Original Research Paper Ophthalmology

To study and compare the central corneal thickness and endothelial cell parameters in patients with open angle glaucoma with normal controls.

Prempal Kaur	Associte Professor Ophthalmology GMC AMRITSAR
Inderjit Kaur	Professor Ophthalmology GMC AMRITSAR
Piyush Goyal	Junior Resident Ophthalmology GMC AMRITSAR
Atish Pradhan	Junior Resident Ophthalmology GMC AMRITSAR

ABSTRACT

Introduction: Glaucoma is the second leading cause of blindness in the world and is responsible for approximately 5.2 million blind which accounts to 15% of the total burden of world blindness.

Aims: To study and compare the central corneal thickness (CCT) and endothelial cell count (ECC) in patients with open angle glaucoma with normal controls.

Material and Methods: This prospective, observational study was conducted on 100 patients (200eyes) of glaucoma and compared with 100 normal age and sex matched individuals(200 eyes).Specular microscope was used to access corneal ECC, hexagonality and coefficient of variance(CV). CCT was measured with ultrasonic pachymeter. The data collected was tabulated and analysed .

Results: The mean central corneal was thicker (513.64±35.64) µm in Group A than in control Group B (515.57 ±27.84 µm) but was not statistically significant (p-value>0.05). The mean corneal ECC was lower (2175.32± 426.67 cells/mm2) in Group A than Group B (2387.86±280.17 cells/mm2) and the mean hexagonality in Group A was lower (65.03±28.57) than control group (87.94±13.26) and the difference was highly significant (p-value<0.05). The mean CV was significantly higher (47.74±17.78) in Group A than control group (35.51±15.39) (p-value<0.05).

Conclusion: Patients with glaucoma have increased central corneal thickness, higher co-efficient of variation, lower corneal endothelial cell density and hexagonality as compared to normal age and sex matched individuals .

KEYWORDS : glaucoma, central corneal thickness, corneal endothelial cell density, and hexagonality.

INTRODUCTION

Glaucoma is the second leading cause of blindness in the world and is responsible for approximately 5.2 million blind.[1] The estimated prevalence of glaucoma in the world was 60.5million in 2010 and is expected to increase to 79.6 million in 2020.[2] There are approximately 11.2 million persons aged 40 years and older with glaucoma in India.Primary open angle glaucoma is estimated to affect 6.48 million persons. The estimated number with primary angle-closure glaucoma is 2.54 million.Those with any form of primary angle-closure disease could comprise 27.6 million persons.[3]

Glaucoma can be defined as a multifactorial optic neuropathywith a characteristic accelerated degeneration of retinal ganglion cells presenting as classical optic nerve head features and correlating visual field changes, which may or may not be associated with angle abnormality in the presence or absence of any cause for the disease. These disorder share features of cupping and atrophy of the optic nerve head with attendant visual field loss and are frequently (but not always) related to the level of intraocular pressure.[4,5,6]

Clinico-etiologically Glaucoma is classified as[6]

1. Open angle Glaucoma
2. Angle Closure Glaucoma
3. Combined mechanism glaucoma

The adult human cornea measures 11 to 12 mm horizontally and 9 to 11 mm vertically. It is approximately 0.5 mm thick at the center, with the thickness increasing gradually toward the periphery, where it is about 0.7 mm thick. Central corneal thickness varies between individuals and is a key determinant of the conventionally-measured intraocular pressure level.[7]

Endothelium is a single layer of corneal endothelial cells covering the posterior surface of Descemet's membrane in a well-arranged mosaic pattern. These cells are uniformly 5 µm in thickness and 20 µm in width and are polygonal (mostly hexagonal) in shape. The uniformity of endothelial cell size has been evaluated by statistical analysis based on photographs taken by a wide-field specular microscope. In young adults, the cell density is about 3500 cells/mm^2. The number of cells decreases at about 0.6% per year and neighbouring cells enlarge to fill the space. The endothelial cells cannot regenerate.[7]

Our study aimed to study and compare the endothelial parameters and central corneal thickness in patients with open angle glaucoma with normal controls.

MATERIALS AND METHODS: After the approval from government medical college thesis and ethical committee the study was conducted on 200 eyes of diagnosed cases of open angle glaucoma (GroupA) and compared with normal age and sex matched normal individuals (GroupB). The written informed consent was taken from all the patients in both the groups in their vernacular language.

Patients (Group A) between 30-70years irrespective of sex with intraocular pressure of more than 21 mm of Hg at least in one eye by Applanation tonometer were included in the study. Patients with any corneal disease or with history uveitis, ocular trauma, secondary glaucoma, diabetes or previous surgical interventions were excluded from the study. Normotensive glaucoma and ocular hypertension patients were also excluded from the study.

The control group (Group B) consisted of people who had intra-ocular pressures <21 mm. of Hg. in both the eyes measured by Goldman's applanation tonometer, had normal optic discs, open angles on gonioscopy, no suspicion of any form of glaucoma, no family history of glaucoma, and did not have any other eye disease.

A complete ophthalmic examination including BCVA, Goldmann Applanatio tonometry, Direct Ophthalmoscopy, Slit-lamp biomicroscopy with 90D lens, Indirect Gonioscopy with a three mirror/ four mirror goniolens, Perimetry on the Humphrey Visual Field Analyser (Static Perimetery), Specular microscopy and ultrasonic pachymetry was performed in each patient

Specular microscopy (TOPCON SP 3000P non contact specular microscope) was done to assess corneal endothelial density, hexagonality and coefficient of variance. Central corneal thickness

was measured by Ultrasonic pachymetry.

The data collected was tabulated and analysed to study the central corneal thickness, corneal endothelial cell density, hexagonality and coefficient of variance in both the groups individually and a comparative analysis was done between both the groups.Data analysis was performed using statistical package for the social sciences, version 21.0 for windows (IBM corp. SPSS, 2012, Armonk, NY). Chi-square test was used to find significance among the number of cases in different age group, gender, best corrected visual acuity. Student's unpaired sample t- test was used to find significant difference of central corneal thickness, corneal endothelial cell density, hexagonality and coefficient of variance in both the groups.

OBSERVATIONS AND RESULTS

Out of 100 patients in Group A 38% were in 61-70 years of age group and 55% were females. Figure 1 and 2

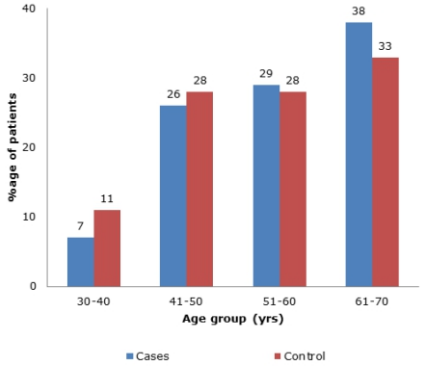

Figure 1 showing age distribution

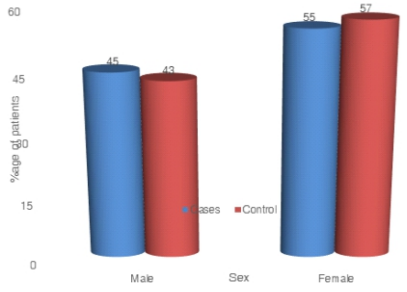

Figure 2 showing sex distribution

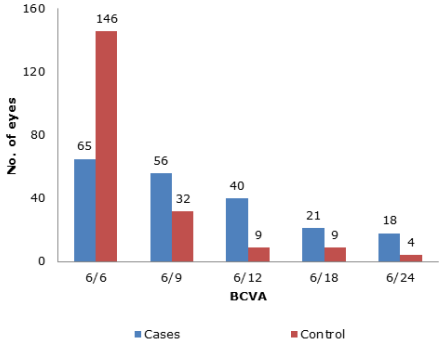

Figure 3. Details of BCVA

In Group A, 65(32.5%) eyes were having best corrected visual acuity of 6/6 whereas in control group, 146 (73%) eyes were having best corrected visual acuity of 6/6. The difference in best corrected visual acuity was statistically significant among the two groups (p-value<0.05). Figure 3.

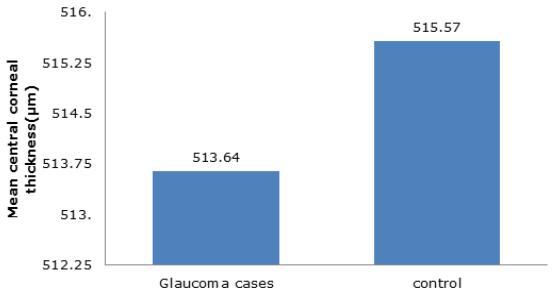

Figure 4 Mean central corneal thickness

The mean central corneal thickness was 513.64±35.64 µm in Group A compared to mean of 515.57 ±27.84 µm in control group and the difference was not found to be statistically (p-value>0.05) (Figure 4).

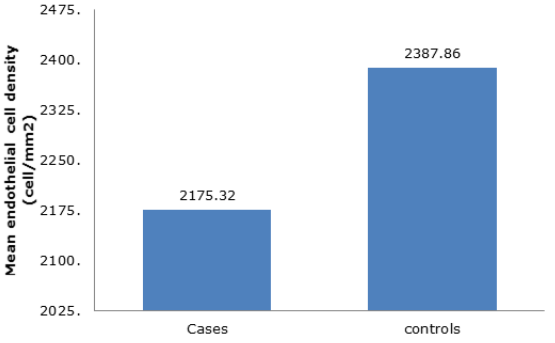

Figure 5 mean endothelial cell density.

The mean corneal endothelial cell density was 2175.32± 426.67 cells/mm^2 in Group A and 2387.86 ±280.17 cells/mm^2 in Group B. The mean corneal endothelial cell density was lower in Group A compared to control group and the difference was statistically highly significant among the two groups (p-value<0.05)figure 5.

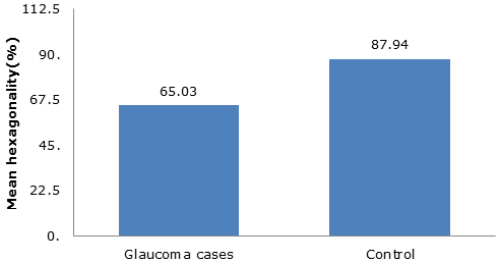

Figure 6 Showing mean hexagonality

The mean hexagonality in Group A was lower than control group with a mean of 65.03±28.57 in patients with glaucoma compared to mean of 87.94±13.26 in control group and the difference in mean hexagonality was highly significant (p-value<0.05)(figure 6).

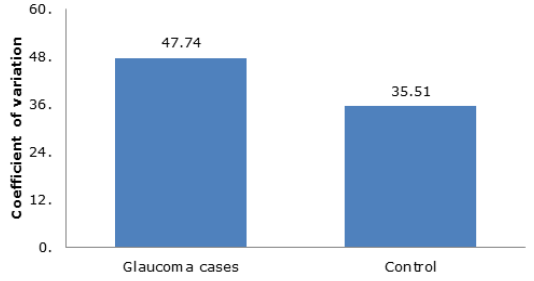

Figure 7 Showing mean coefficient of variation(CV)

The mean coefficient of variation(CV) was 47.74±17.78 in Group A compared to 35.51±15.39 in Group B and the difference in mean coefficient of variation was highly significant between the two groups (p-value<0.05) figure 7.

DISCUSSION

MEAN CORNEAL ENDOTHELIAL CELL DENSITY

In the present study, mean corneal endothelial cell density was lower (2175.32± 426.67 cells/mm^2) in patients with glaucoma compared to control group (2387.86 ±280.17cells/mm^2) and the difference was found to be statistically highly significant(p-value<0.05).

In a study conducted by Gagnon MM et al in 1997, 102 patients with glaucoma were compared with 52 patients without glaucoma. Corneal endothelial cell counts were significantly lower in patients with glaucoma (2,154 ± 419 cells/mm^2) than in controls (2,560 ± 360 cells/mm^2; t test, p < 0.0001).[8]

Luo Y et al in 2000 studied 125 eyes of 68 patients with glaucoma. They were compared with 63 eyes of 32 patients without glaucoma in the same age group. Corneal endothelium density was significantly lower in patients with glaucoma (2386.81 ± 289.76 cells/mm^2) than that in controls (2540.78 ± 195.66 cells/mm^2).[9]

In a prospective study conducted by Novak-Stroligo M et al in 2010 on 50 patients each of glaucoma and control group, specular microscopy was performed on central corneas. This study showed that patients with glaucoma have lower central corneal endothelial cell density than those without glaucoma of the same age group.[10]

In a study conducted by Ranno S et al in 2011, endothelial cell density measured as cells per mm^2 was lower in the glaucoma group comparing treated patients with non treated patients (2826 ± 285 versus 3124 ± 272, P = 0.0003).[11]

Galgauskas S et al in 2012 studied a total of 104 patients and observed endothelial cell density in the glaucoma group as 2484 (±82) where as in healthy elderly group and younger group had 2394 (±416) cells/mm^2 and 2940 (±345) cells/mm^{2}respectively.[12]

In the present study, a weak inverse correlation was observed between corneal endothelial cell density and central corneal thickness (r= -0.127) and it was not statistically significant (p-value >0.05).

HEXAGONALITY

In the present study, the mean hexagonality 65.03±28.57 in Group A was lower than control group 87.94±13.26 and was highly significant (p-value<0.05). The results of our study were in accordance with the study conducted by Galgauskas Setal in 2012 who studied central corneal thickness and corneal endothelial characteristics in healthy, cataract, and glaucoma patients. Hexagonality in the glaucoma group was 60(±10)% which was lower than elderly healthy individuals with hexagonality 64(±10%) as well as young healthy subjects with 66(±10)% hexagonality.[12]

Juan-MarcosL et al in 2013, analysed 30 eyes with pseudoexfoliation glaucoma (PXG), 40 eyes with POAG, and 60 normal eyes. The percentage of hexagonal cells were lower in PEX groups and in the POAG group compared with normal eyes.[13]

COEFFICIENT OF VARIANCE

In the present study, the mean coefficient of variation (CV) was 47.74±17.78 in Group A compared to 35.51±15.39 in control group and the difference in mean coefficient of variation was highly significant between the two groups (p-value<0.05).

Luo Yetal in 2000 found that the area of endothelium became bigger than normal in patients with glaucoma..[14]

Similarly Juan- MarcosL et al in 2013 also found the CV in cell size was greater in PEX group and POAG as compared to normal patients.[13]

CENTRAL CORNEAL THICKNESS

The mean central corneal thickness of Group A patients was 513.64±35.64 µm as compared to mean of 515.57±27.84 µm in control group and the difference was found to be statistically non significant (p-value>0.05). The results of this study were similar to study conducted by LeonW. Herndonetal in 1997 where there was no significant difference in CCT between normal and glaucomatous eyes (P=.40).[15]

Copt R Petal.(1999) also found no significant difference in CCT between controls (552±35 microns) and patients with POAG (543±35 microns).[16]

Kitsos G et al in 2009 and Maya Natarajan et al in 2013 also observed simillar results .[17,18] but in a study conducted by Sibel Kocabeyoglu et al in 2015 , the mean CCT was lower in glaucoma patients on prostaglandin analogues (515.2 ± 18.8 µ) than control subjects (549.6 ± 21.1 µ, *P* < 0.001).[19]

CONCLUSION

Glaucoma patients have increased central corneal thickness as compared to controls but the difference is not statistically significant whereas they have statistically significant lower corneal endothelial cell density, hexagonality and higher coefficient of variation than normal age and sex matched non glaucoma individuals.

REFERENCES:

1. Thylefors B, Négrel AD. The global impact of glaucoma. Bull World Health Organ. 1994;72(3):323–6
2. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol. 2006 Mar;90(3):262–7.
3. George R, Ve RS, Vijaya L. Glaucoma in India: estimated burden of disease. J Glaucoma. 2010 Aug;19(6):391–7.
4. Hitchings RA, Spaeth GL. The optic disc in glaucoma. I: Classification. Br J Ophthalmol. 1976 Nov;60(11):778–85.
5. Kitazawa Y, Yamamoto T. Glaucomatous visual field defects: their characteristics and how to detect them. Clin Neurosci N Y N. 1997;4(5):279–83.
6. Stamper RL, Lieberman MF, Drake MV, Becker B, Shaffer RN. Becker-Shaffer's diagnosis and therapy of the glaucomas. 8th ed. Edinburgh: Mosby, Elsevier; 2009. 568 p.
7. Krachmer JH, Mannis MJ, Holland EJ, editors. Surgery of the cornea and conjunctiva. 3. ed. Maryland Heights, Miss.: Mosby Elsevier; 2011. 1321 p. (Cornea). Gagnon
8. MM, Boisjoly HM, Brunette I, Charest M, Amyot M. Corneal endothelial cell density in glaucoma. Cornea. 1997 May;16(3):314–8.
9. Luo Y, Li J, Jin Y. [Changes of corneal endothelium in patients with primary glaucoma]. Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 2000 Aug;22(4):356–9.
10. Novak-Stroligo M, Alpeza-Dunato Z, Kovacević D, Caljkusić-Mance T. Specular microscopy in glaucoma patients. Coll Antropol. 2010 Apr;34 Suppl 2:209–10.
11. Ranno S, Fogagnolo P, Rossetti L, Orzalesi N, Nucci P. Changes in corneal parameters at confocal microscopy in treated glaucoma patients. Clin Ophthalmol Auckl NZ. 2011;5:1037–42.
12. Galgauskas S, Krasauskaite D, Pajaujis M, Juodkaite G, Asoklis R-S. Central corneal thickness and corneal endothelial characteristics in healthy, cataract, and glaucoma patients. Clin Ophthalmol Auckl NZ. 2012;6:1195–9
13. de Juan-Marcos L, Cabrillo-Estévez L, Escudero-Domínguez FA, Sánchez-Jara A, Hernández-Galilea E. [Morphometric changes of corneal endothelial cells in pseudoexfoliation syndrome and pseudoexfoliation glaucoma]. Arch Soc Esp Oftalmol. 2013 Nov;88(11):439–44.
14. Luo Y, Li J, Jin Y. [Changes of corneal endothelium in patients with primary glaucoma]. Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 2000 Aug;22(4):356–9.
15. Herndon LW, Choudhri SA, Cox T, Damji KF, Shields M, Allingham R. CEntral corneal thickness in normal, glaucomatous, and ocular hypertensive eyes. Arch Ophthalmol. 1997 Sep 1;115(9):1137–41.
16. Copt RP, Thomas R, Mermoud A. Corneal thickness in ocular hypertension, primary open-angle glaucoma, and normal tension glaucoma. Arch Ophthalmol Chic Ill 1960. 1999 Jan;117(1):14–6.
17. Kitsos G, Gartzios C, Asproudis I, Bagli E. Central corneal thickness in subjects with glaucoma and in normal individuals (with or without pseudoexfoliation syndrome). Clin Ophthalmol Auckl NZ. 2009;3:537–42.
18. Natarajan M, Das K, Jeganathan J. Comparison of central corneal thickness of primary open angle glaucoma patients with normal controls in South India. Oman J Ophthalmol. 2013 Jan;6(1):33–6.
19. Kocabeyoglu S, Mocan MC, Irkec M. Decreased keratocyte density and central corneal thickness in primary open-angle glaucoma patients undergoing treatment with topical prostaglandin analogues. Indian J Ophthalmol. 2015 Jan;63(1):15–9.