STUDY OF RETINAL NERVE FIBRE LAYER THICKNESS IN CASES OF PRIMARY OPEN ANGLE GLAUCOMA IN CORRELATION WITH PERIMETRIC CHANGES AND CENTRAL CORNEAL THICKNESS

ABSTRACT

Glaucoma has is one of the leading causes of blindness in the developed countries. In developing countries like India, glaucoma is the second leading cause of blindness after cataract. Primary open angle glaucoma is a multifactorial disorder characterised by death of retinal ganglion cells which results in a characteristic optic neuropathy and concomitant visual field reduction.The central corneal thickness (CCT) as well as the intraocular pressure (IOP) are important for assessing glaucoma since a low CCT will underestimate IOP which will affect the prognosis of glaucoma. In this study, we sought to assess the correlation between central corneal thickness (CCT) and quantitative measurements of retinal nerve fiber layer (RNFL). Our findings indicated that glaucomatous eyes with thinner corneas were associated with larger and deeper optic disc cups, suggesting that these eyes may be at an increased risk for RNFL loss.

KEYWORDS

Primary Open angle glaucoma (POAG), Central Corneal thickness (CCT), Intraocular pressure (IOP), Spectral Domain Optical coherence Tomography (SD-OCT), Retinal nerve fibre layer (RNFL), Ocular hypertension (OHT)

INTRODUCTION

Primary open-angle glaucoma (POAG) is a chronic progressive optic neuropathy with characteristic morphological changes at the optic nerve head and retinal nerve fibre layer in the absence of other ocular disease or congenital anomalies. Progressive retinal ganglion cell death and visual field loss are associated with these changes.[1]IOP is considered the most important risk factor for the development of POAG, and remains the only known modifiable risk factor. Population studies have shown increased prevalence of glaucoma with increasing IOP. In patients with OHT (raised IOP but no signs of glaucomatous optic disc or visual field changes), higher IOP is associated with a higher risk of developing POAG.(1)The prevalence of POAG increases with age.Myopia has been shown to be a risk factor for POAG in several

studies.A thinner cornea has been shown to be a risk factor for OHT patients developing POAG. This may be in part due to IOP measurement error (IOP tends to be read lower in patients with thinner corneas), but there are also theories that a thinner cornea may indicate less rigid support structures around the optic nerve head, and a resultant increased propensity to damage.A first-degree relative with POAG is a risk factor for the development of POAG.Several genes associated with POAG have been identified.A high prevalence of POAG has been found in diabetic patients, and a high prevalence of diabetes has been found in POAG patients. Hypertension may predispose to glaucomatous damage via increased peripheral vascular resistance in small vessels, while a low blood pressure may reduce the perfusion pressure of the optic disc.[1]

PATHOPHYSIOLOGY

MECHANISM OF AQUEOUS HUMOR FORMATION

Three mechanisms are involved in aqueous humor formation: diffusion, ultrafiltration and active secretion.Diffusion occurs when solutes, especially lipid soluble substances, are transported through the lipid portions of the membrane of the tissues between the capillaries and the posterior chamber, proportional to a concentration gradient across the membrane.Ultrafiltration is the flow of water and water-soluble substances, limited by size and charge, across fenestrated ciliary capillary endothelia into the ciliary stroma, in response to an osmotic gradient or hydrostatic pressure.Active secretion is thought to be the major contributor to aqueous formation, responsible for approximately 80% to 90% of the total aqueous humorformation . The main site for active transport is believed to be the nonpigmented epithelial cells. Active transport takes place through selective trans-cellular movement of anions, cations, and other molecules across a concentration gradient in blood-aqueous barrier. This is mediated by protein transporters distributed in the cellular membrane. Aquaporins (AQPs) are molecular water channels which aid with rapid bulk transport of fluid or transport of fluids against an insufficient osmotic pressure gap. The energy required for the transport is generated by hydrolysis of adenosine triphosphate (ATP) to adenosine diphosphate (ADP), which is activated by Na+ and K+ (66) mediated by Na+-K+-ATPase, an enzyme located in both the non-pigmented and pigmented ciliary epithelia.Another enzyme, carbonic anhydrase, found in the nonpigmented and pigmented

ciliary epithelia , mediates the transport of bicarbonate across the ciliary epithelium by the reversible hydration of CO2 to form HCO3-and protons.[2]

PHYSIOLOGY OF AQUEOUS OUTFLOW

The trabecular meshwork (trabeculum) is a sieve-like structure at the angle of the anterior chamber (AC) through which 90% of aqueous humour leaves the eye. It has three components

The uveal meshwork is the innermost portion and offers little resistance to the passage of aqueous.

The corneoscleral meshwork lies external to the uveal meshwork to form the thickest portion of the trabeculum conferring greater resistance to flow.

The juxtacanalicular (cribriform) meshwork is the outer part of the trabeculum, and links the corneoscleral meshwork with the endothelium of the inner wall of the canal of Schlemm.The outer wall is lined by smooth flat cells and contains the openings of collector channels, which leave the canal at oblique angles and connect directly or indirectly with episcleral veins. Septa commonly divide the lumen into 2–4 channels.[3,4]

There are multiple proposed mechanisms of damage, some of which are IOP- dependent, and others are IOP- independent.

Raised IOP is thought to damage the optic nerve head via induced mechanical changes at the lamina cribrosa, or via vascular dysfunction and resultant ischemia.
IOP independent mechanisms of damage

- Reduced ocular perfusion pressure (and hence the association with vascular diseases such as diabetes, hypertension and migraine)

Diagnosis of POAG requires assessment of:

- Intraocular pressure
- Open- normal appearing anterior chamber angle
- Characteristics signs of optic disc damage
- Visual function loss on perimetry [1]

MATERIALS AND METHODS

STUDY DESIGN

This was a cross sectional observational study which was conducted over a period of two years (August 2022-2024).

INCLUSION CRITERIA

1. Patients of age above 18 years.
2. Patients of both gender.
3. Patients presenting with intraocular pressure greater than 21 mm Hg
4. Characteristic VF changes.
5. Patients with co morbidities like diabetes and hypertension.

EXCLUSION CRITERIA

1. Pregnant and lactating women.
2. Patients with history of cornea opacity.
3. Patients with congenital /pathological myopia
4. Disc pathologies like papiloedema
5. Patients with signs of secondary glaucoma
6. Non glaucomatous optic neuropathy.
7. Angle closure suspects
8. Patients not willing to give consent

SAMPLE SIZE

Patients visiting Ophthalmology outpatient department of a tertiary healthcare centre were enrolled in the study.

Sample Size Calculation: By using ‘Cup:disc area ratio 0.71±0.14 0.63±0.13 <0.005 a sample size of Total 72 (36 cases in each arm) completed cases needed to assess the study objective at 80% power and 5% level of significance with 1:1 allocation.

N = 80 (40 in each arm) Considering 10% drop out to be enrolled in this study.

STUDY METHOD

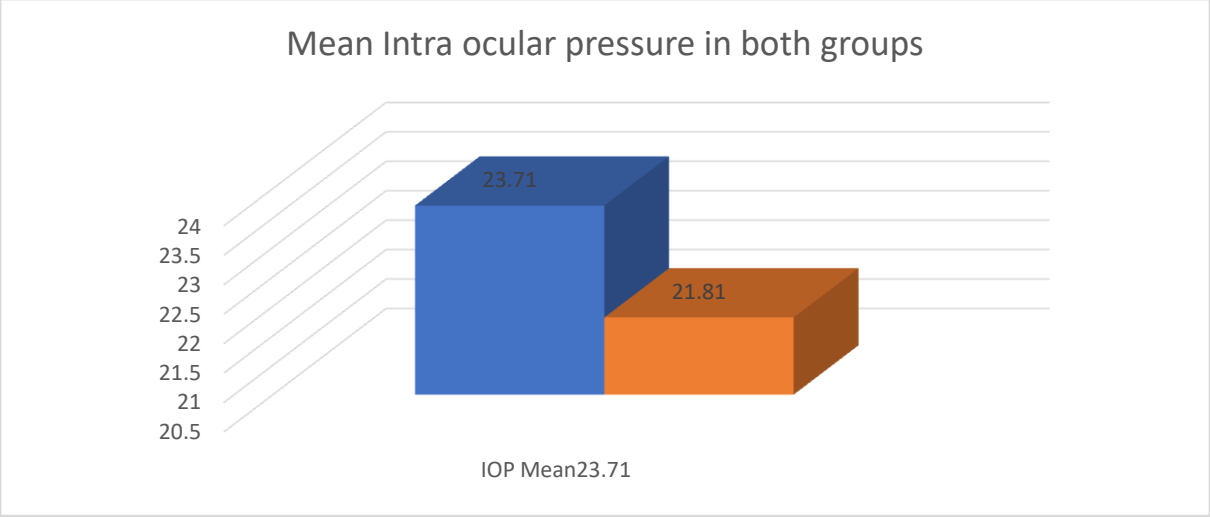
Complete medical history including previous medications, ocular trauma or ocular surgeries were recorded in the case record form. Subjects underwent complete ophthalmological examination including uncorrected and best corrected visual acuity (BCVA) measurement, slit lamp examination, Goldmann Applanation tonometry for IOP measurement, gonioscopic evaluation and fundus examination. Visual field test was carried out using Humphrey octopus perimeter with SITA without pupil dilatation. A Glaucomatous VF was defined as a glaucoma hemifield test outside of normal limits on atleast 2 consecutive baseline tests and the presence of atleast three contiguous test points within the same hemifield on pattern deviation plot at P<1%, with atleast one at P<0.5%.CCT was measured using ultrasound pachymeter. RNFL and ONH parameters were recorded through SD-OCT.All eyes had open-angle observed by gonioscopy, and the patients fulfilled at least two of the following criteria: glaucomatous optic neuropathy, IOP >21 mmHg on at least three occasions, and glaucomatous visual field defects. Eyes were divided into two groups on the basis of their median central corneal thickness (CCT) and classified into thick cornea group CCT ≥540 µm (Group 1) and thin cornea group (Group 2) CCT < 540 µm.

RESULTS AND DISCUSSION

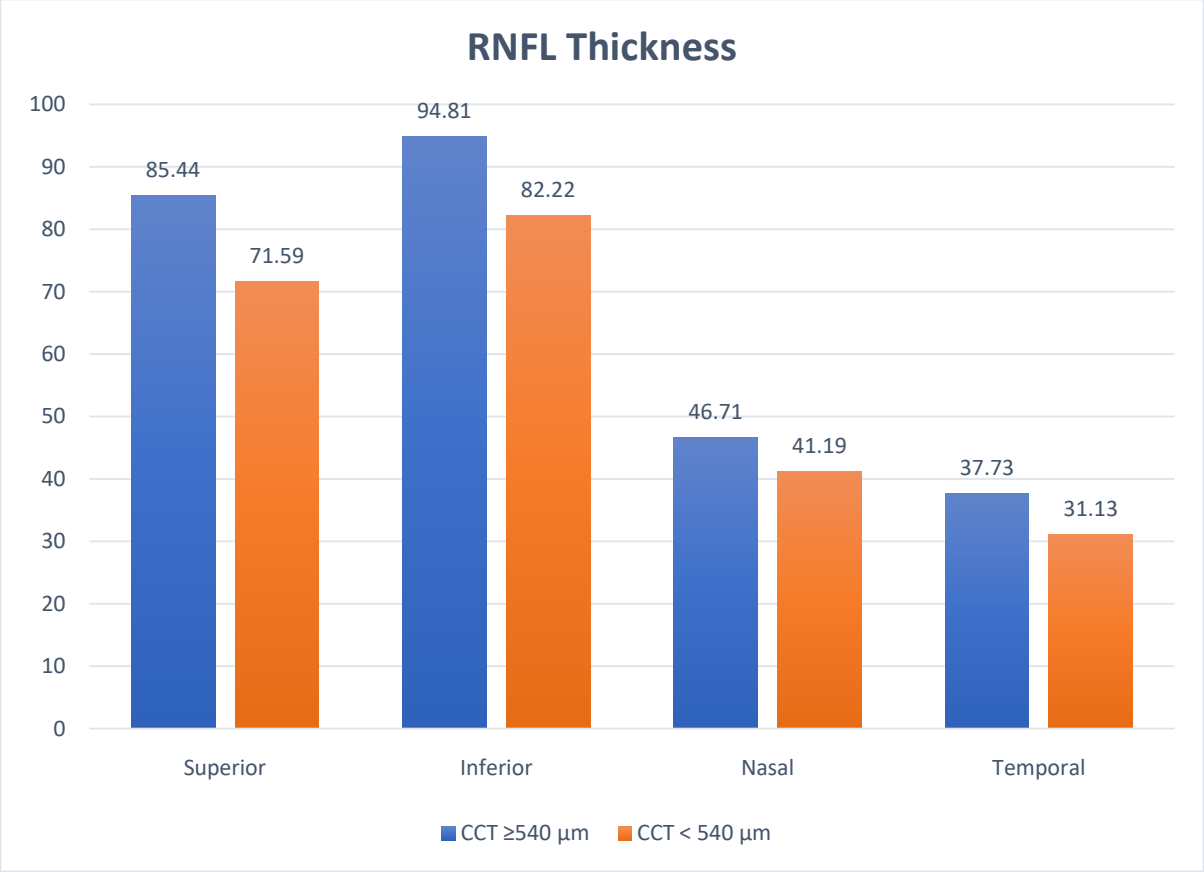
In this study, the age of cases was ranging from **34.00 – 87.00 years** with average age being **61.71** years among CCT ≥540 µm which was comparable to **61.38 years** in CCT < 540 µm and the difference was statistically not significant.In study conducted by Wangsupadilok et al the mean age was 60.96 +/- 7.44 years which was comparable to this study.[5]

62.5% of total cases were males in CCT ≥540 µm which was more as compared to **41.7%** cases in CCT < 540 µm but the difference was not statistically significant. **37.5%** of total cases were females in CCT> 540 µm which was more as compared to **25%** cases in CCT <540 µm but the difference was not statistically significant.

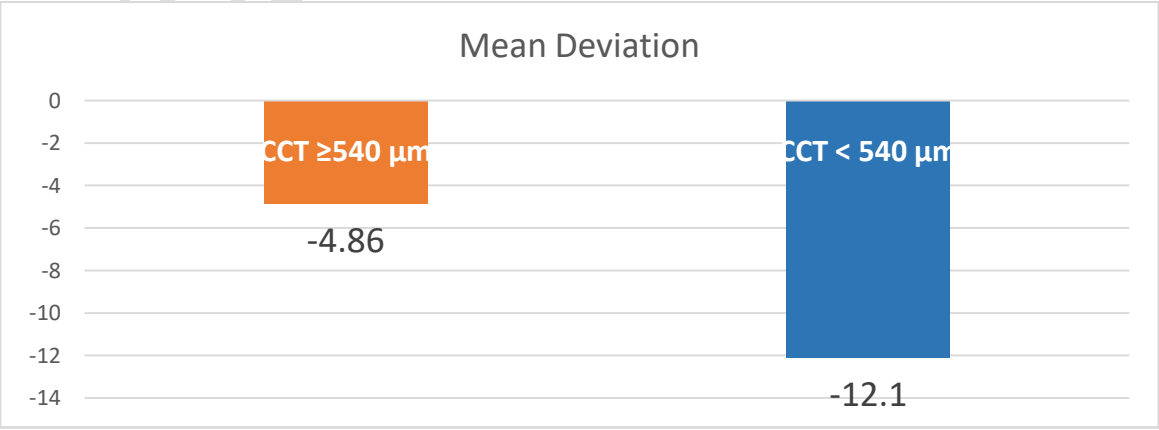
Mean IOP was **23.71 mmHg** among CCT ≥540 µm which was significantly more as compared to **21.81 mmHg** in CCT < 540 µm. A study conducted by Dhiman et al in a cross sectional study on 103 eyes of 58 patients of POAG and divided patients into two groups- thick and thin CCT taking a reference range of 529µm and came to a conclusion that as the CCT increases there is falsely elevated IOP.[6]



The mean average RNFL was **85.85µm** among CCT ≥540 µm which was significantly more as compared to **67.19µm** in CCT <540 µm. Mean Superior RNFL was **85.44 µm** among CCT ≥540 µm which was significantly more as compared to **71.59 µm** among CCT < 540 µm. Mean Inferior RNFL was **94.81 µm** among CCT ≥540 µm which was significantly more as compared to **82.22 µm** in CCT < 540 µm. Mean Nasal RNFL was **46.71 µm** among CCT ≥540 µm which was significantly more as compared to **41.19 µm** in CCT < 540 µm. Mean Temporal RNFL was **37.73 µm** among CCT ≥540 µm which was significantly more as compared to **31.13 µm** in CCT < 540. In a cross sectional study of 234 eyes conducted by Barua et al patients were categorized into three groups POAG, ocular hypertensive and normal and it showed GCC and RNFL parameters had equal predictive capability in perimetric versus normal group.[7]Bhat et al conducted a study on 49 patients of POAG and inferred the average RNFL loss in mild, moderate, and severe POAG was 25.44%, 29.67%, and 44.15%, respectively.[8]A statistically significant correlation ($P < 0.05$) between RNFL loss and severity of glaucoma was found in all except the superior and temporal sectors. A study conducted by Wangsupadilok and associates found a significant correlation was found between CCT and RNFL thickness ($r = 0.487$, $p = 0.001$).[5]Kaushik et al. discovered that the retinal nerve fiber layer (RNFL) in individuals with ocular hypertension and a central corneal thickness (CCT) of 555 µm or less was significantly thinner compared to those with thicker corneas, as measured by optical coherence tomography (OCT).[9]



Mean MD was **-4.86dB** among CCT ≥540 µm which was significantly more as compared to -**12.10dB** in CCT < 540 µm. Mean PSD was **2.46dB** among CCT ≥540 µm which was significantly less as compared to **6.92dB** in CCT < 540 µm. Research has shown that eyes with thinner central corneal thickness (CCT) exhibit more severe visual field (VF) defects compared to those with thicker CCT.[10]



CONCLUSION

In conclusion, SD OCT is an effective tool in evaluating the ONH and RNFL thickness to detect early to moderate glaucomatous changes. The average RNFL thickness and the Superior and inferior RNFL quadrant thickness are the most sensitive parameters to detect glaucomatous changes. Both the ONH and RNFL parameters are equally reliable as a diagnostic tool but their role in detecting the progression needs to be studied further with the long term study. Overall, the study underscores the importance of considering CCT in glaucoma assessment and highlights the role of OCT in providing valuable insights into RNFL and ONH changes associated with glaucoma. This early detection is crucial for timely intervention, helping to monitor glaucomatous damage and potentially reduce the risk of blindness associated with the disease.

LIMITATIONS

The study was undertaken only on known cases of primary open angle glaucoma to evaluate the glaucomatous changes but the efficacy of these parameters in detecting the progression of these changes were not studied. The glaucoma suspects were not included in the study, hence the efficacy to predict future glaucomatous changes with these parameters is not known.The RNFL parameters were not studied for the clock hourwise distribution, hence focal glaucomatous changes could have been.

REFERENCES

1 .Stamper R, Lieberman M, Drake M. Becker-Shaffer's Diagnosis and Therapy of the Glaucomas. 8th Edition. New York, NY: Mosby; 2009:239-265.

2 .Millar C, Kaufman PL. Aqueous humor: secretion and dynamics. In: Tasman W, Jaeger EA, editors. Duane's foundations of clinical ophthalmology. Philadelphia: Lippincott-Raven; 1995.

3. Costagliola C, dell'Omo R, Agnifili L, Bartollino S, Fea AM, Uva MG, Zeppa L, Mastropasqua L. How many aqueous humor outflow pathways are there? SurvOphthalmol. 2020 Mar-Apr;65(2):144-170.

4. Buffault J, Labbé A, Hamard P, Brignole-Baudouin F, Baudouin C. The trabecular meshwork: Structure, function and clinical implications. A review of the literature. J Fr Ophtalmol. 2020 Sep;43(7):e217-e230.

5. Wangsupadilok B, Orapiriyakul L. Correlation between central corneal thicknessand visual field defect, cup to disc ratio and retinal nerve fiberlayerthickness in primary open-angle glaucoma patients. J Med Assoc Thai. 2014;97:751–757.

6. Dhiman R, Sharma G, Tomar M, Singh M. A study for the assessment of central corneal thickness and visual field defects in patients of primary open-angle glaucoma. Sudanese J Ophthalmol2019;11:25-30.

7. Barua N, Sitaraman C, Goel S, Chakraborti C, Mukherjee S, Parashar H. Comparison of diagnostic capability of macular ganglion cell complex and retinal nerve fiber layer among primary open angle glaucoma, ocular hypertension, and normal population using Fourier-domain optical coherence tomography and determining their functional correlation in Indian population. Indian J Ophthalmol2016;64:296-302.

8.Bhat KS, Reddy MV, Pai V. Correlation of retinal nerve fiber layer thickness with perimetric staging in primary open-angle glaucoma - A cross-sectional study. Oman J Ophthalmol. 2022 Mar 2;15(1):36-42.

9. Kaushik S, Gyatsho J, Jain R, Pandav SS, Gupta A. Correlation between retinal nerve fiber layer thickness and central corneal thickness in patients with ocular hypertension: an optical coherence tomography study. Am J Ophthalmol2006;141:884–90.

10. Jonas JB, Holbach L. Central corneal thickness and thickness of the lamina cribrosa in human eyes. Invest Ophthalmol Vis Sci 2005;46:1275-9

239

240

241