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ORIGINAL PAPER

Corneal Endothelial Cell Density and Retinal Nerve Fiber Layer Thickness in Glaucoma

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ABSTRACT

***Purpose**: To evaluate a possible association between corneal endothelial cell density and retinal nerve fiber layer (RNFL) thickness in primary glaucoma patients.*

***Methods**: All patients underwent comprehensive eye examination. Diagnosis of primary glaucoma was done according to the ISGEO criteria. Corneal endothelial count was measured by non–contact specular microscopy. The RNFL thickness was measured by time-domain optical coherence tomography (OCT). Data was analyzed using appropriate statistical methods.*

***Results**: A total of 95 eyes of 50 primary open angle glaucoma (POAG) patients, 97 eyes of 50 primary angle closure glaucoma (PACG) patients and 100 eyes of 50 age matched normal subjects were examined. In all the groups, the endothelial cell density positively correlated with average RNFL thickness ($p<0.0001$) indicating direct correlation of endothelial density with RNFL. The RNFL thickness of the POAG and the PACG groups were found to significantly decrease with increasing IOP ($p<0.001$). Similarly, the endothelial cell count of the POAG and the PACG groups were found to significantly decrease with increasing IOP ($p<0.001$).*

***Conclusion**: Lower endothelial cell density correlates well with thinner RNFL in both glaucomatous and normal eyes. Also, the corneal endothelial cell count and RNFL thickness in both the groups decreased proportionately with increasing IOP.*

***Keywords**: Corneal endothelial cell density, correlation, intraocular pressure, primary glaucoma, retinal nerve fibre layer thickness*

INTRODUCTION

Glaucoma is a progressive optic neuropathy identified by characteristic optic disc, retinal nerve fiber layer (RNFL) and visual field damage and change that occurs as a result of retinal ganglion cell damage and death. Detecting structural and functional change is one of the most challenging aspects of glaucoma management.[1-3]

Reduced endothelial counts are reported in association with primary open angle glaucoma,[4] primary angle closure glaucoma (PACG)[5-7] and other forms of glaucoma's.[5-7] Elevated intraocular pressure likely affects the decrease of corneal endothelial cell density in eyes with glaucoma,[8] though the relationship between the changes in RNFL thickness and endothelial count in glaucomatous patients has not much been studied in detail.

AIMS OF THE STUDY

We assessed if there is any association between corneal endothelial cell density and RNFL thickness in primary glaucoma patients. Moreover, we also investigated the association of corneal endothelial cell density and RNFL thickness with IOP level in primary glaucoma patients. Understanding this relationship may provide new insight

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into the role of corneal endothelial cell density in the diagnosis of primary glaucoma.

METHODS

This case controlled, cross-sectional study which included a total of 95 eyes of 50 primary open angle glaucoma (POAG) patients and 97 eyes of 50 primary angle closure glaucoma (PACG) patients and 100 eyes of 50 normal age matched subjects from July 2013 to February 2014 .The study protocol was approved by the Ethical committee, Srimanta Sankaradeva University of Health Sciences, Guwahati.

Inclusion criteria included all patients, both males and females, above 40 years of age attending the indoor and outdoor departments of the Regional Institute of Ophthalmology, Gauhati Medical College and Hospital, Guwahati, Assam.

Exclusion criteria included patients below 40yrs of age, secondary glaucoma (traumatic, tumours, uveitis, etc), any condition that will hamper visualization of corneal endothelial cells or the posterior segment (corneal scarring, cataract or any other media opacity),patients with history of contact lens use, ocular trauma, patients who had glaucoma medication history, laser treatment history, all conditions affecting endothelial cells (cataract surgery, glaucoma surgery etc), all conditions affecting RNFL(DM, high myopia, retinal disorders, posterior segment inflammations).

A detailed history of the patients was taken and the best corrected visual acquity was checked using Snellen's chart. Patients were examined using slit lamp, Goldman applanation tonometry, Susmann 4-mirror gonioscopy, ultrasonic pachymetry, Humphrey field analyzer (SITA 30-2), and direct and indirect Ophthalmoscopy and disc examination by slit lamp biomicroscopy using +90D lens. Diagnosis of primary glaucoma was done according to the ISGEO criteria. Corneal endothelial cell density was measured by specular microscopy and RNFL thickness by stratus OCT.Corneal endothelial count was measured by non–contact specular microscopy [Topcon SP3000P (TMS Oakland, NJ)]. The endothelial cell count was based on the average of two measurements with the best clarity.

The RNFL thickness was measured by time-domain optical coherence tomography OCT (Stratus OCT, Carl Zeiss Meditec, Inc., Dublin, California, USA), which has a resolution of 10 microns. Fast RNFL scan protocol was used in this study. The average of two measurements was taken with the best signal strengths.

Data was analyzed with appropriate statistical methods, using person's correlation coefficient. $p< 0.5$ was considered significant.

RESULTS

The study population consisted of 150 subjects belonging to the presbyopic age group and the ages ranged from 40yrs to 78yrs (mean + SD was 59+ 19 yrs). In the POAG group, the largest number (25) of patients were in the age group 60-69 years (50%), followed by17 (34%) patients in the 70-79 yrs group,6(12%) patients in the 50-59 yrs age group and 2(4%) in the age group of 40-49 yrs. In the PACG group, the largest number (27) of patients were in the age group 50-59 years(54%), followed by12 (25%) patients in the 60-69 yrs group,8(16%) patients in the 70-79 yrs age group and 3 (7%) in the age group of 40-49 yrs. In the normal group, the largest number (25) of patients were in the age group 50-59 years (50%), followed by15 (30%) patients in the 40-49 yrs group, 6(12%) patients in the 60-69 yrs age group and 4(8%) in the age group of 70-79 years (**Table 1**).

Table 1 Age distribution of all primary glaucoma cases in the study population

Age group(years)	POAG	PACG	Normal
40-49	2(4%)	3(7%)	15
50-59	6(12%)	27(54%)	25
60-69	25(50%)	12(25%)	6
70-79	17(34%)	8(16%)	4

In the POAG group, there were 31 (62%) males and 19 (38%) females, in the PACG group, there were 27(54%) males and 23(46%) females while in the normal group, there were 26(52%) males and 24(48%) females.

The mean endothelial cell densities were 2302.54 ±224, 2344.38±231 and 2482.98 ± 235.08 respectively among the POAG, PACG and the normal groups (**Table 2**).

Table 2 Corneal endothelial cell density among POAG, PACG and Normal

	POAG	PACG	Normal
No. of eyes	95	97	100
Mean density	2302.54	2344.38	2482.98
SD	210.02	235 .08	220.29
Min density	1809	1986	2009
Max density	2722	3202	2923

The mean RNFL thickness were72.13 ±19.79µ, 75.17 ± 20.64µ and 92.55 ±14.99µ respectively among the POAG, PACG and the normal groups (**Table3**).

Table 3 Showing average RNFL thickness in POAG, PACG and Normal

	POAG	PACG	Normal
No of eyes	95	97	100
Mean avg RNFL (µ)	72.13	75.17	92.55
SD	14.24	16.49	17.28
Min avg RNFL (µ)	29.12	35.32	65.15
Max avg RNFL (µ)	110.45	109	140.92

In our study, we found that in all the groups, i.e., POAG, PACG and normal, the mean endothelial cell density positively correlated with average RNFL thickness [Pearson's correlation coefficient, r=0.55, 0.68 and 0.58, (p<0.5) respectively] (**Figure 1**, **2** and **3**).

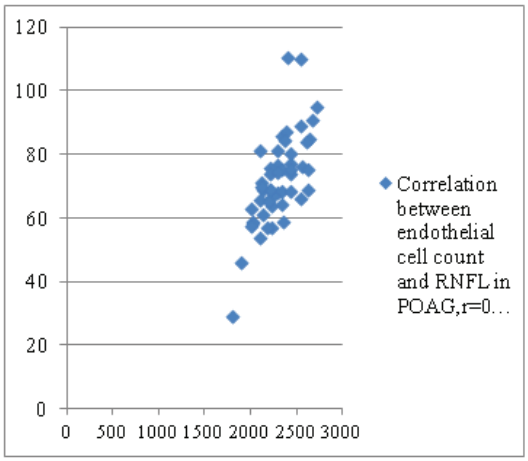

Figure 1 Correlation between corneal endothelial cell count and RNFL thickness in POAG cases

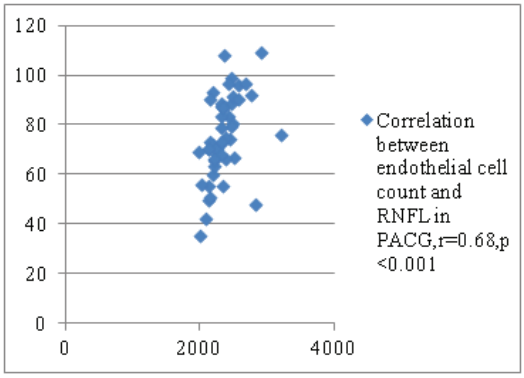

Figure 2 Correlation between corneal endothelial cell density and RNFL thickness in PACG cases

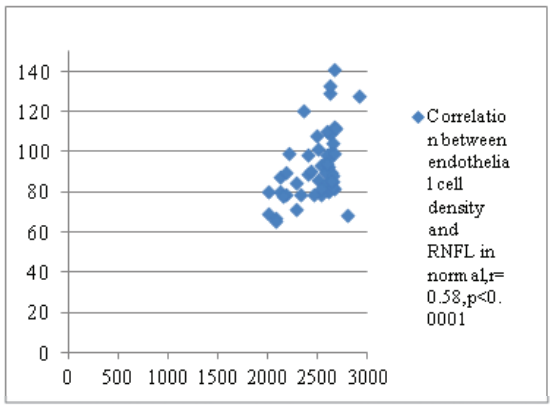

Figure 3 Correlation between corneal endothelial cell density and RNFL thickness among normal population

The difference of the mean IOP of the POAG and PACG groups with the normal subjects was found to be statistically significant [t=16.31, p<0.001and t=15.13, p<0.001) respectively]. Moreover, the difference of the mean IOP between the POAG and PACG group was also found to be statistically significant (t=4.8, p<0.001) (**Table 4**).

Table 4 Mean IOP in POAG, PACG and normal groups

	POAG	PACG	Normal
Mean IOP+-SD (mmHg)	23.96+-4.48	28.87+-8.55	14.2+-3.85

The RNFL thickness of the POAG and the PACG groups were found to significantly decrease with increasing IOP [Multiple regression analysis, (r=- 0.68,p<0.001and – 0.96, p<0.001) respectively]. Similarly, the endothelial cell count of the POAG and the PACG groups were found to significantly decrease with increasing IOP, [Multiple regression analysis, (r= - 0.57, p<0.001 and – 0.96, p<0.0001) respectively]. Also, there seems to be a greater decrease in the endothelial cell count in the PACG group in comparison to the POAG group (**Table 5**, **Figure 4, 5**).

Table 5 Comparison of RNFL and endothelial cell count with IOP level in POAG and PACG patients

IOP (mmHg)	Mean RNFL(μ)				Mean endothelial cell density(μ)			
	POAG	r value	PACG	R value	POAG	r value	PACG	R value
15-20	86.6+ -18.9	r= -0.68p <0.001	79.8+- 17.4	r= -0.57p <0.001	2545+- 245	r= -0.85p <0.001	2399+- 218	r= -0.96p <0.001
20.1-25	81.2+ -15.4		80.1+- 18.53		2456+- 312		2231+- 256	
25.1-30	79.3+ -14.3		70.5+- 16.90		2331+- 256		1931+- 201	
>30	68.2+ -15.4		60.8+- 13.3		2102+- 245		1672+- 189	

DISCUSSION

Glaucoma affects around 60.5 million people worldwide, with 8.4 million people with bilateral blindness and millions more suffering from visual disability.[8] Glaucoma has been declared to be the second most common cause of blindness in adult population in India.[9] Knowledge about the relationship of corneal endothelial cell density and RNFL thickness in primary glaucoma may herald new possibilities towards earlier diagnosis of this potentially blinding condition.

In a previous study by Gagnon et al, it was concluded that corneal endothelial cell counts were significantly lower in patients with glaucoma than in controls. In the glaucoma group, cell counts were inversely proportional to the means of IOPs.[10] Cho SW et al concluded that there was a significant decrease in corneal endothelial cell density in eyes with primary open-angle glaucoma, but not in normal eyes. Elevated intraocular pressure likely affected the decrease of corneal endothelial cell density in eyes with glaucoma.[11] In another study conducted by Kirsi Setala, corneal endothelial cells of 25 patients with unilateral acute glaucoma were photographed with a clinical specular microscope .It was concluded that there was a clear correlation between the duration of elevated pressure and the number of central corneal endothelial cells lost.[12] In our study, there seems to be a greater decrease in the corneal endothelial cell count in the PACG group in comparison to the POAG group. However, we did not take into account the duration of the disease in the two groups, and that might affect the outcome of the study.

Christopher Bowd et al found in their study that quantitative differences in RNFL thickness exist between age-matched normal and glaucomatous eyes.[13] Li Guo et al demonstrated that RGC apoptosis in glaucoma correlates strongly with elevated IOP and is significantly associated with IOP-induced changes in specific ECM components in the RGC layer.[14] In our study, the RNFL thickness and corneal endothelial cell density was seen to significantly decrease with increasing IOP, in both the POAG and the PACG groups. These findings may have significant implications in the early detection of the changes that occurs in glaucomatous eyes.

To our knowledge, ours is the first study, which correlates corneal endothelial cell density with RNFL thickness in primary glaucoma patients. In our study, it was found that in all the three groups (normal, POAG and PACG groups), the corneal endothelial cell density positively correlated with average RNFL thickness parameters (Pearson's correlation coefficient: r=0.55, 0.68, 0.58 respectively). However, further prospective studies are needed to substantiate the correlation between RNFL thickness and corneal endothelial cell density in primary glaucoma patients, while considering other factors which affect the RNFL thickness and corneal endothelial cell density.

CONCLUSION

Lower corneal endothelial cell density correlates well with thinner RNFL in primary glaucomatous eyes. Also, the rate of damage to RNFL and the corneal endothelial cells in primary glaucoma patients is directly proportional to increasing IOP. Knowledge about the relationship of corneal endothelial cell density and RNFL thickness in primary glaucoma may herald new possibilities towards earlier diagnosis of this potentially blinding condition. However, further prospective, longitudinal studies are necessary to substantiate the relationship between RNFL thicknesses with corneal endothelial cell density in primary glaucoma, particularly taking into account the duration of the disease.

Ethical clearance: Taken.

Conflict of interest: No conflict of interest.

Contribution of authors: We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors

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