to enhance the detection of glaucoma in both preperimetric and perimetric groups.²⁸ Since this study did not include long term follow up of patients so further studies are required to study the role of serial RNFL and GCC scans in glaucoma progression.

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