# Diurnal variations in central corneal thickness in glaucoma suspects

**Rajni Sethia[1], Palvee Menon[2,*]**

[1]Associate Professor, [2]Resident, Dept. of Ophthalmology, SBKS&MIRC, Sumandeep Vidyapeeth, Vadodara, Gujarat, India

***Corresponding Author: Palvee Menon**
Email: palveemenon@gmail.com

## Abstract

**Aim:** To analyse 24 hour variations of central corneal thickness in glaucoma suspects.

**Materials and Methods:** 130 glaucoma suspects were hospitalised and underwent circadian evaluations. Total 6 readings of CCT were recorded over a 24-hour period: Immediately after waking up, 8 am, 11 am, 2 pm, 5 pm, & 8 pm. CCT was measured using an ultrasonic pachymeter.

**Results:** Mean CCT measurement at each time point: Immediate after wake up: 549.21 um; 08 AM: 548.97 um; 11 AM: 545.82 um; 2 PM: 544.41 um; 5 PM: 544.34 um; 8 PM: 543.65 um. The mean CCT was highest just after wake up with a slight decline throughout the day without any statistical significance in both groups ($p>0.05$).

**Conclusion:** The mean CCT was found to be highest just after wake up in the right eye and at 08:00 AM in left eye with steady decline throughout the day with statistically significance. The average variation in CCT was less than 1.92% in patients with suspected glaucoma from wake up to 8:00 pm.

**Keywords:** Central corneal thickness, Diurnal variation, Glaucoma suspects, Intraocular pressure.

## Introduction

Corneal thickness measurements are indicative of the metabolic status of the cornea, as they provide an index of corneal hydration.[1] Such measurements give valuable information on the physiological status of the cornea and its changes associated with disease,[2] trauma,[3,4] and hypoxia.[5,6] The healthy human cornea experiences hypoxia on a daily basis beneath the closed eyelid during sleep.[7,8] The reduction in oxygen levels beneath the closed eyelid is thought to induce anaerobic metabolism, which causes an accumulation of lactate within the stroma which is followed by an osmotic influx of water.[5] Other factors could also influence corneal hydration such as the reduced evaporation from the tear film which occurs during the first 2 hours of waking, intraocular pressure which increases rapidly after sleep,[2] and body temperature which changes on a diurnal basis decreasing during night-time sleep and increasing throughout the day.[9]

Upon opening the eyelid at waking the corneal thickness is reputed to return rapidly to normal. Thus, corneal thickness changes on a diurnal basis.

It still remains unclear whether overnight changes in human corneal thickness are truly representative of the diurnal variation occurring throughout any 24 hour period or whether the pattern of thickness changes is the same on consecutive days.

IOP measurement vary according to the Central corneal thickness (CCT), that is especially important in suspected glaucoma.[10] This influence of CCT on measured IOP by applanation is well documented. Goldmann and Schmidt tonometer assumed a standard corneal thickness during measurment but corneal thickness influences the reading. A thick cornea should lead to an overestimation of IOP, and a thin cornea should lead to underestimation. CCT is not routinely measured for glaucoma assessment so this effect is rarely considered in general ophthalmic practice.

The aim of this study was to use ultrasonic pachymetry to elucidate the diurnal variation in human central corneal thickness over the 24-hour period in glaucoma suspects.

## Materials and Methods

This observational study was conducted on 130 glaucoma suspects and was carried out in the department of Ophthalmology, SBKS&MIRC, Vadodara from November 2016 to June 2018. Patients were enlisted after procuring a permission from the Ethical Committee and after obtaining the informed written consent. Subjects with age from 20 to 60 years and of both sexes who fit in inclusion criteria were taken in the study.

Glaucoma suspects are:

Subjects with CDR 0.6 or more in one or both eyes**,** asymmetry of more than 0.2 C/D ratio in a patient with symmetrical disc sizes, and the presence of glaucomatous cup-disc changes such as focal nerve fiber loss, notching, splinter haemorrhage or peripapillary atrophy was taken as a suspect.

A single IOP reading of more than 21 mm Hg in one or both eyes in the clinic setting was taken as a suspect.

Presence of reproducible visual field defects on two or more occasions inconclusive of glaucoma was taken as a suspect.

Other inclusion criteria are as follows: 1) Adequate tear film production 2) With a family history of glaucoma. Exclusion criteria are as follows: 1) Patients who had ocular surface disorder, corneal oedema, corneal opacities and corneal astigmatism 2) Subjects on IOP lowering medication (topical or systemic) 3) Subjects who were alcoholic, diabetic, hypertensive and having systemic diseases like connective tissue disorders 4) Previous history of ocular trauma and surgery 5) History of Contact lens wearers 6) Menstruating females, pregnant and lactating mothers.

A structural performa will be used to collect relevant information for each individual patient selected. A routine investigation like complete anterior and posterior segment examination, gonioscopy, fundus examination, schirmer's test and automated perimetry in glaucoma suspects were done in each patient. iop measurement was done by applanation tonometer (GAT) and the measurement of CCT was performed by ultrasonic pachymetry (PACSCAN 600p). Total 6 readings were taken of IOP and CCT over a 24-hour period: Immediately after waking up (5:30 to 6:30 am), 8 am, 11 am, 2 pm, 5 pm, & 8 pm.

Data was entered into excel file and analyzed by Epi info version 7. Quantitative data was described by mean and standard deviation. Mean difference between quantitative data were analyzed by Z test and ANOVA test. Less than 0.05 of p-value was considered significant. Correlation coefficient R was calculated for the correlation between quantitative data.

## Result

This is an observational study carried out in the Department of Ophthalmology, Dhiraj Hospital, Vadodara from November 2016 to June 2018. One hundred and thirty patients who had suspected glaucoma were enrolled in the study.

**Table 1: Age and gender wise distribution of subjects**

| Age group | Frequency (%) | Female (56, 43.1%) | Male (74, 56.9%) |
|---|---|---|---|
| 20-29 | 6 (4.6) | 3 (5.4) | 3 (4.1) |
| 30-39 | 26 (20.0) | 13 (23.2) | 13 (17.6) |
| 40-49 | 40 (30.8) | 16 (28.6) | 24 (32.4) |
| 50-60 | 58 (44.6) | 24 (42.9) | 34 (45.9) |
| Total | 130 (100.0) | 56 (100.0) | 74 (100.0) |

Age and gender-wise distribution of subjects was given in Table 1. The patients had an age group ranging from 20 to 60 years with a mean age of 46.42 years, among them, 74(56.9%) were males, 56(43.1%) were females. Majority of patients 84 (75.6%) were in 40 to 60 year age group. There is no significant difference in age & gender-wise distribution of subjects.

**Table 2: Mean CCT (um) of right eye at different time point**

| Time point | Mean CCT (um) | SD (um) |
|---|---|---|
| During wake up | 549.21 | 36.70 |
| 8:00 AM | 548.97 | 36.16 |
| 11:00 AM | 545.82 | 36.90 |
| 2:00 PM | 544.41 | 37.32 |
| 5:00 PM | 544.34 | 37.00 |
| 8:00 PM | 543.65 | 37.45 |
| Overall during whole day | 546.06 | 36.9 |

Mean CCT of the right eye of 130 subjects is at each time point is given in Table 2. The mean ± SD corneal thickness during whole day 546.06 ± 36.9 um and it varied with the time point. Mean CCT measurement at each time point: Immediate after wake up, 549.21 um; 08 AM, 548.97 um; 11 AM, 545.82 um; 2 PM, 544.41 um; 5 PM, 544.34 um; 8 PM, 543.65 um. This variation at different time point was not statistically significant (ANOVA F value – 0.57; p-value – 0.72). The mean CCT was found to be highest just after wake up because of swelling of the cornea. Then it was declining throughout the day. The corneal thickness had typically returned close to its mean level around 11:00 AM. Maximum CCT at first reading was found in 95(73.1%) right eyes, another 19 (14.6%) at the 8:00 AM, while only 7(5.3%) exhibited the Maximum CCT at 11:00 AM.

**Table 3: Mean CCT (um) of left eye at different time point**

| Time point | Mean CCT (um) | SD (um) |
|---|---|---|
| During wake up | 546.08 | 36.39 |
| 8:00 AM | 546.96 | 37.22 |
| 11:00 AM | 544.42 | 37.68 |
| 2:00 PM | 544.34 | 37.19 |
| 5:00 PM | 543.73 | 37.44 |
| 8:00 PM | 543.51 | 37.41 |
| Overall during whole day | 544.84 | 37.22 |

Mean CCT of the left eye of 130 subjects is at each time point is given in Table 3. The mean ± SD corneal thickness during whole day 544.84 ± 37.2 um and it varied with the time point. Mean CCT measurement at each time point: Immediate after wake up, 546.08 um; 08 AM, 546.96 um; 11 AM, 544.42 um; 2 PM, 544.34 um; 5 PM, 543.73 um; 8 PM, 543.51 um. This variation at different time point was not statistically significant (ANOVA F value – 0.17; p-value – 0.97). The mean CCT (546.96um) was found to be highest at 8:00 AM. Then it was declining throughout the day. The corneal thickness had typically returned close to its mean level around 11:00 AM. Maximum CCT at first reading (wake-up time) were found in 73 (56.5%) patients, another 26 (30.0%) at the 8:00 AM, while only 21(16.2%) exhibited the Maximum CCT at 11:00 AM.

Mean variation in CCT at different time point was calculated according to below-mentioned formula.

Variation at different time point (%) =

$$\frac{\text{Actual CCT at specific time point} - \text{Mean CCT of day}}{\text{Mean CCT of day}} \times 100$$

**Table 4: Diurnal variation in CCT from mean CCT at different time point**

| Time point | Right eye | | Left eye | | Z Value | p Value |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| During wake up | 0.58 | 0.81 | 0.29 | 1.65 | 1.77 | >0.05 |
| 8:00 AM | 0.55 | 1.27 | 0.45 | 1.59 | 0.56 | >0.05 |
| 11:00 AM | -0.04 | 1.31 | -0.03 | 1.18 | -0.05 | >0.05 |
| 2:00 PM | -0.31 | 0.92 | -0.05 | 0.83 | -2.46 | <0.05 |
| 5:00 PM | -0.32 | 0.86 | -0.16 | 0.91 | -1.47 | >0.05 |
| 8:00 PM | -0.45 | 0.96 | -0.20 | 0.89 | -2.22 | <0.05 |

In the right eye, the CCT was 0.58% higher than mean CCT just after wakeup. At 8:00 AM it was also 0.55% higher than mean CCT. At 11:00 AM, 2:00 PM, 5:00 PM and 8:00 PM, it was respectively 0.04%, 0.31%, 0.32% and 0.45% lower than mean CCT. A very slight decrease (thinning) from the mean corneal thickness was observed from 11:00 AM onwards.

In the left eye, CCT was 0.29% higher than mean CCT just after wakeup. At 8:00 AM CCT was also 0.45% higher than mean CCT. At 11:00 AM, 2:00 PM, 5:00 PM and 8:00 PM, CCT was respectively 0.03%, 0.05%, 0.16% and 0.20% lower than mean CCT.

Mean variation in CCT at each time point was higher in the right eye as compared to the left eye. But all this variation at each time was not statistical significant as p-value greater than 0.05 (except at 2:00 pm and 8:00 PM, $p<0.05$).

**Table 5: Diurnal variation of IOP and CCT**

| Diurnal variation | Mean (%) | SD (%) | Z Value | p Value |
|---|---|---|---|---|
| Right eye IOP | 16.83 | 7.41 | 0.61 | >0.05 |
| Left eye IOP | 16.28 | 7.28 | | |
| Right eye CCT | 1.91 | 2.08 | 0.11 | >0.05 |
| Left eye CCT | 1.94 | 2.53 | | |

Diurnal variation was calculated according to below mentioned formula.

Diurnal variation (%) =

$$\frac{\text{Highest reading of day} - \text{Lowest reading of day}}{\text{Lowest reading of day}} \times 100$$

Diurnal variation in IOP of right eye and left eye is respectively 16.83 ± 7.41 and 16.28 ± 7.28. There is no significant different between the diurnal variation of right or left eye ($p > 0.05$). Diurnal variation in CCT of right eye and left eye is respectively 1.91 ± 2.08 and 1.94 ± 2.53. There is no significant different between the diurnal variation of right or left eye ($p > 0.05$).

**Analysis according to Gender**

**Table 6: Gender-wise comparison of mean CCT of Right eye**

| Time point | Female | | Male | | Z Value | p Value |
|---|---|---|---|---|---|---|
| | Mean CCT (um) | SD (um) | Mean CCT (um) | SD (um) | | |
| During wake up | 552.69 | 36.12 | 546.56 | 37.16 | 0.98 | >0.05 |
| 8:00 AM | 553.08 | 35.43 | 545.85 | 36.62 | 1.18 | >0.05 |
| 11:00 AM | 550.32 | 35.92 | 542.41 | 37.50 | 1.29 | >0.05 |
| 2:00 PM | 547.67 | 37.37 | 541.93 | 37.35 | 0.90 | >0.05 |
| 5:00 PM | 547.55 | 36.30 | 541.90 | 37.58 | 0.92 | >0.05 |
| 8:00 PM | 546.55 | 37.36 | 541.44 | 37.62 | 0.83 | >0.05 |
| During whole day | 549.88 | 36.88 | 543.14 | 37.47 | 1.03 | >0.05 |

Gender-wise mean CCT of the right eye was given in Table 6. The mean CCT in female patients (549.88 ± 36.88) was found to be slightly higher than the male patients (543.14 ± 37.47) but this difference was not statistically significant.

**Table 7: Gender-wise comparison of mean CCT of left eye**

| Time point | Female | | Male | | Z Value | p Value |
|---|---|---|---|---|---|---|
| | Mean CCT (um) | SD (um) | Mean CCT (um) | SD (um) | | |
| During wake up | 549.10 | 36.15 | 543.78 | 36.64 | 0.87 | >0.05 |
| 8:00 AM | 550.50 | 36.86 | 544.28 | 37.51 | 0.93 | >0.05 |
| 11:00 AM | 548.14 | 37.31 | 541.59 | 37.97 | 0.98 | >0.05 |
| 2:00 PM | 548.68 | 36.78 | 541.05 | 37.40 | 1.16 | >0.05 |
| 5:00 PM | 548.17 | 37.40 | 540.36 | 37.36 | 1.18 | >0.05 |
| 8:00 PM | 547.69 | 37.22 | 540.34 | 37.48 | 1.11 | >0.05 |
| During whole day | 548.74 | 37.29 | 541.77 | 37.73 | 1.05 | >0.05 |

Gender-wise mean CCT of the left eye was given in Table 7. The mean CCT in female patients (548.74 ± 37.29) was found to be slightly higher than the male patients (541.77 ± 37.73) but this difference was not statistically significant.

## Discussion

Corneal thickness was found to increase overnight in our glaucoma suspects, which is in agreement with previous studies.[7,11-14] Some previous studies have suggested that the diurnal variation of CCT is too small to have a significant effect on diurnal variation of IOP.[15-17] However, CCT is responsible for only a small proportion of the variation in measured IOP and other corneal biomechanical properties are recognized as having an important influence on IOP measurement.[18]

In our study the mean CCT was found to be highest just after wake up in the right eye and at 08:00 AM in left eye with steady decline throughout the day with statistically significance (Right eye: Immediate after wake up: 549.21 um; 08 AM: 548.97 um; 11 AM: 545.82 um; 2 PM: 544.41 um; 5 PM: 544.34 um; 8 PM: 543.65 um. Left eye: Immediate after wake up: 546.08 um; 08 A M: 546.96 um; 11 AM: 544.42 um; 2 PM: 544.34 um; 5 PM: 543.73 um; 8 PM: 543.51 um). The corneal thickness was highest just after wake up because of swelling of the cornea. It had typically returned close to its mean level around 11:00 AM in both eyes. Similar result was observed in another study.[19] Various studies on healthy patients have investigated the diurnal variation of CCT.[19-21]

Shah et al.[22] have studied CCT and IOP of 56 eyes from 28 glaucoma suspected patients.

Both parameters were measured using an ultrasonic pachymeter and a Goldmann tonometer, respectively at 8 am, 12 pm, 4 pm and 8 pm. They did not find statistically significant correlation between the mean variation of IOP and CCT.

Harper reported a variation of 7.2% (standard deviation, 2.8%) in CCT during a 24-hour period monitoring.[19] our study reported a variation of 1.91% (standard deviation, 2.08%) in right eye CCT and variation of 1.94% (standard deviation, 2.53%) in left eye CCT. There was statistical difference between the CCT measurements at different time point. (Table 4)

Mertz used electronic digital pachymetry and reported overnight swelling of 4.33% in nine subjects (three male, six female).[21] The highest overnight thickness increase in Mertz's study was 9.7%. The most recent published study[21] involved electronic digital pachymetry and reported a 3% overnight increase in corneal thickness. This study was limited to a group of youths of about 19 years of age. Our study includes the widest age range reported so far in a diurnal study of this nature (20 to 60 years).

Our results suggest that overnight changes in corneal thickness are not truly representative of actual diurnal variation. While we can compare our overnight changes in corneal thickness with other studies, it is difficult to compare diurnal studies as most authors do not report the full hour cycle.

## Conclusion

In our study the mean CCT was found to be highest just after wake up in the right eye and at 08:00 AM in left eye with steady decline throughout the day which was statistical significance. The mean variation in IOP did not significantly correlate with mean variation of CCT. Therefore, a change in CCT would not predict change in IOP.

**Conflict of Interest:** None.

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