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RESEARCH ARTICLE
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CORRELATION BETWEEN CENTRAL CORNEAL THICKNESS (CCT) AND RETINAL NERVE FIBER LAYER THICKNESS (RNFL) IN PRIMARY OPEN ANGLE GLAUCOMA

Dr. Wasim Rashid[1], Dr. Mustafeez Zehra[2*], Dr. Sheikh Sajjad Ahmed[3], Dr Areeb[4]

[1]Assistant Professor; [2*]PG Scholar; [3]Professor and Head; [4]PG Scholar
Department of Ophthalmology, SKIMS MCH, Bemina Srinagar

***Corresponding Author:** Dr. Mustafeez Zehra
*Department of Ophthalmology, SKIMS MCH, Bemina Srinagar

ABSTRACT

Objectives: To correlate central corneal thickness and retinal nerve fibre layer thickness in patients with primary open angle glaucoma and compare it with their age matched controls using Ocular Coherence Tomography (OCT).

Material and Methods: This is an observational cross-sectional study in which 127 eyes of 100 patients diagnosed with POAG and 200 eyes of 100 controls were included**.** Ocular coherence tomography (OCT) was used to estimate Central Corneal Thickness (CCT) and Retinal Nerve Fiber Layer (RNFL) thickness in both glaucoma and control groups and correlated. Statistical analysis was done using Pearson's coefficient and p value < 0.005 was considered statistically significant.

Results: The average CCT among POAG cases was 505.7 µm whereas that of controls was 550.5 µm. Average RNFL thickness in POAG group was found to be 67.5± 15.70 µm whereas that in controls was 90.8± 7.89 µm. A positive significant correlation between CCT and average RNFL thickness was found in patients with POAG.

Conclusion and Implications: The results of this study add to the evidence that patients with thinner corneas have greater susceptibility to glaucomatous damage in view of thin RNFL. With the increasing availability of the OCT, CCT and RNFL measurements may be considered useful ancillary investigative tool in patients with POAG, for early diagnosis and timely management.

Key Words: Central corneal thickness, retinal nerve fibre layer thickness, ocular coherence tomography, primary open angle glaucoma.

INTRODUCTION

Glaucoma is a heterogenous group of disorders which have in common, a progressive optic neuropathy specified by a characteristic visual field loss and optic disc morphology changes, in which raised intraocular pressure is usually a key causative factor. Glaucoma is a multifactorial optic degenerative neuropathy characterised by the loss of retinal ganglion cells. It is a combination of vascular, genetic, anatomical and immune factors.[1] Glaucoma poses a significant public health concern as it is the second leading cause of irreversible-blindness worldwide and is associated with a reduced quality of life. It is not easily detected and can thus go undiagnosed, leading to an irreversible loss of vision. When classified according to gender, 2,395,600 of the diagnosed glaucoma cases were females and 1,577,800 were males.[2]

Primary open-angle glaucoma (POAG) tends to progress slowly and patients are often asymptomatic until the disease reaches an advanced stage. Injury due to glaucoma is irreversible, so early detection and prevention is of vital importance. It has been reported that circum-papillary retinal nerve fibre layer thickness begins to decrease during the early stages of glaucoma. Structural damage of optic nerve head (ONH) and RNFL may precede functional loss and it is estimated that between 30-50% of retinal ganglion cells may be lost before detectable changes in visual fields are evident. As retinal ganglion cells are lost, the layer thins out. Thus, RNFL defect is the main sign of early glaucomatous damage and that visual field testing, fundus image and IOP may not be sensitive to detect early damage.[3,4] Fundus photography can provide good qualitative information about glaucomatous damage indicators such as ONH cupping and the presence of optic disc haemorrhages, but more recent advances in ocular imaging technology promise to provide much more objective and quantitative information about the health and thickness of the retinal nerve fibre layer. One such modality is Optical Coherence Tomography (OCT).[5] In addition, within past several years, large glaucoma and ocular hypertension multicentre studies, such as the Ocular Hypertension Study and the European Glaucoma Prevention Study, have been established to determine the significant risk factors and predictors for the development of open-angle glaucoma. One of the risk factors that had been shown to be a powerful predictor of glaucoma development is the central corneal thickness.[6]

Although this relationship has been examined in glaucomatous eyes and eyes with ocular hypertension, there is little information on the relationship between Retinal nerve fibre layer (RNFL) thickness and Central Corneal Thickness in glaucoma patients.

This study is aimed at evaluating the relationship between CCT and RNFL thickness, which we believe is of value in early detection and follow-up of patients with primary open angle glaucoma.

MATERIALS AND METHODS

The study was a hospital based observational cross-sectional study conducted at Department of Ophthalmology, SKIMS Medical College and Hospital from April 2021 to December 2022. The study was approved by IEC SKIMS MCH Bemina. 127 eyes of 100 patients and 200 eyes of 100 controls were included in this study.

INCLUSION CRITERIA

- Open Angle Glaucoma Group

1. Patients diagnosed with POAG on the basis of high IOP (>21 mmHg), characteristic visual field defects and optic disc changes at the time of diagnosis with open angle of the anterior chamber.
2. Age over 40 years.

- Control Group

1. Participants of age over 40 years but normal IOP, normal visual fields, normal optic disc, open angle and absence of any ocular disease.

EXCLUSION CRITERIA

Patients with signs of secondary glaucoma, non-glaucomatous cause of optic neuropathy, known history of corneal disease, trauma. ocular surgery (corneal or retinal), with other retinal diseases like high myopia, hypertensive or diabetic retinopathy or optic disc anomalies and dense cataract obscuring fundus view were excluded from the study.

All those patients fulfilling the inclusion criteria were taken up for the study. Written Informed consent was taken before subjecting the patients to evaluation. SD-OCT (Zeiss Cirrus HD-OCT 500 Ocular Coherence Tomography (OCT) was used to estimate Central Corneal Thickness (CCT) and Retinal Nerve Fiber Layer (RNFL) thickness. The global and average four quadrant RNFL thickness data (superior, nasal, temporal, inferior) was collected and compared in both groups.

Statistical Methods: The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean ± SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by bar diagrams and scatter plots. Student's independent t-test or Mann-Whitney U-test, whichever feasible, was applied for comparing continuous variables. Karl Pearson's correlation coefficient was employed for assessing correlation between central corneal thickness (CCT) and retinal fiber nerve layer (RNFL) thickness in POAG patients. A P-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 127 eyes of 100 patients and 200 eyes of 100 controls were included in this study. Mean age of patients was 60.3±10.16 years ranging from 40-85 years. Mean age of control group was 58.9±9.73 years ranging from 40-81 years. Among POAG group, 61 (61%) were males and 39(39%) were females. Among control group 58 (58%) were males and 42 (42%) were females. Mean of average RNFL thickness among POAG patients was 67.5± 15.70 micrometers (µm) with range from 27-106µm. Mean RNFL thickness of superior quadrant among POAG patients was 81.4±24.79 µm with a range from 77.1-85.2, of inferior quadrant among was 78.2 ±24.30 µm with a range from 38-143, of temporal quadrant was 53.1 ±12.16 µm with a range from 32-85 and nasal quadrant among was 57.4±13.94 µm with a range from 55.1-59.8 µm as shown in table 1.

Table 1: RNFL thickness of POAG Patients

RNFL Thickness	Mean	SD	95% CI	Range
Superior quadrant	81.4	24.79	77.1-85.8	40-142
Inferior quadrant	78.2	24.30	74.0-82.5	38-143
Temporal quadrant	53.1	12.16	51.2-55.3	32-85
Nasal quadrant	57.4	13.94	55.1-59.8	32-95
Average	67.5	15.70	64.7-70.2	27-106

Mean of average RNFL thickness among controls was 90.8 µm with a range from 78-112 µm. Mean of RNFL thickness in superior quadrant among controls was 109.6 ±8.23 µm with a range from 95-12, of inferior quadrant was 104.8 ±14.73 µm with a range from 77-140 µm, of temporal quadrant was 64.9±9.75 µm with a range from 45-86 µm, of nasal quadrant among controls was 78.3± 8.96 µm with a range from 60-96 µm as shown in table 2.

Table 2: RNFL thickness of Controls

RNFL Thickness	Mean	SD	95% CI	Range
Superior quadrant	109.6	8.23	110.0-113.3	95-128
Inferior quadrant	104.8	14.73	101.9-107.8	77-140
Temporal quadrant	64.9	9.75	62.9-66.8	45-86
Nasal quadrant	78.3	8.96	76.5-80.1	60-96
Average	90.8	7.89	93.3-96.4	78-112

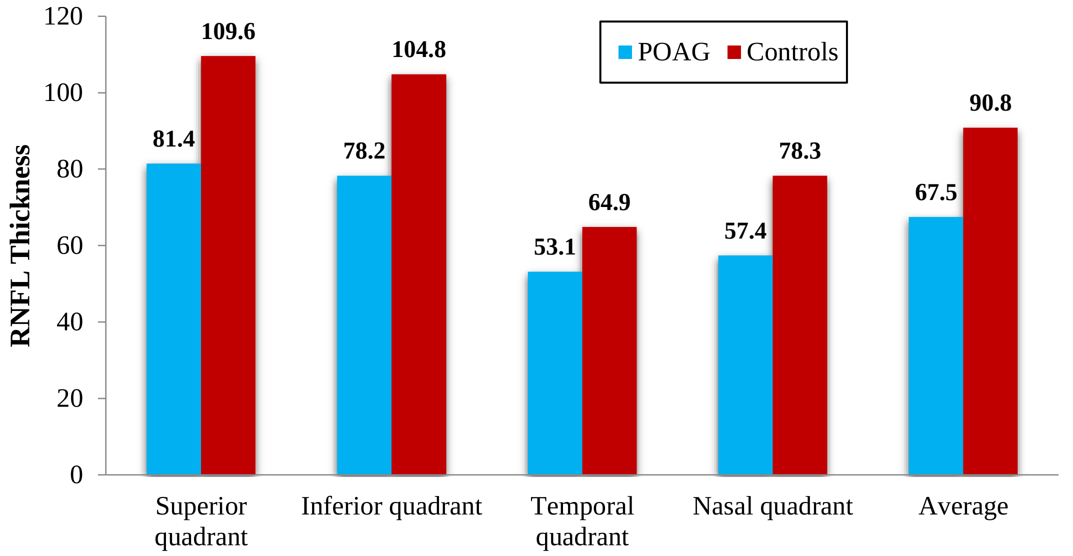
The difference in the average RNFL thickness and RNFL thickness among superior, inferior, temporal and nasal quadrant among POAG cases and controls was statistically significant between two groups (p value < 0.001).

Table 3: Comparison based on RNFL thickness in two groups

RNFL Thickness	POAG		Controls		P-value
	Mean	SD	Mean	SD	
Superior quadrant	81.4	24.79	109.6	8.23	<0.001*
Inferior quadrant	78.2	24.30	104.8	14.73	<0.001*
Temporal quadrant	53.1	12.16	64.9	9.75	<0.001*
Nasal quadrant	57.4	13.94	78.3	8.96	<0.001*
Average	67.5	15.70	90.8	7.89	<0.001*

*Statistically Significant Difference (P-value <0.05)

Figure 1: Comparison based on RNFL thickness in two groups



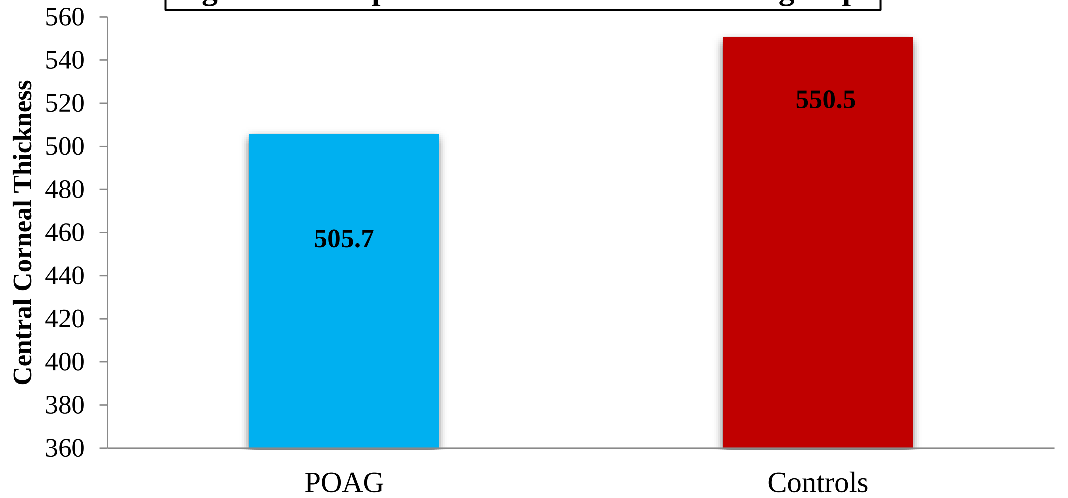
Mean Central Corneal thickness (CCT) among POAG cases was 505.7± 41.32µm with a range from 431-576 µm and among controls was 550.5 ±11.20 µm with a range from 530-569 µm as shown in table 4.

Table 4: Comparison based on CCT in two groups

CCT	Mean	SD	95% CI	Range	P-value
POAG	505.7	41.32	498.5-513	431-576	<0.001*
Controls	550.5	11.20	548.3-552.7	530-569	

*Statistically Significant Difference (P-value <0.05); CI: Confidence Interval

Figure 2: Comparison based on CCT in two groups



Pearson correlation between CCT and average RNFL thickness in POAG patients showed a positive significant correlation between them (r= 0.637, p<0.001) as shown in table 5. Pearson correlation between CCT and RNFL thickness among superior, inferior, temporal and nasal quadrant also showed a positive significant correlation between them (r= 0.591, 0.425, 0.512, 0.472 respectively) (p < 0.001)

Table 5: Correlation between CCT and RNFL thickness in POAG patients		
Quadrant	**Pearson correlation (r-value)**	**P-value**
Superior quadrant	0.591	<0.001*
Inferior quadrant	0.425	<0.001*
Temporal quadrant	0.512	<0.001*
Nasal quadrant	0.472	<0.001*
Average	0.637	<0.001*

*Statistically Significant Correlation (P-value <0.05)

Pearson correlation between CCT and average RNFL thickness among controls showed no significant correlation as shown in table 6. Pearson correlation between CCT and RNFL thickness of superior, inferior, temporal and nasal quadrant among controls, also didn't show any significant correlation as shown in table 6.

Table 6: Correlation between CCT and RNFL thickness in controls		
Quadrant	**Pearson correlation (r-value)**	**P-value**
Superior quadrant	0.137	0.175
Inferior quadrant	0.015	0.882
Temporal quadrant	0.004	0.967
Nasal quadrant	0.032	0.748
Average	0.054	0.594

*Statistically Significant Correlation (P-value <0.05)

DISCUSSION

This study has been done to correlate Retinal Nerve Fiber layer Thickness (RNFLT) with Central Corneal thickness (CCT) measured by Ocular Coherence Tomography (OCT) in patients with Primary open glaucoma (POAG). The correlation was compared with that of control group. Statistical analysis was done using Pearson's coefficient and p value <0.005 was considered statistically significant.

Our study found that the average RNFLT in the POAG group was 67.5 ± 15.70 µm, whereas in the control group, it was 90.8 ± 7.89 µm. This is consistent with previous literature, which demonstrates that POAG is associated with RNFL thinning. For instance, the Singapore Chinese Eye Study[7,8] and the Gutenberg Health Study[9] reported mean RNFLT values of 96.2 µm and 96.0 µm, respectively, for healthy individuals, indicating that our control group findings align closely with these values. The Beijing Eye Study[10] reported a slightly higher RNFLT of 103.2 µm in the Chinese population, showing that variations exist between different ethnic groups.

A study by Zhao L et al., (2014)[11] found that RNFLT follows a decreasing order of thickness: inferior, superior, nasal, and temporal quadrants. Our study supports this general trend, as POAG patients exhibited quadrant-wise thinning, with the superior and inferior quadrants being more affected. This thinning sequence aligns with the Singapore-Malay[12] and Singapore Chinese Eye Studies[7,8].

Our study supports the notion that ethnicity plays a role in RNFLT distribution, and our findings align with studies indicating that Asians have greater RNFLT than European and African populations. The E3 Consortium meta-analysis found RNFL thinning of 3.5 µm per year in predominantly white European populations.[13,14] In contrast, our study did not evaluate the impact of age on RNFL thinning, but age-related RNFL loss has been well-documented in multiple studies, including those by Hashemi H et al., (2017)[15] and histological analyses. Studies suggest an RNFL thinning rate of 2–4 µm per decade after 50 years, which could partially explain the differences in RNFLT values among different populations and age groups.

Our study found that CCT in POAG patients (505.7 μm) was significantly thinner than in controls (550.5 μm), with a p-value <0.001. This is in line with existing studies indicating that thinner CCT is associated with a higher risk of glaucoma progression. Previous research has established that African and Latino populations tend to have thinner corneas than Europeans and Asians, which may contribute to the higher risk of glaucoma observed in these groups[13,14,16,17].

In a study by **Jha B et al., (2017)**[18] changes in RNFL thickness among 100 POAG cases and 100 controls was compared. They found that the overall RNFLT, regardless of severity of glaucoma was thinner as compared to their age matched controls. RNFL thickness in all the quadrants of the optic nerve head was also found to be thinner than in controls and it became thinner as the severity of glaucoma increases. The difference was statistically significant. These results correlate with those of our study.

In the present study, there was a positive significant correlation between CCT and average RNFL thickness in patient with POAG (p<0.001). Also, there was a significant positive correlation between CCT and RNFL thickness of Superior, Inferior, Temporal and Nasal quadrant of ONH. Whereas, no significant correlation between CCT and RNFL thickness was found in the control group. CCT can thus be considered as a predictive factor of POAG. It is used to modify measured IOP, predict the effect on RNFL thickness and therefore determine the plan of therapy. Similarly in a retrospective analytical study by **Wangsupadilok B, Orapiriyakul L (2014)**[19] there were significant correlations between CCT and RNFL thickness in all quadrants and average RNFL thickness with highest correlation for average RNFL (r= 0.487. p<0.001). **Kaushik S et al., (2006)**[20] included a normal subset for comparison to patients with Ocular hypertension (OHT) in their OCT based study, where 51 patients were analyzed. After stratifying their data between CCT less than or equal to 555 μm and CCT more than 555 μm, they found no significant difference in average, inferior average, or superior average RNFLT between the two CCT groups. The correlation between CCT and the three RNFLT parameters and cup-to-disc area ratio was all found to be nonsignificant in their normal subset, except for the inferior quadrant RNFL thickness and average RNFL thickness, which had a Pearson correlation coefficient of 0.482, with a P=0.003. This agrees with this study finding of a positive relationship between CCT and overall average RNFLT as measured by OCT.

In another study by **Mansouri K et al., (2012)**[21] the CCT had no significant correlation with RNFL thickness as measured with OCT, in patients with POAG. However, when the RNFLT was measured by enhanced corneal compensation algorithms of scanning polarimetry, CCT was found to have a significant positive correlation with RNFL thickness.

One of the limitations of our study was that no comparison between different subtypes of glaucoma was done, which would have given us a better insight on the degree of correlation between different variables. Moreover, due to a lack of longitudinal follow-up, RNFL values were recorded at one point of time and were correlated. Glaucoma being a progressive condition, requires a serial follow up with multiple RNFL studies to get a better picture of RNFL loss.

CONCLUSION

Patients with thinner corneas have greater susceptibility to glaucomatous damage in view of thin RNFL. With the increasing availability of the OCT, CCT and RNFL measurements may be considered useful ancillary investigative tool in patients with POAG, for early diagnosis and timely management. Measurement of CCT can not only help in accurate estimation of IOP but can provide further insights into the stage of glaucomatous damage. The understanding that patients with thin CCT are more likely to have functional glaucomatous damage, such patients may require more frequent follow up than those with thicker CCT.

FINANCIAL INTEREST: Nil

CONFLICTS OF INTEREST: There are no conflicts of interest.

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