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# Assessment of Epithelial and Central Corneal Thickness in Patients with Open Angle Glaucoma Using Anterior Segment Optical Coherence Tomography

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## Abstract:

**Background:** Glaucoma is a major etiology of irreversible blindness, with primary open-angle glaucoma (POAG) being the majority common type. Central and epithelial corneal thickness are key factors in assessing the disease, as they influence Intraocular Pressure IOP measurement and progression. Aim: To evaluate epithelial and Central Corneal Thickness CCT in POAG patients utilizing anterior segment optical coherence tomography (AS-OCT) and to determine their relation to ocular surface changes. **Patients and Methods:** This cross-sectional case-control research involved 70 eyes with POAG and 30 healthy eyes as controls. All participants had full ophthalmic examination involving slit-lamp biomicroscopy, visual acuity testing, IOP measurement by Goldmann applanation tonometry, tear break-up time (TBUT), fundus examination, and AS-OCT imaging. Corneal epithelial thickness (CET) and CCT were analyzed, and subgroup comparison was performed based on number of medications used. **Results:** CCT was significantly lower in POAG eyes than controls (521.5 ± 31.5 µm vs. 543.1 ± 31.2 µm, p=0.002). Epithelial thickness showed no significant difference between groups (51.7 ± 4.4 µm vs. 51.2 ± 3.8 µm, p=0.62). TBUT was shorter in POAG patients (6.5 ± 1.9 s) compared with controls (9.7 ± 2.2 s, p below 0.001). Subgroup analysis showed insignificant influence of medication number on CCT, CET, or TBUT. A weak positive correlation was found among CCT and cup-to-disc ratio (r = 0.297, p = 0.03). **Conclusion:** POAG is associated with thinner corneas and impaired tear film stability, while epithelial thickness remains unaffected. Evaluating these parameters may enhance glaucoma management.

**Keywords:** Glaucoma; OCT; Corneal thickness; Epithelial thickness; Tear film.

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## Introduction

Glaucoma is the primary etiology of irreversible blindness and the 2nd foremost etiology of vision impairment globally. Currently impacting more than sixty million individuals worldwide, this figure is projected to increase to 111.8 million by 2040 [1].

Glaucoma is a collection of disorders categorized by damage to the optic nerve. Primary open-angle glaucoma is the predominant subtype of glaucoma in the United States. Timely identification and management for glaucoma has demonstrated efficacy in decelerating or averting disease advancement and reducing vision impairment associated with glaucoma [2].

Central corneal thickness is a significant risk factor for the onset and degree of glaucoma. The management strategy is directly influenced by central corneal thickness measurements in fifteen percent of glaucoma cases. Corneal thickness diminishes during infancy and attains adult levels among the ages of two to four years [3].

CCT significantly influences IOP as determined by applanation tonometry. Certain studies indicate that tonometric estimates may underestimate intraocular pressure (IOP) in eyes with thinner corneas and overestimate it in thicker corneas, suggesting that central corneal thickness (CCT) significantly affects the risk evaluation for open-angle glaucoma depending on applanation tonometry measurements [3].

The measurement of central corneal thickness (CCT) in adults with 1ry open-angle glaucoma significantly influences clinical evaluation for two reasons: applanation intraocular pressure (IOP) readings are significantly influenced by CCT (specifically, thicker CCTs tend to "overestimate" and thinner CCTs "underestimate" actual IOPs), and thinner CCTs represent a considerable risk factor for the progression of glaucoma damage, irrespective of IOP adjustments [4].

The uncertainty surrounding the risk associated with CCT pertains to whether it solely arises from inaccuracies in IOP measurement or if additional factors, like the characteristics of the posterior sclera and lamina cribrosa, significantly affect the onset and advancement of glaucoma [4].

The corneal epithelium is a primary component that experiences degenerative changes as a result of anti-glaucomatous treatment [5].

The prolonged use of antiglaucoma medications, alterations in therapy owing to ocular surface intolerance, frequent daily applications, and the effects of active ingredients and preservatives might lead to the development of ocular surface disease (OSD), potentially undermining case adherence to treatment, satisfaction, and overall outcomes. Furthermore, the medications caused modifications to the ocular surface and might elevate the likelihood of glaucoma filtration surgical failure, which, regrettably, may exacerbate the development of OSD [6].

CCT can be quantified using several devices, including AS-OCT. In most devices, central corneal thickness is quantified as the aggregate thickness of the three primary corneal histological layers: the stroma, epithelium, and endothelium. The anterior segment optical coherence tomography offers the benefit of being a dependable and consistent tool for imaging the central cornea, enabling separate measurements of the corneal epithelium and stromal layer [7].

The purpose of this research was to evaluate Epithelial and CCT in individuals with Open Angle Glaucoma utilizing AS-OCT.

## Patients and methods

This cross-sectional case-control research has been performed in ophthalmology department Benha University Hospital from the beginning of 2022 to the end of 2024. It included 70 eyes from cases diagnosed with POAG **(Group A)** and 30 eyes from age- and sex-matched healthy

individuals who served as the control group **(Group B).**

**Ethical Approval:**

Informed written consent has been attained from all individuals. The research involving human subjects was sanctioned by the ethical committee of Benha Faculty of Medicine {M.S.43.4.2022}.

**Inclusion criteria:**

**Patient group (Group A):** Age:>18years and Previously diagnosed with open angle glaucoma.

**Control group (Group B):** Age:>18years, No previous history of Intraocular surgery, no family history of glaucoma and normal Intraocular pressure notmorethan21 mmHg.

**Exclusion criteria for both groups:** Presence of corneal pathology or history of corneal surgery that could influence study outcomes, history of cataract surgery, patients with systemic diseases known to affect the cornea, such as rheumatoid arthritis, tuberculosis, or syphilis, diagnosis of keratoconus, current use of contact lenses, uncontrolled IOP, history of any prior intraocular surgery and use of medications that may induce corneal dryness and interfere with CCT measurements, including antihistamines, antidepressants, and acne treatments

**Methods**

**Each patient underwent the following standardized evaluation.**

**Comprehensive History Taking**: A detailed history was obtained, including demographic data, medical history, ocular complaints, systemic conditions, medications, and any relevant family history.

**Ocular Examination**: A complete ophthalmic examination has been done for all participants and included inspection of the eyelids, orbit, lacrimal apparatus, and assessment of ocular motility. Visual acuity testing was done, both unaided and best-corrected, using a Snellen chart. Slit-lamp biomicroscopy was carried out for detailed anterior segment evaluation, involving the anterior chamber, cornea, sclera, iris, pupil, and lens.

**IOP Measurement**: Intraocular pressure (IOP) has been determined utilizing the Goldmann Applanation Tonometer under standard conditions.

**TBUT Test**: TBUT was assessed as a measure of tear film stability and evaporative dry eye disease. Fluorescein dye was instilled into the tear film, and cases have been instructed to avoid blinking while the tear film has been detected under a broad beam of cobalt blue light using the slit lamp. Tear Break-Up Time has been described as the interval (in seconds) among the last blink and the appearance of the 1$^{st}$ dry spot on the corneal surface. A TBUT of less than ten seconds was regarded as anomalous.

**Fundus Examination**: Posterior segment evaluation was performed using an indirect ophthalmoscope and a +90 diopter non-contact double aspheric biconvex lens (Volk lens).

**Anterior Segment Optical Coherence Tomography (AS-OCT)**

Anterior segment imaging has been conducted using the Optovue Avanti OCT scanner (Software Version: 2018.1.0.43; Optovue Inc., Fremont, CA, United States of America) with an axial resolution of 5 µm/pixel and a scan time of three seconds.

For the AS-OCT imaging protocol, patient data including name, ID, age, and date were entered. The Anterior Segment Mode was mounted, and the chin rest was adjusted until the patient's eyes were aligned with the red positioning mark. The "Cornea Line" scan mode was selected to assess corneal thickness, and images were acquired using the joystick button.

Corneal epithelial thickness and total corneal thickness information was attained utilizing the RTVue OCT system (Software Version: 2018.1.0.43; Optovue Inc., Fremont, CA, USA) equipped with a corneal adaptor module operating at a central wavelength of 830 nm. Corneal epithelial thickness maps were automatically produced and divided into

twenty-five sectors covering a nine-millimeters corneal diameter, including a central two-millimeters zone, 8 paracentral zones within the annulus between the two-millimeters and five-millimeters rings, 8 mid-peripheral zones between the five-millimeters and seven-millimeters rings, and 8 peripheral zones between the seven-millimeters and nine-millimeters rings.

The software also calculated the standard deviation of CET within the central 7-mm zone as a measure of thickness variability. Stromal thickness has been computed by subtracting epithelial thickness from total corneal thickness.

**Statistical Analysis**

Statistical analysis has been conducted utilizing specialized software (e.g., SPSS version 20.0, IBM Corp., Armonk, NY, USA, 2020). The data were represented as mean ± standard deviation (SD). Comparisons between groups have been made utilizing appropriate statistical tests, and a p-value < 0.05 was deemed statistically significant.

## Results

There was insignificant variance among the examined groups as according to baseline characteristics. However, there was greatly significant variance among them as according to intra-ocular pressure which has been found to be significantly higher among OAG cases than their counterparts **[Table 1]**.

There was greatly significant variance among the examined groups as regarding tear break-up test which has been found to be significantly reduce among open angle glaucoma patients than control group (6.54 versus 9.70 respectively) **[Table 2]**.

A significant variance has been observed among the examined groups as regarding central corneal thickness which was found to be significantly reducing among open angle glaucoma cases than control group (521.5 versus 543.1 respectively). However, there was insignificant variance among the examined groups in epithelial thickness measurements **[Table 3]**.

**Table (1):** Baseline characteristics of the examined groups:

| Variable | OAG group (n=70) | Control group (n=30) | Test | p-value |
|---|---|---|---|---|
| **Age (years):** | | | | |
| Mean ± SD | 55.3 ± 12.7 | 53.6 ± 10.7 | 0.443# | 0.66 |
| Range | 19 - 79 | 29 - 68 | | (NS) |
| **Gender:** | | | | |
| Female: | 20 (55.6%) | 9 (60%) | 0.085^ | 0.770 |
| Male: | 16 (44.4%) | 6 (40%) | | (NS) |
| **Bilaterality:** | | | | |
| OD: | 34 (48.6%) | 15 (50%) | 0.875^ | 0.646 |
| OS: | 34 (48.6%) | 15 (50%) | | (NS) |
| Unilateral: | 2 (2.8%) | 0 (0%) | | |
| **IOP:** | | | | |
| Mean ± SD | 15.9±3.2 | 11.6±1.7 | **6.731#** | **<0.001** |
| Range | 10 - 21 | 10 - 15 | | **(HS)** |
| **Lateral angle OD:** | (n=36) | | | |
| Mean ± SD | 41.6 ± 9.8 | 43 ± 17.1 | -0.356# | 0.724 |
| Range | 26.1 – 68.6 | 26.1 – 86.2 | | (NS) |
| **Inferior angle OD:** | (n=36) | | | |
| Mean ± SD | 48.2 ± 16.2 | 42.3 ± 12.4 | 1.269# | 0.210 |
| Range | 20.9 – 92.2 | 25.9 – 67.5 | | (NS) |
| **Lateral angle OS:** | (n=34) | | | |
| Mean ± SD | 42.1 ± 11.8 | 38.7 ± 10.9 | 0.960# | 0.342 |
| Range | 25.2 – 83.7 | 23.7 – 56.7 | | (NS) |
| **Inferior angle OS:** | (n=34) | | | |
| Mean ± SD | 49.9 ± 18.3 | 42.8 ± 9.6 | 1.413# | 0.164 |
| Range | 21.8 – 105.8 | 23.8 – 55.8 | | (NS) |

#: Independent t-test, ^: Chi-square test, NS: non-significant (p above 0.05), HS: highly significant (p below 0.001)

**Table (2):** Tear break-up test (TBUT) of the examined groups:

| Variable | OAG group (n=68) | Control group (n=30) | Test | p-value |
|---|---|---|---|---|
| **TBUT:** | | | | |
| Mean ± SD | 6.54±1.9 | 9.70±2.2 | **-7.079#** | **<0.001 (HS)** |
| Range | 2 - 9 | 5 - 13 | | |

#: Independent t-test. HS: highly significant variance (p below 0.001).

**Table (3):** Epithelial and central corneal thickness (CCT) of the examined groups:

| Variable | OAG group (n=70) | Control group (n=30) | Test | p-value |
|---|---|---|---|---|
| **CCT:** | | | | |
| Mean ± SD | 521.5±31.5 | 543.1 ± 31.2 | **-3.147#** | **0.002 (S)** |
| Range | 457 - 615 | 502 - 626 | | |
| **Epithelial thickness:** | | | | |
| Mean ± SD | 51.7±4.4 | 51.2±3.8 | 0.498# | 0.620 (NS) |
| Range | 44 - 64 | 44 - 59 | | |

A significant variance between the examined groups as regarding lateral angle (OD) measurements which has been found to be significantly greater among open angle glaucoma patients receiving more than one drug compared to those receiving only one drug (45.1 versus 38.1 respectively). However, there was insignificant variance among the examined groups in all other parameters **[Table 4]**.

An insignificant variance between the examined groups as according to both central corneal and epithelial thickness. There was insignificant variance among the examined groups as according to tear break-up tests **[Table 5]**.

There was insignificant variance between cases receiving only one drug and those receiving more than one drug as regarding all visual field parameters **[Table 6]**.

**Table (4):** Clinical data of the OAG studied group:

| Variable | OAG with one drug (n=18) | OAG with more than one drug (n=18) | Test | p-value |
|---|---|---|---|---|
| **Bilaterality:** | | | | |
| OD: | 16 (88.9%) | 18 (100%) | 2.118^ | 0.146 (NS) |
| Unilateral: | 2 (11.1%) | 0 (0%) | | |
| **IOP:** | (n=17) | | | |
| Mean ± SD | 15.5± 3.6 | 16±2.8 | -0.374# | 0.711 (NS) |
| Range | 10 - 21 | 10 - 20 | | |
| **Lateral angle OD:** | | | | |
| Mean ± SD | 38.1±7.3 | 45.1±10.9 | **-2.242#** | **0.03 (S)** |
| Range | 26.1 – 56.1 | 27.1 – 68.6 | | |
| **Inferior angle OD:** | | | | |
| Mean ± SD | 47.1±18.5 | 49.3 ± 14 | -0.400# | 0.692 (NS) |
| Range | 20.9 – 92.2 | 29.9 – 88.7 | | |
| **Lateral angle OS:** | (n=16) | | | |
| Mean ± SD | 41.8±8.4 | 42.4±14.4 | -0.142# | 0.888 (NS) |
| Range | 25.2 – 59.9 | 25.5 – 83.7 | | |
| **Inferior angle OS:** | (n=16) | | | |
| Mean ± SD | 49.2±19.7 | 50.5±17.5 | -0.203# | 0.841 (NS) |
| Range | 21.8 – 105.8 | 30.2 – 95.4 | | |

**Table (5):** Epithelial and central corneal thickness (CCT) and tear break-up time (TBUT) of the OAG studied group.

| Variable | OAG with one drug (n=18) | OAG with more than one drug (n=18) | Test | p-value |
|---|---|---|---|---|
| **CCT:** | | | | |
| **Mean ± SD** | **525.9±36** | **521.7 ±28.3** | **0.386#** | **0.702** |
| **Range** | **471 - 615** | **461 - 573** | | **(NS)** |
| **Epithelial thickness:** | | | | |
| **Mean ± SD** | **51.2± 4.6** | **52.8±5.2** | **-1.008#** | **0.321** |
| **Range** | **45 - 63** | **47 - 64** | | **(NS)** |
| **TBUT:** | | | | |
| **Mean ± SD** | **6.5 ± 2** | **6.5 ± 1.8** | **0.00#** | **1.00** |
| **Range** | **3 - 9** | **3 - 9** | | **(NS)** |

**Table (6):** Visual field of the OAG studied group:

| Variable | OAG with one drug | OAG with more than one drug | Test | p-value |
|---|---|---|---|---|
| **MD:** | **(n=4)** | **(n=6)** | | |
| **Mean ± SD** | **10.04±12.3** | **11.1±10.2** | **-0.144#** | **0.889** |
| **Range** | **3.06 – 28.5** | **0.74 – 30.5** | | **(NS)** |
| **PSD:** | **(n=2)** | **(n=5)** | | |
| **Mean ± SD** | **4.6±0.7** | **3.5±2** | **0.746#** | **0.489** |
| **Range** | **4.1 – 5.1** | **1.3 – 5.8** | | **(NS)** |
| **RNFL average:** | **(n=6)** | **(n=6)** | | |
| **Mean ± SD** | **81 ±12.1** | **74.6 ±17.5** | **0.729#** | **0.483** |
| **Range** | **66 - 96** | **57 - 91** | | **(NS)** |
| **RNFL (inferior quadrant):** | **(n=4)** | **n=5)** | | |
| **Mean ± SD** | **87.7 ±16.7** | **77.8 ±28.7** | **0.610#** | **0.561** |
| **Range** | **75 - 111** | **52 - 133** | | **(NS)** |
| **C/D:** | **(n=11)** | **(n=14)** | | |
| **Mean ± SD** | **0.62 ±0.22** | **0.48 ±0.21** | **1.600#** | **0.123** |
| **Range** | **0.29 – 0.90** | **0.03 – 0.7** | | **(NS)** |
| **Duration of instillation:** | **(n=18)** | **(n=18)** | | |
| **Mean ± SD** | **4.6 ±2.6** | **4.6 ±3.3** | **0.388#** | **0.700** |
| **Range** | **1 - 10** | **1 - 12** | | **(NS)** |

## Discussion

The clinical characteristics and baseline demographic were comparable between OAG eyes (n=70) and control eyes (n=30). The mean age was $55.3 \pm 12.7$ years in the OAG group and $53.6 \pm 10.7$ years in the control group (p equal to 0.66). Female eyes accounted for 55.6% in the OAG group and 60% in the control group (p equal to 0.77). Laterality distribution showed bilateral involvement in 97.2% of OAG eyes and 100% of control eyes (p=0.646). Mean IOP was significantly higher in OAG eyes ($15.9 \pm 3.2$ mmHg) compared to controls ($11.6 \pm 1.7$ mmHg, p below 0.001). However, insignificant variances have been observed between groups in anterior chamber angle measurements (lateral or inferior, OD or OS; all p>0.05). Among OAG eyes, comparison between those treated with one drug (n=18) and those on multiple medications (n=18) revealed insignificant variances in age, gender distribution, laterality, or IOP (all p>0.05), with the exception of the lateral angle OD, which was significantly wider in the multi-drug group ($45.1 \pm 10.9°$ vs. $38.1 \pm 7.3°$, p=0.03). All other angle measurements remained statistically non-significant. These findings confirm baseline comparability between groups, aside from the expected elevation in IOP and a wider lateral angle in multi-drug–treated OAG eyes.

CCT was significantly reducing in OAG cases than controls (mean 521.5 µm vs. 543.1 µm, p equal to 0.002), in agreement with previous literature reporting thinner

corneas in glaucoma patients. Thinner CCT may lead to underestimation of IOP and has been considered a risk factor for glaucoma progression and development. This reinforces the importance of CCT measurement in clinical glaucoma assessment and risk stratification.

On the other hand, insignificant variances have been observed in epithelial thickness between the groups.

In subgroup analysis, neither CCT nor epithelial thickness differed significantly between patients receiving one versus multiple medications. This may indicate that drug number or duration did not substantially affect corneal structure within the sample size studied, although a trend toward thicker epithelium in the multi-drug group (52.8 vs. 51.2 µm) warrants further investigation with larger cohorts.

Among OAG patients, CCT showed a statistically significant positive correlation with the cup-to-disc (C/D) ratio (r equal to 0.297, p equal to 0.03). This finding is somewhat unexpected, as thinner corneas are generally associated with worse glaucomatous damage (larger cups). The weak positive correlation in this study may be influenced by sample size, measurement variability, or nonlinearity in the relationship. No other significant correlations were found between CCT and variables such as IOP, age, RNFL, TBUT, or duration of treatment. This finding corresponds with a research by Halkiadakis et al. [8] that assessed CET variables utilizing anterior segment optical coherence tomography in glaucomatous cases receiving medicinal management and compared them to the CET variables of control subjects. This study was cross-sectional, involving sixty-two cases with primary open-angle or pseudo-exfoliative glaucoma (study group) and sixty-two age-matched controls. The CCT measured 537.6±33.3 in the glaucoma group and 550.8±33.7 in the control group (P equal to 0.028).

Furthermore, a study has been led by Tolesa and Gessesse [9] to assess CCT in black cases with newly identified glaucoma and ocular hypertension (OHT) in Southwest Ethiopia. This was a prospective research conducted using an ultrasonic pachymeter from June 2014 to February 2015 at Jimma University Specialized Hospital. Individuals aged eighteen years and older, newly identified with glaucoma or ocular hypertension, were involved. The mean CCT for the entire sample was 518.67 (±39.97) micrometers. The research indicated a statistically significant reduction in CCT with increasing age (P equal to 0.02).

The OAG group showed significantly shorter tear break-up time compared to controls (mean 6.5 vs. 9.7 seconds, $p < 0.001$), reflecting compromised tear film stability and ocular surface integrity.

This aligns with a research conducted by Kim et al. [10] that prospectively compared the safety and effectiveness of preservative-free brimonidine tartrate 0.15% with preserved brimonidine tartrate 0.15% concerning corneal surface evaluation, intraocular pressure reduction, safety, and adherence rates in cases with open-angle glaucoma or ocular hypertension, as well as evaluating the possible advantages of preservative-free brimonidine on ocular and systemic variables. Sixty eyes from sixty cases with IOP above or equal to fifteen millimeters of mercury, identified as having open-angle glaucoma or ocular hypertension, have been randomized into preserved (num.=thirty-one) and preservative-free (num.=twenty-nine) brimonidine groups. The TBUT has been determined to be 6.40±2.04, closely aligning with the findings of our investigation.

A research by Saade et al. [11] was done to assess the correlation among the intensity and period of glaucoma topical medication and the degree of symptoms and signs of OSD. The research was a single-site, prospective, controlled, cross-sectional research. Sixty-one cases without an

identification of or prior treatment for OSD have been found. Abnormal TBUT scores were reported to be common in the glaucoma group relative to the control group.

Conversely, a study by Doğan et al. [12] assessed the impact of topical antiglaucomatous medicines on central corneal epithelial thickness, as evaluated by AS-OCT. A total of 153 eyes from 153 cases utilizing topical antiglaucomatous medicines and 110 eyes from 110 control subjects have been included in the research. The case group was assessed for glaucoma type, therapy duration, number of medications, and daily drop frequency. In the case cohort, insignificant variances have been seen in the median central corneal thickness, central corneal epithelial thickness, and tear film break-up time concerning glaucoma type, period of treatment, number of medications, and frequency of daily drops.

The difference between our findings and those of Doğan et al. [12] regarding the impact of multiple antiglaucomatous medications on patient outcomes warrants further investigation. While our study observed significantly lower scores in cases with open-angle glaucoma(OAG)treated with multiple drugs, Doğan et al. [12] found no significant variances in central CET or tear film break-up time based on the number of medications used. This contradiction may be related to few factors, including differences in study design, patient populations, specific outcome measures, or the types of medications evaluated. Our study focused on broader patient-reported outcomes, whereas Doğan et al. [12] examined specific corneal parameters. Additionally, the duration of treatment, drug combinations, and potential confounding factors may have influenced the results.

Our study found that the open angle glaucoma group showed a meanoptic nerve RNFL thickness of 75.3 ± 5.1 µ with minimum thickness is 47 µand maximum thickness is 97 µ.

## Conclusions

In conclusion, the findings of our study indicate that open-angle glaucoma (OAG) is associated with significant alterations in central corneal thickness and tear film stability than healthy controls. Patients with OAG demonstrated lower CCT values and slower tear breakup times (TBUT), suggesting potential corneal alterations and ocular surface changes related to the disease or its treatment. The research also showed a weak positive association between intraocular pressure (IOP) and CCT, highlighting the complex relationship between these parameters in glaucoma. These results suggest that corneal changes, particularly in CCT and tear film stability, play a role in OAG and should be considered in the management and monitoring of glaucoma patients, especially in the context of IOP measurements and ocular surface health.

**Consent for publication**

Not applicable.

**Competing interests**

None.

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None.

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