

How to Cite:

Manade, V., Dhavalikar, S., Kotecha, M., & Paranjpe, R. (2022). Comparative study of retinal ganglion cell complex thickness with retinal nerve fibre layer and visual field changes in cases of suspicious disc or glaucoma suspect. *International Journal of Health Sciences*, 6(S1), 2007–2012.
<https://doi.org/10.53730/ijhs.v6nS1.4958>

Comparative Study of Retinal Ganglion Cell Complex Thickness with Retinal Nerve Fibre Layer and Visual Field Changes In Cases of Suspicious Disc or Glaucoma Suspect

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Abstract---Purpose: To compare and correlate macular ganglion cell complex thickness (GCC) with retinal nerve fibre layer (RNFL) and visual field (VF) changes in cases of suspicious disc or glaucoma suspect. Methods: A total of 60 glaucoma suspects, were included in the study group. These patients were subjected to standard investigations for glaucoma like tonometry, central corneal thickness (CCT), gonioscopy and funduscopy. Visual fields were assessed using automated static perimetry of Humphrey Automated Visual Field Analyser. The test used was central 30-2 SITA standard. Optical coherence tomography was done using RTvue, model 100 (version 5.1) to assess retinal nerve fiber layer (RNFL) and macular ganglion Cell complex thickness (GCC). Correlation of RNFL and GCC was evaluated using Pearson's correlation coefficient and correlation between GCC and VF was assessed using two independent sample t –test. Results: A total of 60 eyes of 60 glaucoma suspects, were enrolled in the study both males and females were included.

Keywords---fibre layer, ganglion cell complex, retinal nerve, suspicious disc, visual field.

Introduction

Glaucoma is an optic neuropathy with characteristic appearance of optic disc changes and specific patterns of visual field defects that is associated frequently but not invariably with raised intraocular pressure (IOP). Although elevated IOP is clearly the most frequent causative risk factor for glaucomatous optic atrophy, it is not the only factor. Three crucial parameters are considered as they relate to current understanding of glaucoma: intraocular pressure, the optic nerve, and the visual field. It is a progressive, irreversible optic neuropathy and the underlying process is the loss of Retinal Ganglion Cells (RGC). Because the macular region contains more than 50% of all the RGCs, assessing ganglion cell changes in the macular region may be more useful in diagnosing glaucoma than measuring peripapillary RNFL thickness (1).

In some cases, detecting RGC loss in the macula may allow for earlier detection of glaucoma which is essential for the initiation of pressure-reducing treatment to stop or delay progressive loss of visual function. Glaucoma is associated with characteristic structural changes in the optic disc and the RNFL, accompanied by functional VF loss. Thus, both structural and functional assessments are mandatory in glaucoma diagnosis. Often, structural change precedes functional deficit, as assessed by standard automated perimetry (2,3,4). The Fourier-domain optical coherence tomography (FD-OCT) offers comprehensive glaucoma evaluation by providing assessment of RNFL thickness, optic disc morphology, and GCC thickness, which is a combination of nerve fibre, ganglion cell, and inner plexiform layers. Glaucoma causes RGC loss and most of the ganglion cells are present in the posterior pole. Loss of RGCs lead to nerve fibre layer thinning and optic nerve head cupping. FD-OCT not only allows us to detect this measurable loss of RGCs and RNFL surrounding the optic nerve, but also can detect their loss in the macula with newly developed algorithms.

In nearly all cases, however, blindness from glaucoma is preventable. This prevention requires early detection and proper treatment. And hence distinguishing normal patients from those at risk for developing chronic open-angle glaucoma (COAG), that is, glaucoma suspects (GSs), is important because GSs need to be followed up more carefully to decide whether and when to begin prophylactic therapy. This study was done to find out diagnostic capability of macular GCC thickness and correlate it with RNFL and visual field changes in glaucoma suspects.

Materials and Method

A prospective observational study was conducted at a tertiary level ophthalmic institute in western Maharashtra over a period of 1 year. Institutional ethical committee approval was taken for the study. A total of 60 eyes of 60 patients were included in the study. The patients coming to the hospital outpatient department or being referred to the hospital were selected and included in the study as per inclusion and exclusion criteria. Written informed consent was taken from each patient before the study. Glaucoma suspect patients i.e., patients with any one of the following criteria: IOP >21 mmHg, C:D ratio >0.5, asymmetric C:D ratio i.e.,

difference of >0.2 between the two eyes or family h/o glaucoma were included in study.

Patients with age < 40 or > 79 years, Best-corrected visual acuity $< 20/40$, Spherical equivalent refractive error $> + 3.00$ or >-7.00 diopters, diabetic retinopathy or other diseases that could cause VF loss or optic disc abnormalities were excluded from study. Detailed history of patient was noted. Best corrected visual acuity and refraction were done to determine the refractive error. Thorough external ocular examination was done with torch light, followed by slit lamp examination. Intraocular pressure was recorded using Goldmann Applanation Tonometer. Gonioscopy was performed using Goldmann 3 mirror contact lens. The optic nerve head was examined using direct ophthalmoscopy and findings confirmed using $+90$ D non -contact fundus lens. CCT was measured using ultrasonic pachymeter. Visual fields were assessed using Humphery Automated Visual Field Analyser Model 740. The test used was central 30-2 SITA standard. OCT was done using RTvue, model 100 (version 5.1) to assess RNFL and Macular GCC thickness.

The p-value associated with a given measure is classified by the software as being 'within normal limits', 'borderline' and 'outside normal limits. A given result is color coded based on this classification where green indicates 'WNL', yellow indicates 'borderline' and red indicates 'ONL'. Statistical convention is to define the normal cut-off as a p-value of 5%. Results with p- value greater than 5% are classified as 'WNL', less than 5% are classified as 'borderline' and less than 1% are classified as 'ONL'. RNFL was considered normal when RNFL thickness was WNL and abnormal when RNFL thickness was borderline or ONL. Normal values were taken as average RNFL \pm sd = 105.66 ± 8.77 and average GCC \pm sd = 96.30 ± 7.10 , FLV \pm sd = 0.82 ± 0.79 , GLV \pm sd = 4.52 ± 3.43 . Statistical methods – Correlation of GCC and RNFL was shown by Pearson's correlation coefficient. Correlation between GCC and VF, two independent sample t -test was used.

Results

60 glaucoma suspect patients were included in this study out of which, 33 were males and 27 were females. The mean age of the study group was 55.93 ± 7.55 years. Out of 60 patients, 31 had IOP ranging between 16-21mm Hg, 20 had IOP less ≤ 15 mm Hg and 9 had IOP >21 mm Hg. Mean CCT of study population was $513.32 \pm 31.73 \mu$. Out of 60 glaucoma suspects, 7 had C:D ratio between 0.3-0.5 and 53 had C:D ratio between 0.6 -0.8. mean corrected IOP was 17.12 ± 4.04 mm of Hg and mean C:D ratio was 0.65. Table 1 shows correlation between GCC parameters and RNFL

Table 1
Correlation between GCC parameters and RNFL

	Avg GCC	GCC FLV	GLV	RNFL Avg RNFL
Normal readings	39	39	33	40
Abnormal Readings	21	21	27	20

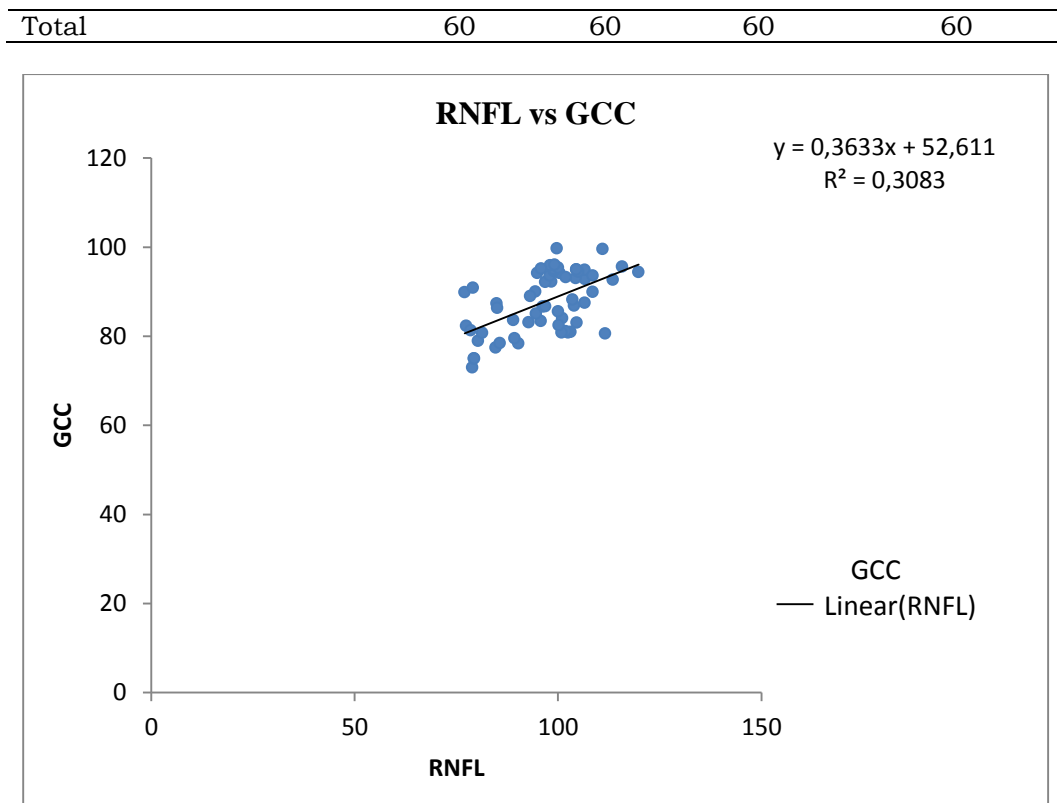


Figure 1. Scatter plot showing correlation of RNFL and GCC

Above scatter plot shows correlation of RNFL and GCC with Pearson's correlation coefficient (0.555), p-value < 0.001. It shows that there is a positive but weak correlation between RNFL and GCC. Out of 60 glaucoma suspect patients, RNFL abnormality was seen in 20 (33.33%) patients, whereas GCC abnormality was seen in 28(46.67%) patients, and RNFL+GCC abnormality is seen in 12(20%) patients. Table 2 shows Correlation of GCC parameters and RNFL with visual field changes. Table 3 shows correlation of GCC with Visual field

Table 2
Correlation of GCC parameters and RNFL with visual field changes

RNFL & GCC	(VF) MD < -6	(VF) MD > -6
Avg RNFL (μ)	97.28	96.81
Avg GCC (μ)	85.86	88.36
FLV (%)	3.09	2.70
GLV (%)	10.84	8.61

Mean FLV (Focal loss volume) of the study population was 2.78 +/- 2.42
Mean GLV (Global loss volume) of the study population was 9.09 +/- 4.001

Table 3
Correlation of GCC with Visual field

	MD in dB	No of patients	Mean(μ)	SD	P –value
GCC	<-6	13	85.87	5.01	0.163
	>-6	47	88.36	7.17	

To find out correlation between GCC and VF, two independent sample t –test was used. P-value was 0.163 which was statistically not significant.

Discussion

Glaucoma is one of the leading causes of global blindness. The aim of glaucoma treatment is to detect the disease in its early phase in order to prevent significant visual loss. Thus, it is important to screen general population to find out high risk cases (glaucoma suspects) for observing them to establish proper diagnosis before functional disability to the eyes takes place. Glaucoma is associated with characteristic structural changes in the optic disc and the RNFL, accompanied by functional VF loss. Often, structural change precedes functional deficit. In this study we measured macular GCC and peripapillary RNFL on OCT (structural changes) and correlated it with visual field changes on perimetry (functional). The mean age of the study group was 55.93 +/- 7.55 years. Out of 60 glaucoma patients studied, 33 were males and 27 were females. Mean CCT was 513.32 +/- 31.73 μ m and mean corrected IOP was 17.12 +/- 4.04 mm of Hg. Mean C:D ratio was 0.65.

Out of 60 glaucoma suspect patients, 47 (78.33%) had MD greater than -6 and 13 (21.67%) had MD less than -6 on visual field testing. In this study 46.67% eyes had an abnormal GCC and 33.33% had an abnormal RNFL thickness in the glaucoma suspect group. A positive but weak correlation was found between RNFL and GCC ($P < 0.555$). A study by Ganekal S, showed 38% eyes having an abnormal GCC and 13% having an abnormal RNFL thickness in the glaucoma suspect group; GCC thickness had a strong correlation with RNFL thickness (Correlation coefficient = 0.763, $p < 0.001$) (5). In a study by Tan O et al, GCC detected an additional 11% of pre-perimetric glaucoma case that were not detected by RNFL which were consistent with our results.6 In patients with MD < -6, mean (Avg RNFL) was 97.28 +/- 8.61 μ whereas it was 96.81 +/- 10.92 μ in patients with MD > -6. In patients with MD < -6, mean (Avg GCC) was 85.86 +/- 5.01 μ whereas it was 88.36 +/- 7.17 μ in patients with MD > -6. Mean FLV of the study population was 2.78 +/- 2.42. Mean GLV of the study population was 9.09 +/- 4.001. The results are comparable with other studies; in a study by Rolle T et al, Avg RNFL was 100.1 +/- 9.3 μ , Avg GCC was 90.22 +/- 6.49 μ , FLV was 1.34 +/- 2.10 and GLV was 7.19 +/- 5.39.7 In a study by Tan O et al, Avg GCC was 87.0 +/- 9.3 μ , FLV was 2.3 +/- 2.7 and GLV was 10.2 +/- 7.0.6

In this study, correlation between GCC and VF was seen clinically, but it was not found to be statistically significant ($P = 0.163$). In a study by Tan o et al, regional correlation between VF and GCC loss was studied which showed for each VF loss the correlation was highest to the corresponding GCC region (5,2). Correlation of

GCC and VF in the present study is not seen to be statistically significant probably because sample size was not sufficient enough. Thus it can be concluded that GCC and RNFL are comparable and good alternative to each other to help in early diagnosis of glaucoma, before the visual field changes appear.

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