Central Corneal Thickness-An important variable for prognostication in Primary Open Angle glaucoma; A Kolkata based study in Eastern India

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Abstract:
Introduction: Few studies have been conducted to find out any relationship between central corneal thickness (CCT) and other parameters of Glaucoma. In the present work we have tried to find out any possible relationship between CCT and severity of visual field loss in Primary Open Angle Glaucoma (POAG) patients and we have used Glaucoma Staging System for categorizing the POAG patients under study according to visual field loss.

Methods: Informed consent was taken from all patients selected for the study. 50 patients diagnosed as having POAG were included in the study and both eyes were examined as POAG is a disease affecting both eyes. Patients who were one-eyed or one eye not matching the inclusion criteria of this study were excluded. These were all under treatment for POAG in the Glaucoma Clinic of Regional Institute of Ophthalmology, Kolkata.

Conclusion: Patients with thinner CCT showed worse visual field damage than those with thicker CCT. Patients with worse visual field loss had thinner CCT than those with better visual fields. Strong negative correlation between visual field damage and CCT was noted.

Keywords: central Corneal Thickness, POAG, Prognostication

Introduction
Glaucoma is a chronic progressive optic neuropathy causing damage to retinal ganglion cells and thereby retinal nerve fiber layer. It is a leading cause of blindness all over the world. Primary open angle glaucoma (POAG) is a common form of glaucoma encountered in practice. POAG can be considered a chronic, progressive, anterior optic neuropathy that is accompanied by characteristic cupping and atrophy of optic disc, visual field loss, open angles, an IOP too high for the continued health of the eye and no obvious causative ocular or systemic conditions. Glaucoma Staging System (GSS) was designed to provide a reliable and comprehensive staging system and it allows accurate staging of 100% of Glaucoma patients based on their visual field loss. Results of Ocular Hypertension Treatment Study was in univariate analyses, baseline factors that predicted the development of POAG included older age, race (African-American), sex (male), larger vertical cup-disc ratio, larger horizontal cup-disc ratio, higher intraocular pressure, greater Humphrey visual field pattern standard deviation, heart disease, and thinner central corneal measurement. But few studies have been conducted to find out any relationship between central corneal thickness (CCT) and other parameters.
of Glaucoma. It is proved that CCT has effect on measuring intra-ocular pressure by applanation tonometry and 1mm Hg correction is needed for every 25micron deviation from CCT 550 micron. Several recent studies have shown that eyes of POAG patients with thinner cornea had worse progression of visual field loss which can not be explained solely by the effect of CCT on applanation tonometry.

In the present work we have tried to find out any possible relationship between CCT and severity of visual field loss in POAG patients and we have used Glaucoma Staging System for categorizing the POAG patients under study according to visual field loss.

Aims and objectives

1) To find out any difference in severity of visual field loss in patients with CCT<540 micron and in patients with CCT>540 micron.
2) To find out any difference of CCT in different GSS stages of these patients
3) To find out any correlation between CCT and severity of visual field loss of the POAG patients under study.

Materials and methods

It is a hospital based prospective case series study conducted in Regional Institute of Ophthalmology, Kolkata.

Informed consent was taken from all patients selected for the study. 50 patients diagnosed as having POAG were included in the study and both eyes were examined as POAG is a disease affecting both eyes. Patients who were one-eyed or one eye not matching the inclusion criteria of this study were excluded. These were all under treatment for POAG in the Glaucoma Clinic of Regional Institute of Ophthalmology, Kolkata.

DIAGNOSIS OF POAG:

For diagnosis of patients of POAG following criteria were used:

- Medical and ophthalmological history
- Slit lamp examination
- Intraocular pressure by Goldmann Applanation Tonometry
- Gonioscopy by Goldmann two mirror goniolens
- Fundoscopy with Volk 90D lens and slit lamp biomicroscope
- Standard automated perimetry Swedish Interactive Threshold Algorithm (SITA) standard 24-2/30-2
- Central corneal Thickness(CCT) estimation using Ultrasound Pachymeter( Pascan 333 P Digital Biometric Ruler)

INCLUSION CRITERIA:

- Best corrected visual acuity > 20/200 (6/60)
- Bilateral POAG
- Anterior chamber angle open on gonioscopy
- Reliable automated perimetry
- Informed consent

EXCLUSION CRITERIA:

- Spherical refractive error > 5D and cylindrical error > 2.5D
- Concomitant ocular disease leading to raised IOP
- Contact lens wearer
- Corneal pathology
- Cloudy optical media interfering in fundus evaluation
- H/O neurological disease
- Ocular trauma

www.ijbamr.com  P ISSN: 2250-284X  E ISSN : 2250-2858
• H/O intraocular surgery

GLAUCOMATOUS EYES:
POAG patients were diagnosed by presence of abnormal visual field, presence of raised IOP (>22 mmHg) in previous records even if that is controlled by drugs at the time of evaluation, evidence of glaucomatous optic neuropathy by disc examination like asymmetry of disc between 2 eyes of VCDR 0.2, NRR thinning, notching, excavation or RNFL defects.

GLAUCOMA STAGING SYSTEM:
In GSS staging for glaucoma patients 6 stages are there. But our study population was between stage1 to stage 4. Because stage 0 includes patients who have no visual field defect, they were not included in this study. Whereas stage 5 or end stage disease includes patients who had no Humphrey visual field in the worse eye attributable to the visual acuity of 20/200 or worse, which doesn’t fit in our inclusion criteria for the study.

Results
Total study population: 50, Male: 34, Female: 16

Table 1

<table>
<thead>
<tr>
<th>Age</th>
<th>30-40yr</th>
<th>40-50yr</th>
<th>50-60 yr</th>
<th>60-70yr</th>
<th>70-80yr</th>
<th>&gt;80yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>4</td>
<td>5</td>
<td>9</td>
<td>11</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Female</td>
<td>1</td>
<td>7</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>5</td>
<td>12</td>
<td>14</td>
<td>14</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>

Total eyes under study: 100
CCT<540 micron: 59  CCT>540 micron: 41
Fig 1: Distribution of POAG patients under study according to Glaucoma Staging System:

Total eyes under study = 100
Eyes in GSS Stage 1 = 19
Eyes in GSS Stage 2 = 37
Eyes in GSS Stage 3 = 25
Eyes in GSS Stage 4 = 19

Fig 2: Distribution of patients according to CCT & GSS stage:
Table 2: Analysis of CCT in different stages of GSS in POAG patients

<table>
<thead>
<tr>
<th>Stage</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
<th>Stage 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avg CCT</td>
<td>560.55</td>
<td>540.19</td>
<td>515.24</td>
<td>495.05</td>
</tr>
<tr>
<td>SD</td>
<td>19.06</td>
<td>24.91</td>
<td>24.20</td>
<td>14.92</td>
</tr>
</tbody>
</table>

Fig 3: Average CCT in different GSS stages of POAG patients:

T-test is done to find out statistical differences of CCT between different stages:

Table 3:

<table>
<thead>
<tr>
<th>Differences in CCT</th>
<th>Statistical significance</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between stage1 &amp; stage2</td>
<td>present</td>
<td>0.0014</td>
</tr>
<tr>
<td>Between stage2 &amp; stage3</td>
<td>present</td>
<td>0.0003</td>
</tr>
<tr>
<td>Between stage3 &amp; stage4</td>
<td>present</td>
<td>0.0016</td>
</tr>
</tbody>
</table>
Table 4:
Differences in MD & PSD in eyes with CCT>540 micron & CCT<540 micron:

<table>
<thead>
<tr>
<th></th>
<th>Avg MD</th>
<th>SD</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCT&lt;540 micron</td>
<td>16.09</td>
<td>7.45</td>
<td>59</td>
</tr>
<tr>
<td>CCT&gt;540 micron</td>
<td>6.19</td>
<td>3.18</td>
<td>41</td>
</tr>
</tbody>
</table>

There is statistically significant differences between mean MD in these two groups (p<0.05)

Table 5

<table>
<thead>
<tr>
<th></th>
<th>Avg PSD</th>
<th>SD</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCT&lt;540 micron</td>
<td>8.3</td>
<td>2.89</td>
<td>59</td>
</tr>
<tr>
<td>CCT&gt;540 micron</td>
<td>5.07</td>
<td>2.33</td>
<td>41</td>
</tr>
</tbody>
</table>

There is statistically significant differences between mean PSD in these two groups (p<0.05)

Fig 4: Linear regression analysis of correlation between CCT & MD:

Pearson coefficient = - 0.697
Fig 4: Linear regression analysis of correlation between CCT & PSD:

Pearson coefficient = -0.576

Fig 5: Linear regression analysis of correlation between CCT and GSS stage:
### Correlation between Pearson coefficient Strength of correlation

<table>
<thead>
<tr>
<th>Correlation between</th>
<th>Pearson coefficient</th>
<th>Strength of correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD &amp; CCT</td>
<td>- 0.697</td>
<td>Strong</td>
</tr>
<tr>
<td>PSD &amp; CCT</td>
<td>- 0.576</td>
<td>Strong</td>
</tr>
<tr>
<td>GSS &amp; CCT</td>
<td>- 0.714</td>
<td>Strong</td>
</tr>
</tbody>
</table>
Discussion

From the results of this study several factors regarding POAG patients, their visual field loss and CCT have come into light. Those points need some discussion. In the study population number of male patients is more than female patients. This does not mean POAG is more prevalent in male population. On the contrary these pictures signify the socio-economic condition of our country because of which male patients seek medical attention more than females. The age distribution of the study population shows most patients belong to 50-70 years of age group. This signifies POAG is a disease of elderly population. This finding is supported by Ocular Hypertension Treatment Study which indicated increasing age as a risk factor of glaucoma.

In the study conducted by Papadia M, et al. among the POAG patients mean CCT was 554micron +/- 45.03. Based on CCT value, the sample was split at the mode in two groups (group 1 <535 micron, n=49; group 2 >or=535 micron, n=50). A significant difference was found between the two groups for both MD and PSD. Linear regression analysis showed a significant correlation between CCT and PSD (P<0.001). These results are similar to our study results where we also found a statistically significant difference in MD and PSD among groups with CCT >540 micron and CCT <540 micron and correlation was found between PSD & CCT as well as MD & CCT.

A study was conducted by Hong S, et al. which was on chronic primary angle closure glaucoma. Here readings were taken initially and at 3 years follow-up. On the basis of the CCT value, the sample was split in two groups (group 1 <540 micron; group 2 > or =540 micron). There was no significant difference for initial MD (P = .979). But in our study we found significant difference of MD in these two groups. In the above mentioned study, however, significant difference of MD was noted after 3 years follow-up.

Shah H, et al. conducted a study on role of CCT as a baseline parameter and in progression of visual field loss in POAG. Charts of consecutive patients with POAG were reviewed to obtain visual field data. Visual field was measured by standard threshold static perimetry. Variables analyzed included mean deviation (MD) and pattern standard deviation (PSD). A significant negative relationship between CCT and PSD (correlation coefficient: -0.02, p<0.05) was found. Analyses comparing CCT to change in PSD and MD (visual field progression) were statistically not significant. This study showed negative correlation between CCT and PSD which resembles our study but failed to find out any relationship of field progression and CCT.

A study by Kim JW, et al. showed that the mean CCT in patients with visual field progression was significantly lower than the mean CCT in patients who did not progress (529 +/-36 mum vs. 547 +/-35 mum; P = 0.02). Those with thinner CCT were more likely to progress than those with thicker CCT as identified by Cox proportional hazards regression analysis (P = 0.01; hazard ratio, 1.44 for a 40-mum thinner CCT; 95% confidence interval, 1.12-1.80), and CCT was the only risk factor identified to be significantly associated with visual field progression. Since our study was cross-sectional, we did not note the progression of visual field.
Two similar studies\textsuperscript{10,11} conducted among Nepalese and South Indian populations have been compared and all the results have been presented in the form of the following table:

<table>
<thead>
<tr>
<th>Author</th>
<th>Study population</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Papadia M, et al, 2007</td>
<td>Italians</td>
<td>Significant correlation between CCT and PSD (P&lt;0.001).</td>
</tr>
<tr>
<td>2. Hong S, et al, 2007</td>
<td>Seoul, Korea</td>
<td>There was no significant difference for initial MD (P = .979). But in our study Significant difference of MD was noted after 3 years follow-up.</td>
</tr>
<tr>
<td>3. Shah H, et al, 2007</td>
<td>United States</td>
<td>A significant negative relationship between CCT and PSD (correlation coefficient: -0.02, p&lt;0.05). Analyses comparing CCT to change in PSD and MD (visual field progression) were statistically not significant.</td>
</tr>
<tr>
<td>4. Kim JW, et al, 2004</td>
<td>Seattle, Washington, USA</td>
<td>Those with thinner CCT were more likely to progress than those with thicker CCT as identified by Cox proportional hazards regression analysis (P = 0.01; hazard ratio, 1.44 for a 40-mum thinner CCT; 95% confidence interval, 1.12-1.80</td>
</tr>
<tr>
<td>5. Natarajan M, et al 2013</td>
<td>South Indians</td>
<td>There is no significant difference in CCT between POAG patients and normal controls.</td>
</tr>
<tr>
<td>6. Adhikari P, et al, 2014</td>
<td>Nepalese</td>
<td>CCT in glaucoma suspects is similar to normal subjects and POAG, but thicker than NTG.</td>
</tr>
<tr>
<td>7. Bhattacharya A, et al 2016</td>
<td>Eastern Indians</td>
<td>Patients with thinner CCT showed worse visual field damage than those with thicker CCT; &amp; Strong negative correlation between visual field damage and CCT was noted</td>
</tr>
</tbody>
</table>

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Conclusion
Measurement of CCT is recommended in all patients in work up for POAG, since visual field loss is the most important handicap these patients suffer from and this study clearly points out the relationship of CCT and visual field loss. Importance of CCT measurement is far more than its effect on IOP measurement as it is related to severity of visual field loss.

References
3) Gordon MO, Beiser JA, Brandt JD, et al. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open angle glaucoma. Arch Ophthalmol 2002;120:714-20, discussion 829-30