GANGLION CELL COMPLEX (GCC) THICKNESS ANALYSIS BY SPECTRAL DOMAIN OPTICAL COHERENCE (SD-OCT) IN GLAUCOMA SUSPECTS IN THE EARLY PREDICTION OF GLAUCOMA

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ABSTRACT

BACKGROUND

Glaucoma is irreversible, chronic, progressive optic neuropathy leads to characteristic visual field loss1. Studies have shown that, structural changes of glaucoma primarily affect Retinal Ganglion Cells (RGC) and their axons. Studies have found that, 15%-50% of glaucoma patients who were started on antiglaucoma medications, did not meet the criteria of Glaucoma. Glaucoma Suspect is defined as a person who has one of the following in at least one eye: like Optic nerve or nerve fibre layer defect suggestive of glaucoma, visual field abnormality consistent with glaucoma, IOP (Intra Ocular Pressure) consistently more than 21mmhg, diffuse or focal narrowing of disc rim and disc haemorrhage.

Optical Coherence Tomography (OCT) is a non-invasive imaging system gives high-resolution cross-sectional images of layers of retina.

METHODS

Hospital based Descriptive Cross-sectional study done for 1year period in Minto Ophthalmic Hospital attached to BMCRI. Macular Ganglion cell complex thickness analysed by Spectral domain optical coherence tomography. After obtaining approval and clearance from the institutional ethical committee, the patients fulfilling the inclusion criteria will be enrolled for the study after obtaining written informed consent and their Socio-demographic data (age, gender, address, occupation).Study will be done as per study design.

RESULTS

The study included 140 eyes 70 patients. It showed significant decrease in the macular GCC thickness in glaucoma suspects. Total GCC thickness of Right eye has decreased in 23 % of glaucoma suspects, and normal in 77 % of glaucoma suspects. Total GCC thickness has reduced in 26 % of glaucoma suspects, and normal in 74 % of glaucoma suspects.

CONCLUSION

MGCC thickness measurements may be good alternative or complentary measurements to peripapillary RNFL thickness and visual field test in the clinical evaluation and management of glaucoma.

KEYWORDS

GCC, Glaucoma suspect, SD-OCT.

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INTRODUCTION

Glaucoma is irreversible, chronic, progressive optic neuropathy leads to characteristic visual field loss.[1] Since it remains asymptomatic until a relatively late stage in most cases, usually the diagnosis will be missed or delayed. In 2013, global prevalence of glaucoma for population aged 40 to 80yrs is 3.54 % which is estimated to be 64.3 million people, and this number might increase to 76 million in 2020 and 111.8 million in 2040.[2]

Studies have found that, 15 % - 50 % of glaucoma patients who were started on antiglaucoma medications, did not meet the criteria of Glaucoma.[3] Glaucoma Suspect is defined as a person who has one of the following in at least one eye: like Optic nerve or nerve fibre layer defect suggestive of glaucoma, visual field abnormality consistent with glaucoma, IOP (Intra Ocular Pressure) consistently more than 21mmhg, diffuse or focal narrowing of disc rim and disc haemorrhage.[4]

Studies have shown that, structural changes of glaucoma primarily affect Retinal Ganglion Cells (RGC) and their axons.[5] RGC made of 3 layers: inner plexiform layer which is ganglion cell dendrites, ganglion cell layer made of ganglion cell bodies, Retinal Nerve Fibre Layer (RNFL) made of ganglion cell axons, these 3 layers together known as Ganglion Cell Complex (GCC).[6-8] Optical Coherence Tomography (OCT) is a non-invasive imaging system gives high-resolution cross-sectional images of layers of retina.[9] It is important to eliminate both under and over diagnosis of all glaucoma Suspects, so it aids in early diagnosis of glaucoma and prevents inadvertent use of antiglaucoma medications in normal patients. OCT enables us to objectively quantify the GCC thickness which is affected early in glaucoma patients, Hence the need for study.

METHODS

Source of Data

Patients attending the OPD and in patients at Minto Ophthalmic hospital, Regional Institute of Ophthalmology and Hospitals attached to Bangalore Medical College and Research Institute.

Methods of Collection of Data

A. Study design: Hospital based Descriptive Cross-sectional study.

B. Study period: November 2019 - May 2021.

C. Place of study: Regional institute of Ophthalmology, Minto Ophthalmic Hospital and Hospitals attached to BMCRI.

D. Sample size:

Based on previous study of Ganekal et al,

The mean value of total GCC in Glaucoma suspects is 95.40 ± 8.11.

$$n = \frac{(Z_{\alpha})^2(\sigma)^2}{}$$

Where, Zα = 1.96 at standard table value for 95 % of CI

σ =Standard deviation = 8.11

d=considering 2 as absolute Precision value.

n=sample size

$$n = 63.4$$

Total sample size =70.

E. Inclusion criteria:

1. Patients willing to give informed written consent.
2. Patients of Age ≥ 18years of either Gender.
3. Patients with Optic disc changes like enlarged cup disc ratio ≥ 0.6, asymmetry of the cup of > 0.2

Between 2 eyes, localized notching, narrowing of the neuro retinal rim, disc haemorrhage.

4. Patients with Intra ocular pressure (IOP) < 21mmhg.
5. Patients with Normal visual fields.
6. Patients with Open anterior chamber angle.

F. Exclusion criteria:

1. Patients with Poor fixation of eyes.
2. Patients with Significant media opacities, any associated ocular pathology like uveitis,

Vitreoretinal diseases.

3. Patients with non-glaucomatous Optic neuropathy.

G. Methodology:

After obtaining approval and clearance from the institutional ethical committee, the patients fulfilling the inclusion criteria will be enrolled for the study after obtaining written informed consent and their Socio-demographic data (age, gender, address, occupation).Study will be done as per study design. Patients will be explained about the test being performed in the language that they understand. History will be taken and patients will undergo a detailed ocular examination along with the measurement of ganglion cell complex thickness by SD - OCT.

Assessment Tools

1. Visual acuity and refraction.
2. Anterior segment evaluation by Slit lamp bio microscopy examination.
3. Posterior segment evaluation by 78D / 90D lens and indirect ophthalmoscopy.
4. Pachymetry for central corneal thickness.
5. Intraocular pressure measurement using Goldman applanation tonometer.
6. Dilated funds examination.
7. Visual field testing.
8. Measurement of GCC thickness by SD - OCT.

Outcome Measure

H. Statistical analysis:

The data collected will be entered in excel sheet and will be analyzed using SPSS v.23.

For descriptive statistics-mean, standard deviation,

Percentage and Proportion wherever applicable will be used. It will be presented in the form of tables, figures and graphs as appropriate.

RESULTS

Age	Frequency	Percentage
20 to 30 years	5	7.14
31 to 40 years	10	14.28
41 to 50years	25	35.71
51 to 60years	17	24.28
61 to 70years	9	12.85
71 to 80 years	4	5.71
Total	70	100

Table 1: Age Distribution In Study Population

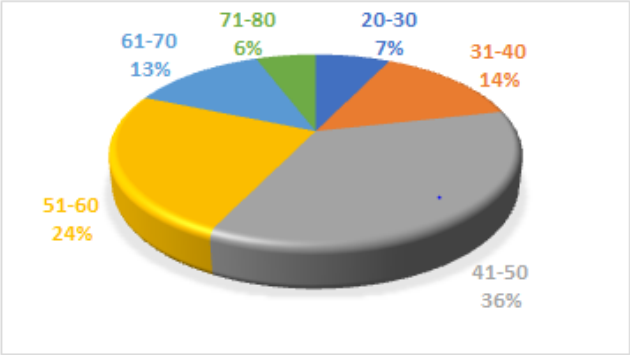

Fig 1: Age Distribution of Study Population

Age distribution of study population was found to be 7.14 %(20 - 30yrs),14.28 %(31 - 40yrs),35.71 %(41 - 50yrs),24.28 %(51 - 60yrs),12.85 %(61 - 70yrs),5.71 %(71 - 80yrs).

Gender distribution			
		Frequency	Percent
Valid	F	35	50
	M	35	50
	Total	70	100

Table No 2: Gender Distribution of Study Population

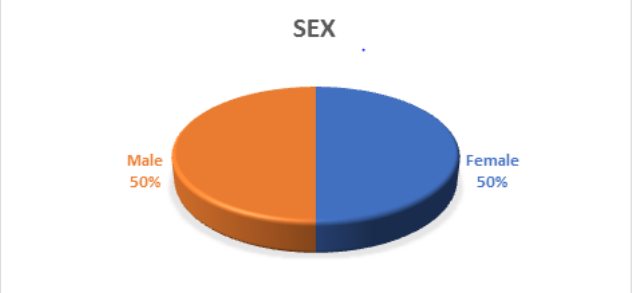

Fig 2: Gender Distribution of Study Population

Gender distribution of the study population was found to be 50 % males, 50 % females.

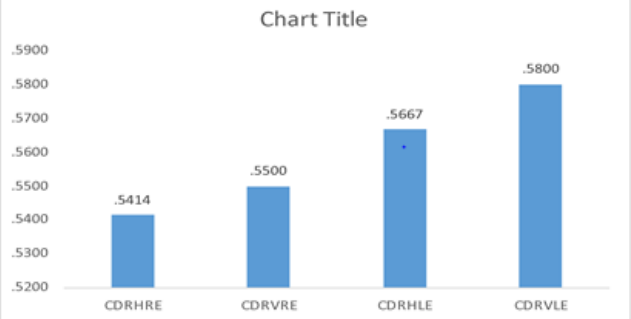

Fig 3: Average Cup Disc Ratio of Study Population

Total GCC RE			
		Frequency	Percent
Valid	Normal	54	77.1
	<95	16	22.9
	Total	70	100

Table No 3: Total GCC Thickness In Right Eye

Total macular GCC thickness in RE was 96.557 ± 7.2505µm,

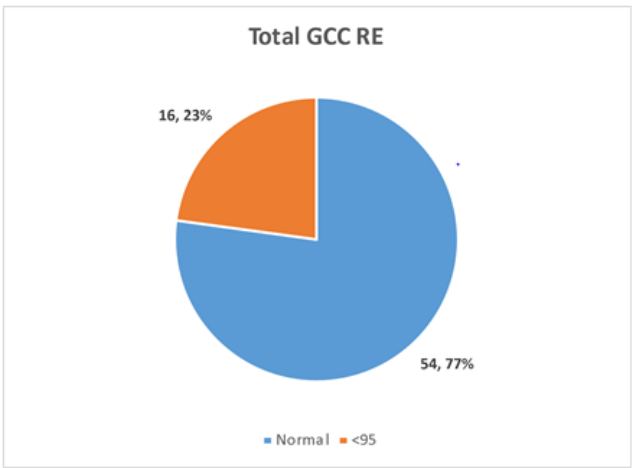

Fig 4:Total GCC Thickness In Right Eye

Total GCC thickness of Right eye has decreased in 23 % of glaucoma suspects, and normal in 77 % of glaucoma suspects.

Total GCC LE			
		Frequency	Percent
Valid	Normal	52	74.3
	<95	18	25.7
	Total	70	100

Table No 4: Total GCC Thickness In Glaucoma Suspects

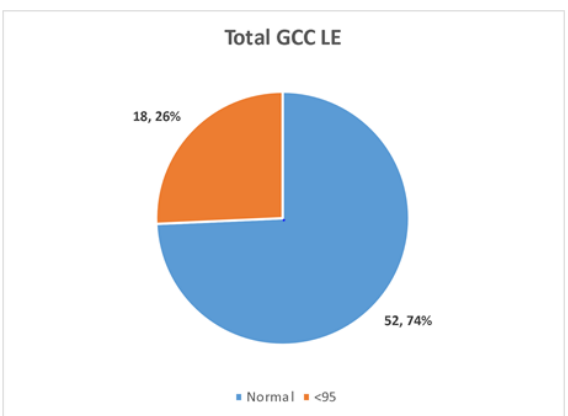

Fig 5:Total GCC Thickness In Left Eye

Total GCC thickness has reduced in 26 % of glaucoma suspects, and normal in 74 % of glaucoma suspects.

DISCUSSION

Glaucoma is the leading cause of irreversible blindness in the India. It is characterized by the death of Retinal Ganglion Cells (RGC) which is the reason for impaired visual function and Blindness. Clinically, Glaucoma is characterized by progressive optic neuropathy with typical excavation of the Optic nerve head, progressive loss of peripheral visual sensitivity in the early glaucomatous stage. On further progression of disease, it impairs central visual aquity.[10] Glaucomatous optic neuropathy is typically observed in glaucoma cases with raised intraocular pressure, High

percentage of population have findings anatomically without actual rise of intraocular pressure.[2]

Glaucoma is no longer considered as pathology occurs only due to elevated Intra ocular pressure. Damage to optic nerve initiated by many factors like ischemia, excitotoxicity, neurotropic insufficiency, inflammatory cytokine damage, aberrant immunity, neuronal-glial interaction, complement regulation of synaptic transmission.

Early, accurate diagnosis of glaucoma is very much important for glaucoma management. Misdiagnosis which results in delay in starting treatment for glaucoma or over diagnosis leads to unnecessary treatment which is potentially harmful and highly expensive. There is no single/any particular test which gives definitive diagnosis of glaucoma. According to previous studies, RNFL thinning is sensitive indicator of the extent of glaucomatous damage. Ganglion cell complex thickness analysis is new advanced technique that helps us in early diagnosis glaucoma. It detects ganglions cell death via loss of synapses and loss of cell bodies at early stage than like other techniques which only measures nerve fibre/axonal loss.[10] Around 1 / 3rd of retinal ganglion cells are in macula and RGC layer is more than 1 cell layer thick, with less variability in cell density as compared to peripheral retina. Hence detection of RGC loss at macula allows earlier detection of glaucoma. So, GCC thinning and progressive loss of GCC aids in making decision to treat glaucoma suspects.

Clinical Profile Data

Our study showed mean age distribution of 49.614 ± 12.7134µm,with 7.14 %(20 - 30yrs),14.28 %(31 - 40yrs),35.71 %(41 - 50yrs),24.28 %(51 - 60yrs),12.85 %(61 - 70yrs),5.71 %(71 - 80yrs). Studies conducted by Sania vidas et al, showed mean age of 56.60 ± 11.08yrs.[11]

Our study showed Gender distribution of the study population was found to be 50 % males, 50 % females. Sania vidas et al showed 35.8 % were males 64.19 % were females.[11]

Our study showed mean BCVA of 0.3629 ± 0.42942, 0.3329 ± 0.42108µm in right and left eye respectively.Sania vidas et al study showed mean BCVA was 0.96 ± 0.09.[11]

Study by Ganekal et al, analyzed 20 glaucoma suspects and 20 glaucoma patients. It showed statistically significant difference in average GCC and average RNFL in glaucoma suspects and glaucoma patients. 38 % of eyes had an abnormal GCC and 13 % had an abnormal RNFL thickness in glaucoma suspects.98 % had abnormal GCC, 90 % had abnormal RNFL thickness in glaucoma group, which showed ability to diagnose glaucoma mGCC thickness is comparable to that with peripapillary RNFL thickness.[12]

Study by bhagat et al, analysed 200 eyes including 68 normal eyes, 70eyes with pre - perimetric glaucoma, 62 eyes with perimetric glaucoma. The average GCC was thickest in normal group and thickness decreased with severity of glaucoma. Mean mGCC was 94.86 ± 8.31, 82.48 ± 13.21, 79.80 ± 12.88, 102 ± 7.42 in preperimetric, perimetric and normal individual. This study concluded GCC analysis definitely plays an important role to detect preperimetric glaucoma earlier than perpapillary RNFL.[13]

Oli A et al did prospective observational study on 33 glaucoma patients, 45 pre perimetric glaucoma, and 30 controls. RNFL thickness was 71.6 µ and GCC was 69.19 µ in glaucoma patients. RNFL thickness was 77.31 µ and GCC was 71 µ in pre-perimetric glaucoma and 99.6 µ and 85.16 µ in controls respectively. The difference of mean for RNFL and GCC by ANOVA was statistically significant for controls, glaucoma patients and pre-perimetric glaucoma patients. RNFL ($p < 0.001$) and GCC ($p < 0.001$). Receiver operating characteristic curve for GCC was 0.83 ($p < 0.000$). This concludes that, GCC is newer tool in early diagnosis of glaucoma and can pick up pre perimetric glaucoma.[14]

In our study

- Total macular GCC thickness in RE was 96.557 ± 7.2505µm, LE was 97.614 ± 6.9788µm.
- Total macular GCC thickness was reduced in 23 % in RE, 26 % in LE.

By above findings in our study, we conclude that 'mGCC thickness changes significantly in glaucoma suspects'. Hence mGCC can be good alternative to pRNFL in early detection of glaucoma or can be complentary to pRNFL and visual fields in early detection of glaucoma.

CONCLUSION

- Early diagnosis of glaucoma and early commencement of treatment is immensely important which slows down the further progression of disease and prevents the vision loss.
- There is no single test or clinical finding which helps in making definitive diagnosis of glaucoma.
- Macular GCC measurement with spectral domain OCT provides extra information for detection and evaluation of glaucoma.
- In our study, Macular Ganglion Cell Complex Thickness (mGCC) thinning was present with normal visual fields and normal intra ocular pressure in glaucoma suspects.

Hence, mGCC thickness measurements may be good alternative or a complentary measurement to peripapillary RNFL thickness and visual field test in the clinical evaluation and management of glaucoma.

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