

## **Corneal Endothelium: Boon to Glaucoma patients A Major Review on Role of Cornea in Glaucoma Patients**

**Dr.Shubhangi Deshmukh Giradkar, Dr.SmitaSingh, Dr.AKShukla,  
Dr.V R Venkatramanan**

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### **I. Introduction**

Glaucoma is one of the most common cause of blindness second only to cataract in magnitude worldwide. Unfortunately the visual loss in glaucoma cannot be restored by any known means at our present level of knowledge.

Corneal transparency is essential to its role as the principal lens which refracts light entirely in the eye. This optical quality is the result of the unique and regular arrangement of the tissue elements constructing it. This transparency is maintained by the optimal function of the endothelium. The endothelium has minimal capacity to regenerate and any loss or defect in the endothelial cell layer is compensated by sliding of the adjacent cells and increase in the cell size of remaining cells. If the density of the endothelial cells comes below a critical level then the cornea starts to swell up. A number of factors are known to decrease the density of endothelial cells. Aging is one such factor. Clinically we can appreciate corneal dysfunction by the appearance of corneal oedema and bullous keratopathy.

Three methods are available for studying endothelium – measuring the thickness of cornea (pachymetry), measuring the endothelium's permeability to fluorescein and morphometric measurement obtained by the specular microscope. With the help of the specular microscope, the endothelium of the cornea can be photographed and analysed. The Non contact Specular Microscope also measures the Central Corneal Thickness.

Persistently raised Intraocular Pressure is known to produce corneal endothelial damage which can result in diminution of the total endothelial cell count . A proposed mechanism may be direct damage from the intra-ocular pressure (IOP)or altered corneal endothelium in patients with glaucoma.

Patients who are at risk of corneal decompensation and glaucomatous damage can be identified and steps can be taken to prevent further damage to the vision of the patients.

This present study was undertaken to evaluate the corneal endothelium and central corneal thickness in eyes suffering from various types of glaucoma to understand specular microscopic corneal status of patients of glaucoma so that necessary steps may be taken to improve visual outcome in the patients of glaucoma.

### **II. Review Of Literature**

Glaucoma can be regarded as a group of diseases that have as a common end point a characteristic optic neuropathy, which is determined by both structural changes (optic disk appearance) and functional deficit (measured by visual field change). This concept of 'end organ damage' provides a uniform definition across the different mechanisms by which glaucoma is caused. (Johnson et al, 2003) Glaucoma (congenital or infantile, primary open angle, primary angle-closure and secondary glaucoma) is an important cause of blindness in developing and developed countries. Approximately 15% of all blindness is due to glaucoma and it is estimated that around 600 000 persons per year go blind from glaucoma worldwide. (Sihota, 2003)

Quigley in 1996 suggested there were 72.8 million glaucoma patients worldwide.

The incidence of glaucoma was estimated to be 0.24% per year. (Bengtsson, 1989) These figures definitely draw our attention to the cause of glaucoma and timely efforts to take active measures in the prevention of blindness.

Once the blindness of glaucoma has occurred, no known treatment will restore the lost vision. However in nearly all cases, blindness from glaucoma is preventable. This prevention requires early detection and proper treatment. Detection depends on the ability to recognize the early clinical manifestations of the various glaucomas. (Allingham, 2005).

The cornea is a transparent avascular tissue with a smooth, convex surface and concave inner surface. Its structure gives some indication of the diverse functional demands upon the tissue. The cornea must be transparent, refract light, contain the intraocular pressure and provide a protective interface.(Edelhauser and

Ubels, 2003)

Transparency of the cornea stroma is achieved by the regularity and fineness of its collagen fibrils and the closeness and homogeneity of their packing. Water is constantly pumped out of the cornea by its posterior layer, the endothelium. This maintains the optical homogeneity of the corneal layers and prevents swelling and clouding. (Bron et al, 1997)

**Anatomy of the Cornea** The axial thickness of the cornea is 0.52mm with a peripheral thickness of 0.67mm. In its central third, the optical zone, the radius of curvature of the anterior surface is about 7.8mm and that of the posterior 6.5mm in adult males. Peripheral cornea is more flattened. (Bron et al, 1997).

Behind the precorneal tear film are five tissue layers - Epithelium, Bowman's layer, Stroma, Descemet's membrane and Endothelium.

The corneal epithelium is stratified, squamous and non-keratinized. The epithelium is 50-90 $\mu$  thick and consist of five or six layers of nucleated cells. (Edelhauser and Ubels, 2003).

Bowman's layer is a narrow acellular homogeneous zone, 8-14 $\mu$  thick, immediately subjacent to the basal lamina of the corneal epithelium. Although at normal or raised intraocular pressure Bowman's layer is under tension and appears smooth, a series of convex ridges can be generated at its surface when tension is relaxed, as during corneal indentation applanation tonometry. (Bron et al 1997).

The stroma about 500 $\mu$  thick, consists of regularly arranged lamellae of collagen bundles (200-300 centrally and 500 in the periphery) these vary between 9 and 260 $\mu$  in width and 1.15 and 2 $\mu$  in height, and lie in a proteoglycan ground substance together with a relatively small population of cells, the keratocytes.

Descemet's membrane is the basal lamina of the corneal endothelium. It measures 10 microns in thickness. At the periphery of the cornea, there are small protusion of this membrane known as Hassall-Henle bodies. (Snell and Lemp, 1998).

The endothelium is a single layer of hexagonal coboidal cells applied to the posterior aspect of Descemet's membrane. (Edelhauser and Ubels, 2003). There is a great individual variation in cell counts.

In infants, the cells are closely arranged and the cytoplasm is small. As the cornea matures, the cytoplasm increases as the cell body, which assumes a hexagonal shape, spreads.

In older patients the regular hexagonal pattern is no longer distinct and the endothelium becomes pleomorphic, containing both small and large cells. (Mishima, 1982).

### **Physiology of Corneal Endothelium**

The endothelium plays a major role in maintaining corneal transparency. The transparency of cornea is essential to its role as the principal lens that enables the eye to function. This optical quality is the result of the uniformity of the tissue elements and the regularity of their arrangement, qualities maintained by a constant level of hydration. (Mishima, 1982).

The constant level of hydration depends on tissue metabolism and removal of fluid from corneal stroma. (Edelhauser and Ubels, 2003). The corneal epithelium and endothelium maintain a steady fluid content of the corneal stroma. Trauma to either of these layers produces oedema of the stroma (Bates, 1988).

Essential nutrients (such as glucose and amino acids) must pass across its surface to supply the cellular needs of all the corneal layers; oxygen derived from the aqueous supplies the requirements of the endothelium and posterior stroma. (Mishima, 1982)

### **Fluid regulation**

Physiological studies have shown that this delicate monolayer of cells is responsible for maintaining the corneal stroma free of oedema, in a state of relative deturgescence. This it does in two ways. First it provides a barrier function to the ingress of salt and metabolites into the stroma, which has a spontaneous tendency to take up salt and consequently, by osmosis, water; second it actively reduces the osmotic pressure of the stroma by mechanically pumping the bicarbonate ions out of the stroma and back into the aqueous humour (Mishima, 1982).

### **Corneal Thickness and hydration:**

Fluid in the corneal stroma is absorbed in the inter fibrillar matrix and because of characteristics arrangements of collagen fibrils, any increase in corneal hydration is manifested as increased corneal thickness. Thus, the relationship between hydration and thickness of cornea is linear (Mishima, 1982).

For human cornea it is:  $H = 7.0q - 0.64$

Where,  $H$  – hydration (weight of tissue water / weight of dry tissue)

$q$  – Thickness in mm

Therefore, measuring corneal thickness allows changes in corneal hydration to be studied quantitatively (Ytteborg and Dohlman, 1965).

Swelling and imbibition pressure of the corneal stroma swells in aqueous medium, producing a swelling

pressure that is a function of stromal hydration. This pressure is normally about 50 – 60mmHg.

### **Injury and Repair**

Physical and chemical damage to the human corneal endothelium result in loss of endothelial cells, and because of the poor reparative power of human endothelium. When the cell layer is injured the wound is repaired by covering of the denuded area by cell migration from the surrounding areas (Chi et al,1960). The loss on continuity of the endothelial sheet is made up by a sliding process in which neighboring cells move up to fill the gap. This is accompanied by the enlargement of the cells to cover the original area. Thus after injury, the endothelial cell density falls, the cell area increases and the cell height decreases. This sliding phenomenon is not distributed equally across the whole of the corneal surface and after a localized injury will be confined to the immediate neighbourhood of the injury. Although the healed endothelium may exhibit a regular hexagonal pattern, some endothelial polymorphism is common. Endothelial injury produces corneal edema due to loss of the specialized junctions between endothelial cells and of the pumping functions of the cells at the site of injury. (Bron, 1997).

### **Specular Microscopy**

More than 100 years ago, Leber's ingenious experiments showed that the endothelium prevents the absorption of the aqueous humor. The first direct visualization of the endothelium was demonstrated by Vogt in 1918. In 1924, Graves used similar methods to describe Fuch's dystrophy in elderly patients. It was not, however until 1968 that David Maurice described the first laboratory specular microscope that could be used to study excised living corneas. Modifications of this specular microscope were made by Laing et al and later by Bourne and although this technique eliminated corneal manipulation and decreased apprehension in some patients, the constant adjustment and refocusing required by the movement of the eye often made observations and photography of the endothelium more tedious.(Lohman,1981) (Krachmer et al,2005).

### **Optical Principles Of Specular Microscopy**

Light striking a surface can be reflected, transmitted or absorbed. Of primary importance in clinical specular microscopy is the light that is reflected specularly, (ie mirror like) where the angle of reflection is equal to the angle of incidence. As light passes through the cornea, it encounters a series of interfaces between optically distinct regions. At each interface, some light is reflected back and some is transmitted deeper into the cornea. The greater the difference in index of refraction between the regions, the greater the intensity of reflected light. The more edematous the tissue, the more light is scattered. A portion of this reflected light is collected by the objective lens of the specular microscope and forms, at the film plane of the microscope, an image of that part of the cornea on which the instrument is focused. According to Laing, if the beam is narrowed sufficiently, four zones of reflection can be seen. Zone 1 is the brightest region and is formed by the interfaces formed by the lens, coupling fluid, and epithelium. Zone 2 is a larger region and represents light reflected from the stroma. Zone 3 is the endothelial region, and Zone 4 represents light reflected from the aqueous, as a result of this Zone 4 is usually dark. (Krachmer et al, 2005).

The clinical specular microscope is extremely useful for studying and documenting the condition of the corneal endothelium before an intraocular surgical procedure, and for assessing the effects of ageing, drugs, operations, inflammation, and the like on the endothelial cells. In addition, it may be possible to demonstrate endothelial disease or damage before it is detectable by other methods of examination.(Bourne and Kaufman, 1976).

### **Quantitative Cell Analysis**

The aim of Quantitative analysis of specular microphotograph is to assign a number that can provide a measure endothelial status (Trinkaus-Randal et al 1998). A variety of morphologic parameter can be quantified. (Laing, 1998).

These included :

- Cell size (cell area or Average Cell Size [ACS])
- Polymegathism (variation of cell size, such as coefficient of variation [CV] of mean cell area)
- Pleomorphism (variation of cell shape, such as percent of hexagonal cells [H] or coefficient of variation of cell shape thick)
- Endothelial cell density [ECD]
- Central Corneal Thickness (CCT)

**Corneal Endothelium and Ageing**

It is well established that the central endothelium changes as a function of age. In most individuals the cell density decreases from birth to death. Changes in the variability of cell size (polymegathism), and other nonsized related parameters have been found to correlate with age. ( Laing ,1998).

While mitosis may occur in young human endothelial cells it is infrequent in the adult and it appears that cornea is supplied with a relatively fixed population of about 5,00,000 cells which are replaced in a limited way after injury (Brightbill,1999).

A gradual decrease in density and increase in graph variation (polymegathism) occur with age (Shah et al 1978). In youth the cells are predominantly hexagonal in shape in the plane of the cornea but with age become increasingly polymorphic.

The endothelial density is about 6000 cells /mm<sup>2</sup> at birth and falls by about 26% in the first year. (Sherrard et al 1987).A further 26% is lost over the next 11 years but the rate of loss slows and possibly stabilizes around middle age, especially in polymegathous endothelium (Rao, 1979) The corneal endothelium continues to lose cells through ageing, but normal cell density decreases only slightly during an individuals life span, enabling the cornea to maintain its normal thickness and transparency. When the number of cells fall below the critical level, the cells can no longer fulfill their barrier function and the corneal swelling develops. (Mishima, 1982).

Different studies have quoted different endothelial cell counts in different subset of population. Waring et al, 1980 stated that endothelium at birth consisted of approximately 3,50,000 cells (approximately 3,000 cells/mm<sup>2</sup>) arranged in the continuous monolayer 4 to 6 μm. Laing et al, 1979 reported that normal endothelial cells are similar in size and shape with no abnormally dark or bright structures. The cell density is between 2000 cell/mm<sup>2</sup> to 3500 cells/mm<sup>2</sup>.

Corneal endothelial cell density is highest at birth, as high as 7500 cells /mm<sup>2</sup>. Rapid decline in density during the first year of life is compatible with the spread of a fixed population over an enlarging cornea. Specular microscopy of normal children from age 5-14years shows that cell density is variable among individuals, with a range from 3591 ± 399 cells /mm<sup>2</sup> at 5 years to 2697 ± 246 cells /mm<sup>2</sup> in older subjects. Decreases in cell density of 13% between the ages of 5 and 7 years and of 12% between 7 and 10 year of age have been recorded . The rate of approx 0.52% loss per year continue into old age.

The critical endothelial cell density below which the human cornea decompensates is approximately 300 – 500 cells/mm<sup>2</sup>. (Brightbill,1999) .

In childhood , normal endothelial cells are of uniform size and hexagonal shape. As cell density decreases with age, individual cells enlarge and loose their hexagonal shape. Polymegathism , irregularity in the normally regular mosaic pattern , may be quantified as a coefficient of variation in cell size. Increased polymegathism or CV of cell size, occurs when the endothelium is stressed and is more susceptible to traumatic cell loss. (Brightbill,1999).

The probability of occurrence of an endothelial cell density of less than 2000 cells/mm<sup>2</sup> is more from the seventh decade onwards (Abib and Barreto, 2001).

The transparency of the cornea is essential to its role as the principal lens that enables the eye to function. This optical quality is the result of the uniformity of the tissue elements and the regularity of their arrangement , qualities maintained by a constant level of tissue hydration.(Mishima, 1982).

Rao et al (2000), found the central endothelial cell density was 2525 ±337 cells/mm<sup>2</sup> in 537 normal Indian volunteers. The decrease in endothelial cell density with age was statistically significant (p <0.001). They also found statistically significant increase in mean cell area (p<0.001) and coefficient of variation (p=0.002) with age. There was a statistically significant correlation between the mean cell size in the central cornea and the age of the subjects. (Mishima, 1982).Sturrock et al (1978) studied the relationship between the axial cell count and age in a group of 67 subjects ,the mean cell count was found to decrease significantly with increasing age of the subject. (p< 0.001).In a study comparing the cell density in the older normal patients and the younger normal patients, there was a significantly low cell density of the endothelium in older patients. (Blackwell, 1984).

Hoffer in 1990 concluded that endothelial cell count decreases statistically with age but the amount of decrease is not statistically significant.(Table I).

**TABLE I: Mean Endothelial Cell Count and Age**

Age Group	Mean ECD cell/mm <sup>2</sup>
41-50	2322
51-60	2490
61-70	2387
71-80	2378
81-90	2257
<b>Average</b>	2370

➤ Source: Hoffer and Kraff, 1980

In a study done on 254 patients (both glaucomatous and non glaucomatous) increasing age was associated with a decrease in central corneal endothelial cell density (P = .001) in younger adults the central mean endothelial density was 2905 ± 132 and in older adults it was found to be 2406 ± 144 (Korey, 1982).

**Corneal Endothelium and Gender**

Rao et al (2001), examined 1235 eyes of patients with ages ranging from 40 – 75 years and found that females had 2.9 % higher cell density than males (p=0.0001). No significant difference in mean cell density was noted according to age. Vanathi et al (2003) noted that there is no statistically significant difference between cell densities either between males and females patients.(See Table II).

**TABLE II: Mean Count Of Corneal Cell Population Of Male And Female Eye (Mean ± Standard Deviation)**

Corneal parameter	Males			Females		
	Left Eye	Right Eye	p Value	Left Eye	Right Eye	p Value
Endothelial cell density (cells/mm <sup>2</sup> )	2780.6±518.7	2757.1±223.3	0.85	2979.5±313.01	2772.9±304.3	0.05
Hexagonal endothelial cell %	44.7±11.5	47.16±11.4	0.51	36.8±10.6	38.4±11.5	0.68
Endothelial cell area(μm <sup>2</sup> )	414.7±44.4	375.2±28.1	0.02	361.1±42.7	388.8±37.8	0.05
Coefficient of variation	32.8±3.2	33.5±3.4	0.49	30.9±2.8	31.6±2.04	0.38

• Vanathi et al, 2003

**Right Vs Left Concordance**

Axial endothelial cell counts were performed on both eyes of 31 subjects (15 males , 16 female, aged 13 to 88 years). A comparison between the mean cell counts from right and left eyes of each subject showed closed agreement (P < 0.001) (Sturrock et al, 1978).

There were significant variation in cell size distribution among individuals but practically no difference between the fellow eyes of the same individual. In 53 subjects 13 to 88 years of age, the mean and standard deviation of cell sizes averaged 303 ± 63.9μ and 97.9 ± 26.5μ for the right eye and 302.8 ± 67.7μ and 97.6 ± 28.5μ for the left eye. (Mishima , 1982).

Rao et al (2000) found that there was no significant difference in endothelial cell density, average cell size, hexagonality and coefficient of variation in fellow eyes of 537 normals Indian volunteers (p<0.05).

Vanathi et al, 2003 conducted study on 50 central corneas of healthy subject to study the corneal cell population and found that there was no statistically significant difference between the Endothelial Cell Densities, Hexagonality, Average Cell Size and Coefficient of Variation in right and left eye. As can be seen in Table III.

**Table III: Mean Counts Of Corneal Cell Population Of Right And Left Eyes (Mean ± Standard Deviation)**

Corneal cell population	Left eye (n=36)	Right eye (n=38)	P Value
Endothelial cell density (cells/mm <sup>2</sup> )	2874.6±439.6	2764±261.2	0.19
Hexagonal endothelial cell (%)	41.01±11.5	43.02±1.9	0.46
Endothelial cell area(μm <sup>2</sup> )	389.4±50.8	381.6±33.3	0.44
Coefficient of cell size variation	31.9±3.1	32.26±2.9	0.3

• Vanathi et al 2003

**Corneal Endothelium in Glaucoma**

Persistently elevated intraocular pressure is believed to result in the gradual loss of endothelial cells and a progressive loss in endothelial function (Irvine, 1956).

This is manifested physiologically by an inverse relation between the level of IOP and the ability of cornea to pump electrolytes and water from the stroma (Harris et al, 1956).

Specular microscopic studies in patients with unilateral glaucoma or with a history of unilateral attacks of glaucomatocyclitic crisis often shows a lower endothelial cell density in the eye afflicted with glaucoma. (Laing et al ,1998 ). The acute increase in the IOP in acute angle closure glaucoma leads to a massive damage of the corneal endothelium (Laing et al ,1998 ).

Bigar and Witmer (1982), studied corneal endothelium in 20 patients after an attack of angle closure glaucoma and concluded that the mean cell density was 1534 per mm square in the affected eyes (mean decrease 33%, P = 0.002) as compared to 2243 in normotensive eyes.(Table IV).

**Table IV: Comparison of Endothelial Cell Density in Normal and Glaucomatous Eyes**

Author, Year	Type of Glaucoma	No. of Patients	ECD In Normal Eyes(Cells/mm <sup>2</sup> )	ECD In Glaucomatous Eyes(Cells/mm <sup>2</sup> )	P Value
Bigar F, 1982	PACG	20	2243 ± 401	1534± 818	0.002
Korey M, 1989	POAG	54	2117 ± 373.2	2079 ± 271	0.38
Sihota R, 2004	PACG	30	2294 ± 305	1597 ± 653	< 0.001
Gagnon, 1997	POAG	52	2560 ± 360	2154 ± 419	< 0.0001

Sihota et al (2004) conducted a study on corneal endothelium and pachymetry in the subtypes of primary angle closure glaucoma in 30 patients and found that there was a significant decrease in the corneal endothelial cell density in eyes that have had an acute attack of angle closure glaucoma and in eyes of chronic PACG. The endothelial count was significantly lower in eyes with chronic PACG as compared to control eyes ( $P < 0.001$ ) there was increased pleomorphism and polymegathism of the corneal endothelial cells seen in eyes with resolved acute and chronic PACG. The mean endothelial cell counts in the four groups were as follows: subacute PACG  $2396 \pm 271$  cells /mm<sup>2</sup>, acute PACG  $1597 \pm 653$  cells/mm<sup>2</sup>, chronic PACG  $2229 \pm 655$  cells/mm<sup>2</sup> and controls  $2461 \pm 321$  cells/mm<sup>2</sup>. The mean endothelial cell count in the fellow eyes of subacute PACG, acute PACG and chronic PACG patients was  $2294 \pm 305$  cells/mm<sup>2</sup>,  $2388 \pm 226$  cells/mm<sup>2</sup> and  $2108 \pm 203$  cells/mm<sup>2</sup> respectively (Not Significant). The acute PACG patients had significantly lower endothelial cell counts ( $P < 0.001$ ).

Koreyet al (1989), assessed the effect of increased intraocular pressure on corneal endothelium in 54 patients of Primary Open Angle Glaucoma and compared them with 103 normals subjects and found that neither mean ECD nor CCT differed significantly among them. ( $p > 0.12$ ).

Gagnon et al (1997), evaluated the corneal endothelial cell density in 102 patients with primary open angle glaucoma and found that corneal endothelial cell counts were significantly lower in patients with POAG ( $2154 \pm 419$  cells/mm<sup>2</sup>) than in controls ( $2560 \pm 360$  cells/mm<sup>2</sup>)  $p < 0.0001$ .

Luo et al (2000), observed the density and morphology of the corneal endothelium in patients with glaucoma and concluded that patients with acute PACG might have lower endothelial counts and bigger cell area than those without glaucoma in the same group. This study was conducted on 125 eyes of 68 patients with glaucoma of the same group. Corneal endothelium density was significantly lower in patients with glaucoma [ $(2368.81 \pm 289.76)$ cells/mm<sup>2</sup>] than that in controls [ $(2540.78 \pm 195.66)$ cells/mm<sup>2</sup>]. Cell density of primary angle closure glaucoma (PACG) [ $(2262.65 \pm 338.64)$ cells/mm<sup>2</sup>] was significantly low, especially in acute ACG [ $(1925.16 \pm 403.38)$ cells/mm<sup>2</sup>].

Stals et al (1984) studied the endothelial cell density of 44 eyes after an acute attack of ACG and found cell density to be statistically lower than control eyes.

In 3204 normal eye with normal intraocular pressure the cell count was observed to be age dependent and to have average value of  $2293 \pm 394$  cells/mm<sup>2</sup> in 302 eyes with primary, chronic, open angle glaucoma with intraocular pressures between 19 and 32 mms of Hg, there was a significant ( $P < 0.001$ ) reduction, in cell count to  $1582 \pm 248$  cells/mm<sup>2</sup> (Knorr et al, 1991).

## ROLE OF CENTRAL CORNEAL THICKNESS IN GLAUCOMA EVALUATION

Mean central corneal thickness was found to be  $573.0 \pm 39.0 \mu$  (Brandt et al, 2001)

The central corneal thickness is necessary to adjust the mean IOP in clinical practice to evaluated the patients at risk of developing glaucoma. Each patients with thick cornea showed a 1.22mmHg increased in mean IOP per decade. This difference was statistically significant ( $P=0.0001$ ) (Phillips, 2003).

Burvenich and De Clercg (2000) observed in a prospective study in 245 healthy emmetropic or ametropic eyes that there is a linear relation between IOP measurement and CCT. In eyes with ocular hypertension there is a manifest elevated CCT. Central corneal thickness influences intraocular pressure measurements. The effect of central corneal thickness may influence the accuracy of applanation tonometry in the diagnosis, screening and management of patients with glaucoma.

In a case study reported by Johnson et al, 1978 it was found that the intraocular pressure measurement in a eye in a thick but nonedematous cornea will give values that are artificially high. The measurement of central corneal thickness may be of value in selected cases of suspected glaucoma especially if the other clinical findings do not seem to correlate with the IOP.(Johnson, 1978)

The corneal thickness decreases during ageing. CCT together with other risk factors can help in establishing a target pressure. (Hornova, 1999).

Peplinski and Torkelson( 1997 ) observed that increased corneal thickness leads to high readings of intraocular pressure.

When CCT is low, underestimation of IOP may occur, and the converse may be true when CCT is high. Thus CCT is important in the diagnosis and treatment of glaucoma because having low CCT may lead to underdiagnosis and undertreatment of glaucoma while overestimation of the IOP in normal subjects who have

thicker corneas may lead to a misdiagnosis of OHT. (Aghaian et al , 2004).and ( Copt et al, 1999).

The central corneal thickness should be taken into account when assessing risk for the development of glaucomatous damage among the ocular hypertension patients.(Medeiros et al, 2003).

Patients with thinner cornea had a greater chance of developing visual field abnormalities during the followup period. The mean CCT was significantly lower for patients with glaucomatous optic neuropathy who developed visual field loss than those who retained normal visual field. These findings implicate that during the management of glaucoma patients, patients with thinner corneas may need more aggressive treatment to reduce IOP and prevent glaucomatous progression. (Medeiros et al, 2003).

The mean CCT in patients with visual field progression was significantly lower than the mean CCT in patients who did not progress ( $525 \pm 36 \mu$  vs  $547 \pm 35 \mu$ ;  $P=0.02$ ). Those with thinner CCT were more likely to progress than those with thicker CCT. (Kim et al, 2004).

Central corneal thickness is greater in children with ocular hypertension than in control subjects or those with glaucoma. The values for CCT in children closely correlated with values reported for adults. The CCT in control subjects was  $555 \pm 37 \mu$  and those for glaucoma patients was  $563 \pm 33 \mu$ . The difference was found to be significant ( $P<0.02$ ). (Muir et al, 2004).

In 352 controls studied the mean central corneal thickness was found to be  $537.4 \mu$ m, ranging from  $427$ - $630 \mu$ m, with a maximal difference of  $42 \mu$ m in between the eyes. There was no difference between the sexes and no significant association with age. Linear regression analysis showed an increase of  $0.19$ mm of Hg in intraocular pressure with each  $10 \mu$ m increase in central corneal thickness (95% confidence interval,  $0.09$ - $0.28$ mmHg). (Wolfs, 1997).

Shah et al, 1999 proposed that the CCT measurement is desirable in patients attending for glaucoma assessment to avoid misclassification resulting from the relationship between CCT and tonometric pressure. Many eyes diagnosed as having NTG have thin corneas which would tend to lower the tonometric recorded intraocular pressure so, the finding of less than normal thickness cornea introduces some error as to the diagnosis of NTG.

Doughty et al (2000) found that mean corneal thickness of eyes reported as normal was 534 microns, for slit lamp based optical pachymetry the mean corneal thickness was 530 microns and for ultrasonic pachymetry 544 microns. Previous studies have reviewed that central cornea thickness tends to decrease with increasing age and found that a statistically significant negative correlation between each and central corneal thickness that corresponds to an age related thinning of 6.3 microns per decade.

The mean Central Corneal Thickness (CCT) by specular microscopy was  $572 \mu$ m. In a study conducted on 31 healthy volunteers in Canada, the CCT measurements by specular microscopy was  $572 \mu$ m. Which were significantly less reproducible than those by ultrasound Pachymetry and ultrasound biomicroscopy the error levels were clinically expectable (Tam and Rootman, 2003).

The central corneal endothelial cell density and thickness were determined in 65 healthy eyes of 39 patients using non contact (Topcon SP-2000P, Topcon corporation) and contact microscope. The central corneal thickness was found to be  $543 \mu$ m. To determine endothelial cell density, contact and noncontact specular microscopy may be used interchangeably. However for combined measurements of endothelial cell density and pachymetry, the use of the same specular microscopy is recommended for long term patients followup.(Modis et al, 2002).

#### **CENTRAL CORNEAL THICKNESS IN PRIMARY OPEN ANGLE GLAUCOMA**

In a study on 28 ocular hypertensives CCT was significantly greater ( $0.606 \pm 0.041$ mm) than that of glaucomatous eyes ( $0.554 \pm 0.022$ mm) ( $p < .001$ ) or of normal controls ( $0.561 \pm 0.026$ mm). Increased CCT may give an artificially high IOP measurement by applanation tonometry. The CCT must be considered when developing a treatment approach for patients with glaucoma. ( Herndon et al, 1997).

In a study on 200 consecutive glaucoma patients corneal pachymetry was performed and compared in three sub groups of glaucoma. The mean CCT in glaucoma patients was  $561 \pm 49.4 \mu$ m with a minimum of  $448 \mu$ m and maximum of  $732 \mu$ m. In control subjects the mean CCT was  $555.9 \pm 34.6 \mu$ m. The central corneal thickness in patients with normal tension glaucoma was significantly lower as compared to control subjects. (Dave, 2004).

Corneal thickness is significantly reduced in patients with normal tension glaucoma compared with patients with primary open glaucoma ( $p=0.0028$ ) and normal subjects ( $p=0.0037$ ). This may lead to underestimation of intraocular pressure and misdiagnosis in some of these patients. (Morad et al, 1998).

Argus, (1995) examined 36 ocular hypertensive patients and compared their central corneal thickness measurements with 29 normal subjects and 31 glaucomatous patients and reported that there was a significantly greater central corneal thickness in patients with ocular hypertension compared with the other groups.

Sobotka et al (2001), found that Central Corneal Thickness was significantly higher ( $p<0.001$ ) in patients with ocular hypertension than in normal individuals or in subjects with primary open angle glaucoma and pseudoexfoliation glaucoma.

With all races grouped together, Glaucoma suspects and eyes with POAG, CACG, NTG, and PEX had CCTs less than those of normal eyes. Another Implication of the importance of corneal thickness on IOP measurements is that IOP measurements are modified by both photorefractive keratectomy and laser in situ keratomileusis being lower in post laser patients hence chances of underdiagnosis to be high in this patients. (La Rosa et al, 2001).

These studies signify the importance of cornea and its important parameters in complete evaluation of patients with glaucoma.

#### CENTRAL CORNEAL THICKNESS IN PRIMARY ANGLE CLOSURE GLAUCOMA

In a study, CCT was measured in 328 eyes of 167 patients. The mean CCT of glaucoma patients was 561  $\mu$ . The CCT for right eyes were  $0.567 \pm 0.035$ mm, for left eyes  $0.569 \pm 0.037$ mm. There was no statistical difference in CCT between hypermetropic, emmetropic and myopic eyes. (Sihota, 2004)

In a cross-sectional study conducted on 30 consecutive patients in each subtype of PACG, subacute, acute and chronic patients of ACG. The mean central corneal thickness was  $531.4 \pm 25.3 \mu$  in eyes with subacute PACG,  $567.9 \pm 37.3 \mu$  in eyes acute PACG,  $526.4 \pm 31.9 \mu$  in eyes with chronic PACG and  $525 \pm 12.6 \mu$  in control eyes. The acute PACG eyes had a significantly higher corneal thickness ( $p < 0.001$ ) when compared to all the other groups. (Sihota et al, 2004).

#### CENTRAL CORNEAL THICKNESS IN PSEUDOEXFOLIATION SYNDROME

Seitz (1995), et al studied the morphological changes of corneal endothelium in patients with pseudoexfoliative syndrome and observed that there was a significant decrease in the endothelial cell density as compared to normal eyes.

White deposits and guttae were significantly more frequent and intensive in PSX eyes. In PSX eyes regardless of the presence of glaucoma in the patients, the corneal endothelial cell density is decreased and the cornea is thin. (Inoue, 2003)

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