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Evaluation of Correlation among Retinal Nerve Fibre Layer Thickness, Cup Disc Ratio and Perimeteric Indices in Primary Open Angle Glaucoma and Glaucoma Suspects

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Abstract: ***Background: Primary open angle glaucoma (POAG) is the most common type of glaucoma which is considered chronic progressive optic neuropathy, accompanied by a characteristic cupping and atrophy of the optic disc, visual field loss, open angle and no obvious systemic or ocular cause. This study aims at evaluating the correlation between optic disc parameters like Cup - to - Disc Ratio (CDR) and retinal nerve fibre layer thickness (RNFL - T) with Visual Field (VF) defect parameters like Mean Deviation (MD) and Pattern Standard Deviation (PSD) in Primary Open - Angle Glaucoma (POAG) patients and Glaucoma suspects. The study also aims to detect early structural changes in Glaucoma suspects. Methods: This prospective study was conducted at Sankara Eye Hospital, Ludhiana from July 2019 to June 2020.50 eyes with diagnosed POAG and glaucoma suspects were analyzed each. Various optic disc parameters like CDR and RNFL - T was correlated with MD and PSD on perimetery. Results: Mean age of study population was 62.16±8.22 years in glaucoma group and 57.48±9.34 in suspects. There was a statistically significant difference in RNFL - T, CDR and perimeteric findings between POAG and glaucoma suspects (P<0.005). Average RNFL thickness was 67.31±16.56 in POAG and 84.63±3.21 in glaucoma suspect which is statistically significant (P<0.05). There was significant correlation of CDR with RNFL - T and MD in POAG where as no such correlation exist in suspects. Conclusion: There is significant direct correlation between average retinal nerve fibre layer thinning and visual field mean deviation in patients with POAG. Optic disc parameters get severely affected as the stage of glaucoma progresses which has also strong correlation with visual field changes and RNFL thickness. In Glaucoma suspects, these parameters are minimally affected or may show no change at all.***

Keywords: Primary open angle glaucoma, Cup-to-Disc Ratio, Retinal nerve fibre layer thickness, Visual Field defect, Mean Deviation, Pattern Standard Deviation, Spectral-domain optical coherence tomography

1. Introduction

Glaucoma is a progressive irreversible optic neuropathy characterized by the loss of retinal ganglion cells and the retinal nerve fiber layer (RNFL), with an associated visual field loss. Primary open angle glaucoma has an open anterior chamber angle of normal appearance and an intraocular pressure which is detrimental to the structural and functional integrity of optic nerve head [(3).] All the epidemiological surveys have concluded that the disease is highly under diagnosed, and most of the patients remain un - diagnosed till later stages, where advanced damage has already taken place [(4).] Individuals with "Glaucoma Suspects" have at least one clinical feature of the disease, including an elevated IOP, optic disc cupping, repeatable visual field abnormality consistent with optic nerve damage, or a strong family history of glaucomatous disease [(5).] Imaging of the RNFL has potential clinical value, because RNFL thinning can occur before irreversible functional visual field loss [(6).] In glaucoma, the precise nature of the relationship between the structure and function is important, as it can be used for detecting glaucomatous damage, determining the stage of the disease, and monitoring the progression of the disease. Standard VF examinations is used in the diagnosis and follow - up of glaucoma, but one of its drawbacks is that the abnormalities do not appear until 20–40% of ganglion cells are lost. Earlier defects in the retinal nerve fiber layer (RNFL) measured by optical coherence tomography (OCT) provide an excellent objective and quantitative method in the diagnosis and management of glaucoma [(7).] Unlike visual field testing that is subjective and prone to interest variability [(8),] OCT imaging of RNFL - T measurements are objective.

In routine clinics, spectral - domain optical coherence tomography (SD - OCT) has rapidly become one of the most widely used technologies due to its high image resolution and measurement precision. As a way of improving our ability to detect the presence and progression of glaucomatous damage, a number of studies have used SD - OCT to specifically focus on the relationship between the structural and functional damage. Results of these studies have demonstrated there are high correlations between the global VF sensitivity and the peripapillary RNFL [(9, 10).] Therefore, the purpose of our current study was to examine the relationship between the RNFL - T and VF measurements, and then evaluate the ability of using these findings to determine progression in patients with early glaucoma.

2. Materials & Methods

We prospectively analysed patients who were seen at the Glaucoma Clinic in Sankara eye hospital, Ludhiana between July 2019 to June 2020. Keeping significance level of 5% and confidence level of 95%, a sample size of 50 glaucomatous and suspected eyes each was taken. Patients from either gender, aged between 40 - 70years, diagnosed as POAG, IOP > 21mmHg on diagnosis, open anterior chamber, characteristics HVF defects, absence of signs secondary glaucoma or a non - glaucomatous cause

for the optic neuropathy were included. Patients with known history of corneal diseases, trauma, ocular surgery, history of laser surgery (Corneal, Retinal), hereditary causes of RNFL thinning like high myopia, cataract obscuring view of fundus, retinal diseases like diabetes and hypertension, optic disc anomalies like papilledema were excluded. Subjects fulfilling the inclusion criteria underwent ophthalmic examination including uncorrected and BCVA measurement, slit lamp examination for IOP measurement and exclusion of corneal diseases. The patients underwent measurement of CCT using Topcon SP 3000P Specular Microscope (Topcon Corporation, Tokyo, Japan). Three reading were taken and mean calculated for analysis. VF was assessed using HVF Analyser with background luminance set at 31.5 asb, Goldmann perimeter stimulus size III, using fast Swedish Interactive Thresholding Algorithm (SITA) without pupil dilation and after correction of near vision. A glaucomatous VF was defined as a glaucoma hemifield test outside of the normal limits on at least two consecutive baseline tests and the presence of at least three contiguous test points within the same hemifield on the pattern deviation plot at $P < 1\%$, with at least one at $P < 0.5\%$ (excluding those points on the edge of the field or those directly above and below the blind spot). Printouts showing VF result with MD and PSD were collected. All OCT scans were performed through a dilated pupil. Scan protocols used were Fast Optic Disc Scan and Fast RNFL - T protocol.

3. Statistical Analysis

Data was evaluated and analyzed using Statistical Program for Social Sciences (SPSS) version 21. Data were analyzed using a paired t - test. All statistical values are presented as mean ± standard deviation (SD), with P values < 0.05 considered statistically significant.

4. Result

A prospective study consisting of 50 Glaucoma suspect patients and 50 patients diagnosed with POAG were undertaken to evaluate the correlation between Optic disc Parameters, RNFL - T with visual field changes. Mean age of study population was 62.16±8.22 years in glaucoma group and 57.48±9.34.

Comparison of Optic Disc Parameters among POAG and Suspect

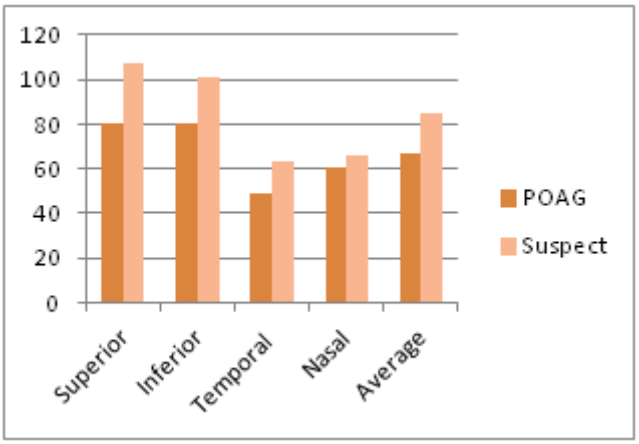
There was significant correlation in optic disc C/D ratio between POAG and glaucoma suspects as shown in the graph below (P<0.05).

	G		S		t	p - value
	Mean	SD	Mean	SD		
OCDR	0.77	0.09	0.65	0.07	7.776	0.001
CD Horz	0.82	0.10	0.69	0.08	7.610	<0.001
CD Vert	0.75	0.08	0.63	0.08	7.393	<0.001

Comparison of RNFL Thickness among POAG and Suspect

Superior, Inferior, Temporal RNFL thickness were found to be highly statistically significant between POAG and glaucoma suspects (P<0.05) and Nasal RNFL thickness was also slightly significant. Average RNFL thickness was 67.31±16.56 in POAG and 84.63±3.21 in glaucoma suspect which was statistically significant (P<0.05).

	G		S		T	p - value
	Mean	SD	Mean	SD		
Sup RNFL	80.34	24.67	107.70	6.75	- 7.563	0.000
Inf RNFL	80.20	30.19	101.40	9.14	- 4.753	0.000
Tem RNFL	48.58	14.17	63.50	11.80	- 5.719	0.000
Nas RNFL	60.38	15.85	66.00	12.69	- 1.958	0.043
Avg RNFL	67.31	16.56	84.63	3.21	- 7.259	0.000



Comparison of Visual Field Indices among POAG and Suspect

VF	POAG	SUSPECT	P value
MD (decibels)	- 15.44±7.90	- 2.42±0.79	<0.001
PSD (decibels)	- 7.67±2.96	- 2.07±0.70	<0.001

This graph depicts comparison of MD indices. In POAG, the MD was found to be –15.49±8.26 and in suspects -2.82±0.73. This was shown to be statistically significant (P<0.05). Pattern Standard Deviation was also found to be statistically significant between two groups.

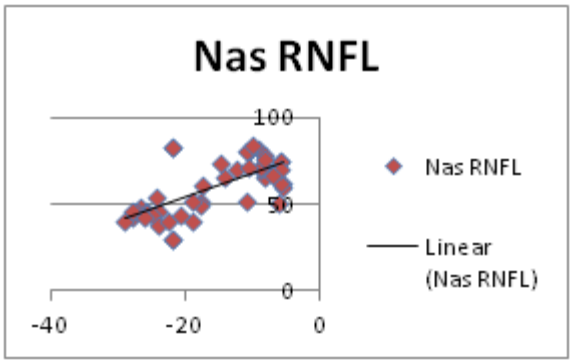
Correlation of RNFL Thickness and Visual Field Indices in POAG

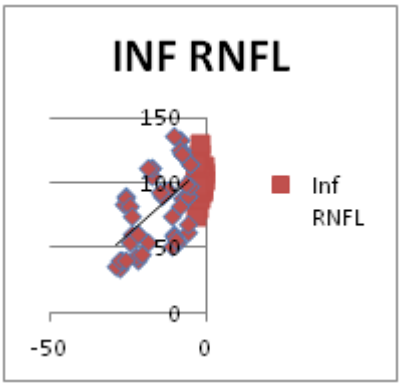
It is evident from the table below that RNFL thickness and Visual field indices in POAG showed high correlation in Superior, Inferior, Temporal, Nasal quadrant. Average RNFL thickness and mean deviation were highly correlated (r=0.867)

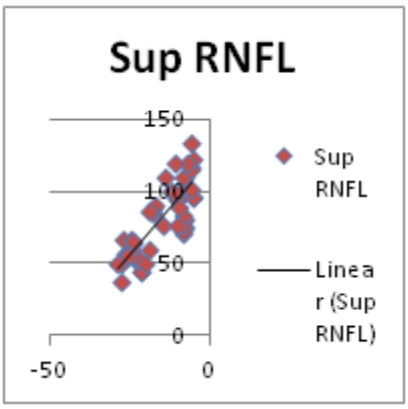
Correlation of RNFL thickness and Visual field indices in suspects showed no correlation between two parameters.

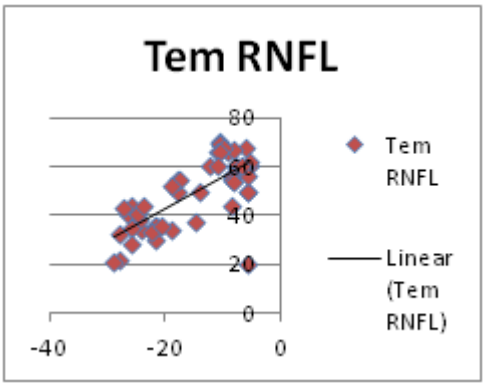
		MD (glaucoma)	PSD (GLAUCOMA)	MD (Suspect)	PSD (suspect)
Sup RNFL	Pearson Correlation	0.812	- 0.313	- 0.072	- 0.248
	p - value	0.000	0.027	0.618	0.083
Inf RNFL	Pearson Correlation	0.544	- 0.368	0.116	- 0.108
	p - value	0.000	0.008	0.424	0.456
Tem RNFL	Pearson Correlation	0.714	- 0.080	- 0.277	0.224
	p - value	0.000	0.582	0.051	0.118
Nas RNFL	Pearson Correlation	0.693	0.011	0.290	- 0.459
	p - value	0.000	0.938	0.041	0.001
Avg RNFL	Pearson Correlation	0.867	- 0.298	0.077	- 0.454
	p - value	0.000	0.036	0.596	0.001

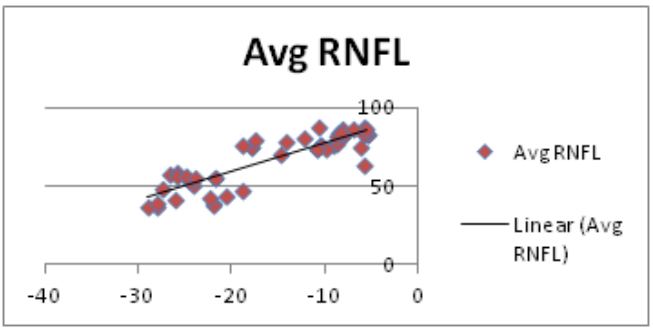
Graph Depicting Correlation of RNFL Thickness and Visual Field Indices in POAG









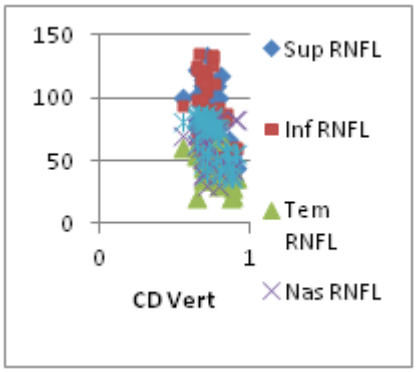


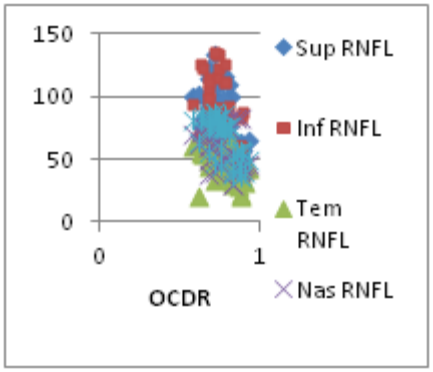
Correlation of RNFL Thickness, Optic Disc Parameters and Visual Field Indices in POAG

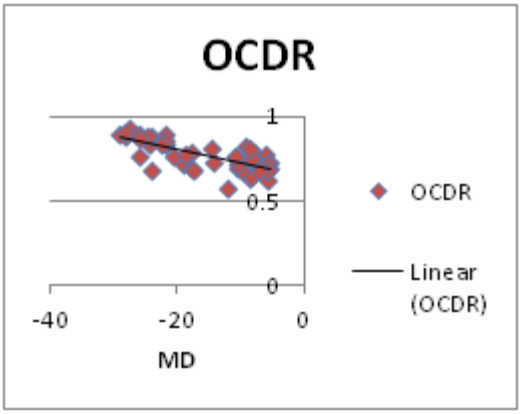
Correlations	G	Sup RNFL	Inf RNFL	Tem RNFL	Nasal RNFL	Avg RNFL	MD	PSD
OCDR	Pearson Correlation	- 0.619	- 0.514	- 0.521	- 0.410	- 0.674	- 0.716	0.213
	p - value	0.000	0.000	0.000	0.003	0.000	0.000	0.137
CD Horz	Pearson Correlation	- 0.641	- 0.543	- 0.540	- 0.404	- 0.700	- 0.717	0.256
	p - value	0.000	0.000	0.000	0.004	0.000	0.000	0.073
CD Vert	Pearson Correlation	- 0.584	- 0.489	- 0.479	- 0.241	- 0.599	- 0.623	0.186
	p - value	0.000	0.000	0.000	0.092	0.000	0.000	0.195

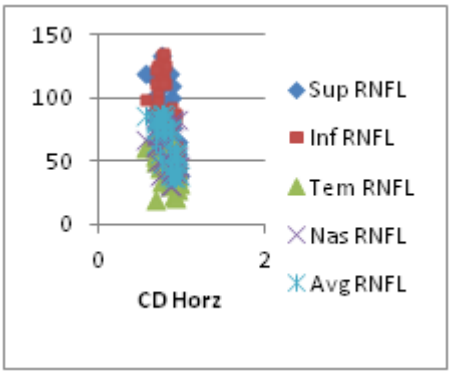
Correlation of optic disc parameters and RNFL thickness in POAG group showed that both the groups were highly correlated where as no such correlation exists in glaucoma suspects.

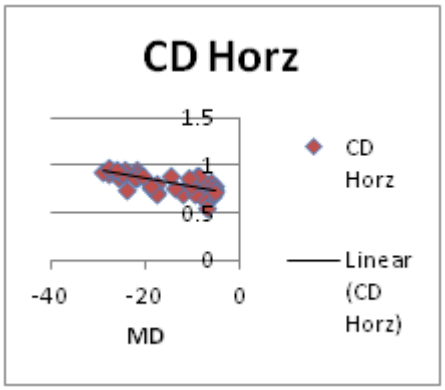
Graph Depicting Correlation of RNFL Thickness, Optic Disc Parameters and Visual Field Indices in POAG

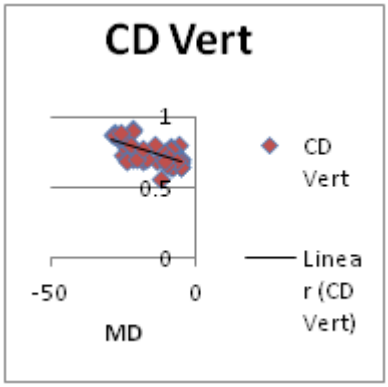












Correlation of optic disc parameters and visual field changes in POAG showed CD ratio and mean deviation were highly correlated.

Correlation of optic disc parameters and visual field changes in suspects showed no correlation between 2 parameters.

Correlation of CD Ratio with RNFL Thickness in Suspect

Correlations	S							
		Sup RNFL	Inf RNFL	Tem RNFL	Nas RNFL	Avg RNFL	MD	PSD
OCDR	Pearson Correlation	- 0.108	- 0.476	- 0.148	0.137	- 0.397	0.072	0.257
	p - value	0.456	0.000	0.304	0.344	0.004	0.618	0.072
CD Horz	Pearson Correlation	- 0.068	- 0.439	- 0.159	0.159	- 0.337	0.112	0.230
	p - value	0.639	0.001	0.271	0.272	0.017	0.438	0.108
CD Vert	Pearson Correlation	- 0.159	- 0.385	- 0.228	0.190	- 0.379	0.095	0.162
	p - value	0.271	0.006	0.111	0.186	0.007	0.512	0.261

5. Discussion

Worsening of optic disc parameters, RNFL thinning and deterioration in visual field indices are all used to detect the progression of glaucoma. If progression is confirmed, treatment needs to be modified or enhanced in order to prevent further irreversible loss of the patient's visual function. In this study, we have correlated optic disc parameters and RNFL thickness with visual field changes in 50 eyes of with POAG and 50 eyes of Glaucoma suspect patients.

Regarding the comparison between average retinal nerve fiber measurements, optic disc parameters in patients with glaucoma and suspects, the present study found that patients with POAG had significantly thinner average RNFL thickness measurements when compared with patients of glaucoma suspects (67.31±16.56 in POAG and 84.63±3.21in suspects). This is in harmony with the study of Mansoori et al. who assessed the utility of SD - OCT to differentiate normal eyes from those with early glaucoma in Asian Indian eyes. The study recruited 178 eyes (83 patients with glaucoma and 95 age - matched healthy persons). The mean RNFL thickness in healthy controls and patients with glaucoma was 105.7±5.1 and 90.7± 7.5 µm, respectively (P=0.001).

Kaw et al. [11] in their study aimed to compare SD - OCT evaluation of RNFL thickness in normal controls and POA glaucoma of various stages and found that normal patients had the thickest RNFL thickness when compared with patients with the severe glaucoma that was associated with thinner RNFL.

The study of Firat et al [12] measured RNFL thickness in POAG, normal tension glaucoma (NTG) and normal subjects using SD - OCT. RNFL thickness parameters were significantly greater in normal subjects, followed in order by the NTG, and POAG ($p < 0.05$).

In our present study, significant correlation was found between RNFL thickness and VF indices in POAG but no such correlation was found in glaucoma suspects. This is in accordance with the study of Sehi et al. [13] who compared prospectively detection of progressive RNFL atrophy identified using time - domain optical coherence tomography with visual field progression using standard automated perimetry in glaucoma suspect and preperimetric glaucoma patients or perimetric glaucoma patients. They found that structural progression is associated with functional progression in glaucoma suspect and glaucomatous eyes. Average and superior RNFL thickness may predict subsequent standard automated perimetry loss.

Study by Sujata subbaih et al [14], analysed the results of 30 normal, 30 ocular hypertensives and 30 glaucoma patients. The mean age of patients in the glaucoma group was 53.77±15.24 years, in the ocular hypertensive group was 48.64±11.52 years. The mean CD ratio was 0.4 and 0.78 in ocular hypertensive and glaucoma group. The mean RNFL thickness was 52.95±31.00µm in glaucoma eyes,

82.87±17.21 in ocular hypertensive group. With reference to glaucoma indices, MD was - 5.54±5.82 and PSD was 4.74±2.82. in the glaucoma group, mean RNFL showed correlation with VF indices. In the ocular hypertensive group, RNFL did not show any statistically significant correlation with global indices.

6. Conclusion

There is significant direct correlation between average retinal nerve fibre layer thinning and visual field mean deviation in patients with POAG. optic disc parameters gets severely affected as the stage of glaucoma progresses which has also strong correlation with visual field changes and RNFL thickness. in Glaucoma suspects, theses parameters are minimally affected or may show no change at all. OCT is capable of detecting changes at the level of RNFL in Glaucoma suspects with normal appearing discs and visual fields. OCT can quantitatively measure RNFL thickness difference between suspects and glaucoma patients. Structural damage owing to RNFL loss can be correlated with functional damage shown in VF loss. This finding may be the cornerstone for upcoming OCT - based staging of glaucoma, combined to automated perimetry. RNFL thickness gradually decreases while visual field defect increases with the development of POAG.

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