Central Corneal Thickness and its Relationship to Intra-Ocular and Epidemiological Determinants

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ABSTRACT

Objective: To measure central corneal thickness in Pakistani population and determine its relationship to intra-ocular pressure, age, gender and ethnicity.

Study Design: Cross-sectional observation study.

Place and Duration of Study: Pakistan Institute of Medical Sciences, Islamabad, Pakistan, between December 2013 and February 2015.

Methodology: The right eyes of 1000 cases (496 males and 504 females) were recruited for this study. Inclusion criteria were Pashtun or Punjabi ethnicity, intra-ocular pressure < 22 mmHg, gonioscopically open angles, cup-disk-ratio < 0.5, and age matched normal visual fields. Cases with prior ocular surgery, contact lens use, corneal pathologies, myopia or hypermetropia > ±3.0 diopters, astigmatism of > ±1.0 diopters were excluded. Central corneal thickness was measured using a TopCon non-contact specular microscope. Intra-ocular pressure was measured using Goldmann application tonometer. Frequency distribution, test of significance, and regression analysis was carried out using Statistical Package for Social Sciences version 20.0.

Results: Mean age was 47.31 ±11.78 years. Ethnic composition was 51.6% (n=516) Pashtun and 48.4% (n=484) Punjabi. The mean central corneal thickness was 503.96 (±12.47) µm, while the mean intra-ocular pressure was 15.61 (±2.68) mmHg. Regression analysis showed a significant association between central corneal thickness and intra-ocular pressure (p=0.00) and age (p=0.00). A ±100 µ change in central corneal thickness was associated with change in IOP of ±3.30 mmHg, whereas central corneal thickness decreased by 0.12 µm per year. No significant association could be established between central corneal thickness and ethnicity (p=0.19).

Conclusion: Central corneal thickness of the studied races was comparable to non-Caucasians which affects intra-ocular pressure measurements, and decreases with increasing age. No relationship was observed between central corneal thickness and ethnicity or gender.


INTRODUCTION

Central corneal thickness is a recognized parameter that influences the measurement of intra-ocular pressure by Goldmann application tonometer.¹ The design of this tonometer assumed a nearly constant central corneal thickness,² which has now shown to be incorrect.¹ Evidence regarding the relationship of central corneal thickness to age, gender and ethnicity is inconsistent.³⁻⁸ With respect to age, studies on healthy (non-glaucomatous) eyes of South-East Asian,³ Western Asian,⁴ Middle Eastern⁵ populations have demonstrated a significant association with central corneal thickness, while the North American literature does not supports this study.⁶ East-Asian and Middle Eastern populations also show significant relationship between gender and central corneal thickness,³⁵ while the Western African population does not.¹ Genome and population studies based on diverse race and ethnic backgrounds in different parts of the world have revealed significant variations in central corneal thickness.⁷⁻⁸ This seemingly contrasting evidence points to strong regional variation in determination of how central corneal thickness is related to age, gender and ethnicity necessitating regional investigations.

Data from Pakistan, in medline indexed literature, is markedly limited. An exhaustive search reveals a solitary publication that investigated the relationship between central corneal thickness and intra-ocular pressure (IOP).⁹ No investigation has been carried out to explore the relationship of central corneal thickness and ethnicity.

The objectives of this study were to measure the central corneal thickness and explore its relationship to intra-ocular pressure, age, gender and ethnicity in Northern Pakistani population; thus instituting the formation of baseline parameters for diagnosis and management of open angle glaucoma.
METHODOLOGY

A total of 1000 right eyes of 1000 cases were recruited from the ophthalmology outpatient department of Pakistan Institute of Medical Sciences, Islamabad, Pakistan, between December 2013 and February 2015 through stratified sampling. Approval for this study was taken from the institutional review board. The study population was stratified, based on their ethnicity, either Punjabi or Pashtun. Inclusion criteria for recruitment was cases of Pashtun or Punjabi ethnicity and intra-ocular pressure of < 22 mmHg as measured with a Goldmann applanation tonometer, gonioscopically open angles, Schaffer Scale ≥ 3, a cup disk ratio of < 0.5 with no visible superior or inferior pole notching, and an age matched normal 30-2 visual field performed on Humphrey automated perimeter. Exclusion criteria for this study were cases with prior ocular surgery, contact lens use, corneal pathologies, and refractive errors of myopia or hypermetropia > ±3.0 diopters or astigmatism of > ±1.0 diopters.

A full disclosure of the study objectives and methods were made to the cases, and informed consent was taken from them. Ethnicity was determined using a caste and language based self-reporting questionnaire. The participants were asked to report their caste, language used for daily communication, and whether the same language was spoken in their family for the last 3 generations. Explanation concerning the significance and measurement of IOP and central corneal thickness (CCT) was provided to all the cases. In addition, all the cases were made familiar with the procedure of measuring IOP and CCT by demonstration. All patients’ queries were answered to their satisfaction. After a detailed history, the cases underwent a complete ocular examination.

The central corneal thickness was measured by a single investigator who was blind to the study. A TopCon non-contact specular microscope (SP-3000) was used to measure the CCT of the right eye using semi-automatic mode. The readings were recorded in micrometers (µm). The IOP was measured using a Goldmann applanation tonometer (GAT) by a separate investigator who was also blinded to the study. Data was collected during morning hours to reduce the bias of time-based variation of IOP. After proper sterilization of the GAT head, the eye was anesthetized with topical 1% Proparacaine eye drops. The tear film was stained, using a commercially available fluorescein dye strip. The pressure of the right eye was then measured and recorded in mmHg. The CCT, IOP, age, gender and ethnicity measurements of all the cases were entered into the database. Univariate analysis (mean with standard deviation) was done for age, gender, ethnicity, CCT, and IOP (total number and percentage of all the cases). To check for bias of age and gender in the two ethnic groups, independent t-test (for age) and chi-square test (for gender) were used.

Independent samples t-test was used to investigate the statistical relationship between CCT in cases of two different ethnic backgrounds and genders. Linear regression analysis was performed to demonstrate the relationship between CCT and IOP and develop a prediction model of change in measurement of IOP with regards to CCT. Similar prediction model was created for change in CCT with age. Statistical Package for Social Sciences Version 20.0 was used to perform all data analysis. A p < 0.05 was considered to be significant in all analyses.

RESULTS

A total of 1000 right eyes of 1000 cases (496 males and 504 females) were studied. The ethnic composition of the population was 51.6% (n=516) Pashtun, and 48.4% (n=484) Punjabi. The mean age of subject was 47.31 ±11.78 years while the mean CCT and IOP were 503.96 ±12.47 µm and 15.61 ±2.68 mmHg, respectively, as shown in Table I.

There was no difference between mean age (p=0.05) of males (46.59 ±11.66 years) and females (48.02 ±11.87 years), mean CCT (p=0.34) of males (504.34 ±12.52 µm) and females (503.60 ±12.42 µm) and mean IOP (p=0.11) of males (15.48 ±2.68 mmHg) and females (15.75 ±2.68 mmHg) as shown in Table II. No statistically significant difference existed between mean age (p=0.32) of Pashtuns (47.67 ±11.64 years), and Punjabis (46.93 ±11.93 years), and gender composition (χ²=0.15, p=0.69) of Pashtuns 50.20% (n=259) males, and 49.80% (n=257) females, and Punjabis 49.00% (n=237) males, and 51.00% (n=247) females cases, as shown in Table III, thus reducing systemic bias due to difference in population demographics.

The mean CCT and IOP of the Pashtuns (504.45 ±13.03 µm and 15.75 ±2.78 mmHg) and Punjabis (503.44 ±11.83 µm and 15.47 ±2.57 mmHg) showed no significant difference (p=0.11) as shown in Table II.

Table I: Mean age, central corneal thickness, and intra-ocular pressure of cases.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td>47.31 ±11.78</td>
</tr>
<tr>
<td>Central corneal thickness</td>
<td>503.96 ±12.47</td>
</tr>
<tr>
<td>(in µm)</td>
<td></td>
</tr>
<tr>
<td>Intra-ocular pressure</td>
<td>15.61 ±2.68</td>
</tr>
<tr>
<td>(in mmHg)</td>
<td></td>
</tr>
</tbody>
</table>

Table II: Mean age, central corneal thickness, and intra-ocular pressure of male and female cases.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Gender</th>
<th>Mean ±SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td>Males</td>
<td>46.59 ±11.66</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>Females</td>
<td>48.02 ±11.87</td>
<td></td>
</tr>
<tr>
<td>Central corneal thickness</td>
<td>Males</td>
<td>504.34 ±12.52</td>
<td>0.34</td>
</tr>
<tr>
<td>(in µm)</td>
<td>Females</td>
<td>503.59 ±12.42</td>
<td></td>
</tr>
<tr>
<td>Intra-ocular pressure</td>
<td>Males</td>
<td>15.48 ±2.68</td>
<td>0.11</td>
</tr>
<tr>
<td>(in mmHg)</td>
<td>Females</td>
<td>15.75 ±2.68</td>
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</table>
Channa glaucoma. Because of the significant difference in the mean CCT of Pakistani versus African-American population, it can be inferred that this population is at an equally greater risk of developing open angle glaucoma.15 As CCT of Pakistani population closely approximates to the African-American population, it can be inferred that this population is at an equally greater risk of developing open angle glaucoma.

There are several ethnic groups of these populations that have demonstrated genetic factors that are responsible for variations in CCT.22 However, evidence of ethnic groups.

### DISCUSSION

The objectives of this study was to measure the CCT and explore its relationship with IOP, age, gender and ethnicity of this study population. To the authors’ knowledge, this is the only study to date that addresses the aspect of ethnicity in relationship to CCT in a Pakistani population. CCT is a useful predictor for the development of open angle glaucoma as concluded by ocular hypertension study (OHTS).1 Establishment of baseline CCT in our population will aid in developing IOP measurements.

The mean CCT in the study population was 503.96 ±12.47 µm (Table I). The mean CCT as determined by our study was in close approximation to several non-Caucasian (African-American, Korean, African, Indian, and Japanese) populations,10-14 while being lower than those of Caucasians,14 and corroborate the findings of Channa et al.9 The investigations of OHTS revealed that African-American population, whose CCT was lower than those of Caucasians, was at a greater risk of developing open angle glaucoma.15 As CCT of Pakistani population closely approximates to the African-American population, it can be inferred that this population is at an equally greater risk of developing open angle glaucoma.

The mean IOP measured in this study was 15.61 ±2.68 mmHg (Table I). To assess the relationship between IOP and CCT, linear regression analysis was performed. This showed a statistically significant (r=0.15, p < 0.01), positive relationship (beta = 0.15), i.e. a higher CCT tends to produce higher measurements of IOP and vice versa. This result is in agreement with those reported in literature.12,16,17

IOP measurement is known to be affected by CCT. Thin corneas lead to underestimation while in thicker corneas, IOP is overestimated when measured by GAT.18 In this study, a ±100 µm change in CCT was associated with a change in IOP of ±3.30 mmHg (co-efficient of regression for CCT = 0.033). To the authors’ knowledge, this is the only reported quantitative association between CCT and IOP in a Pakistani population. It has been reported that a variation of ±10% in CCT would result in a ±1.1 mmHg change in IOP of healthy eyes.16 In South Indian population a 100 µm increase in CCT was associated with a 1.96 mmHg increase in intra-ocular pressure in the rural population versus 2.45 mmHg for every 100 µm in the urban population.19 Mathematical formulae have been devised to factor in effects of CCT on IOP as measured by GAT.20

Regression analysis showed a statistically significant (r=0.11, p < 0.01) and inverse relationship (beta = -0.11) between CCT and age. The co-efficient of regression for age was -0.12. The analysis predicts that each advancing year of age results in a 0.12 µm reduction in CCT. There is a considerable disparity in evidence pertaining to the relationship between CCT and age.3-6,21 The evidence is strongly divided along geographical lines. Asian,3 African,4 Middle Eastern,5 and European,21 populations show a statistically significant change in CCT with advancing age, while this is evidently not so for North-American population.6 As North American and European populations comprise largely of Caucasians, factors excluding race are likely to be responsible for this variation.

In this study, there was no relationship between CCT and gender (males = 504.34 ±12.52 µm, females = 503.60 ±12.42 µm, p=0.34, Table II), which is in agreement with investigation on Pakistani,9 and other populations.3,5 Interestingly, North American population also shows no significant relationship between CCT and gender. These results are similar to this population base with regard to gender, but not age; which again highlights the importance of conducting region specific investigations to elucidate the complex relationship of CCT to its potential determinants.

The mean CCT in Pashtun and Punjabi populations were 504.45 ±13.03 µm and 503.44 ±11.83 µm, respectively; a difference which is not statistically significant (p=0.19, Table III). There is no prior local data to compare these findings. Investigations on multi-ethnic populations have demonstrated genetic factors that are responsible for variations in CCT.22 However, evidence

### Table III: Mean central corneal thickness, intra-ocular pressure, and age of ethnic groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Ethnicity</th>
<th>Mean ±SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td>Pashtun</td>
<td>47.67 ±11.64</td>
<td>0.32</td>
</tr>
<tr>
<td></td>
<td>Punjabi</td>
<td>46.93 ±11.93</td>
<td></td>
</tr>
<tr>
<td>Gender composition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% (n)</td>
<td>Pashtun</td>
<td>Males 51.60 (516) Females 48.4 (484)</td>
<td>0.69</td>
</tr>
<tr>
<td></td>
<td>Punjabi</td>
<td>Males 50.20 (259) Females 49.80 (257)</td>
<td></td>
</tr>
<tr>
<td>Central corneal thickness (in µm)</td>
<td>Pashtun</td>
<td>504.45 ±13.03</td>
<td>0.19</td>
</tr>
<tr>
<td></td>
<td>Punjabi</td>
<td>503.44 ±11.83</td>
<td></td>
</tr>
<tr>
<td>Intra-ocular pressure (in mmHg)</td>
<td>Pashtun</td>
<td>15.75 ±2.78</td>
<td>0.10</td>
</tr>
<tr>
<td></td>
<td>Punjabi</td>
<td>15.47 ±2.57</td>
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</tbody>
</table>

statistically significant differences (p=0.19 and p=0.10), respectively as shown in Table II.

Linear regression analysis between CCT (taken as the independent variable) and IOP (taken as dependent variable) showed a positive (beta = 0.15) statistically significant relationship (r=0.15, p=0.00). On the basis of this analysis, a ±100 µm change in CCT was associated with a change in IOP of ±3.30 mmHg.

Linear regression analysis between age (taken as independent variable) and CCT (taken as dependent variable) showed a negative (beta =-0.11) statistically significant relationship (r=0.11, p=0.00). On the basis of this analysis, the CCT decreased by 0.12 µm for every year of advancing age.
from population based studies is disparate and sharply regionally demarcated. Countries with clearly defined ethnic groups in South-East Asia have central corneal thickness that is strongly related to the ethnic background of its populace, while in other regions with ethnically distinct populations, this is not the case. The reasons for these disparate associations are not clear. Exploration into genetic basis of determination of CCT will provide a greater insight into association observed by the authors and other investigators.

The limitation of this study was that it was hospital-based rather than general community-based study. Though cases were resourced from a public hospital, which provides highly subsidized healthcare and thus available to a large population base, they formed a select cross-section with limited exposure to diverse ethnic groups and population demographics. The limitation of ethnicity is largely due to the location of the study center, situated in the north of the country. A larger population-based study would allow substantiating these results for general applicability.

CONCLUSION

There exists a significant relationship between CCT and IOP; and CCT and age, among the studied population. However, no relationship could be established between CCT and gender or ethnicity. The lower CCT in our case places them at a higher risk of developing open angle glaucoma at a lower level of IOP as well as under-estimation of IOP which may confound the diagnosis and management of open angle glaucoma. It is recommended that clinicians factor in CCT while measuring IOP in all cases for screening as well as management of glaucoma. A large population-based study should be undertaken to validate these findings and provide generalized guidelines applicable across our population spectrum.

REFERENCES