Comparison of uveal parameters between acute primary angle-closure eyes and fellow eyes in South Indian population

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Purpose: To analyze the ocular biometric parameters of eyes with acute primary angle closure (APAC) as compared to fellow eyes. Methods: A cross-sectional study was conducted on 27 patients presenting with recent onset APAC to a tertiary eye institute in India. Anterior and posterior ocular biometric parameters were measured simultaneously by anterior segment optical coherence tomography (AS-OCT), A-scan, ultrasonic biomicroscopy (UBM), and B-mode ultrasonogram (USG). The parameters measured were anterior chamber depth (ACD), anterior chamber angle (ACA), angle opening distance (AOD500, AOD750), lens vault (LV), axial length (AL), ciliary body thickness maximum (CBTmax) and at the point of scleral spur (CBT0), anterior placement of the ciliary body (APCB), and retinochoroidal thickness (RCS). Results: Mean age ± SD of patients with APAC was 55.66 ± 7.2 years with female preponderance (21:6 patients). Mean presenting IOP ± SD of the affected eye and fellow eye were 54.74 ± 11.67 mm Hg and 18.7 ± 11.67 mm Hg, respectively. Eyes with APAC had statistically significant narrower anterior ocular biometric parameters, higher LV, decreased ciliary body thickness, more APCB, and longer AL than the fellow eyes. CBTmax is the only variable that had significance (β = -0.421, 95% CI: -0.806 to -0.035, P = 0.034) in the univariate analysis with RCS thickness in APAC eyes. Further, there was a correlation between CBT0 and APCB with CBTmax both in univariate (β = 0.894, P < 0.0001 and β = -0.351, P = 0.039) and multivariable analysis (β = 0.911, P < 0.0001 and β = -0.416, P = 0.016). Conclusion: Compared to the fellow eyes, APAC eyes had different ocular biometric parameters. In addition to known biometric parameters associated with pupillary block (narrower anterior biometric parameters-ACA, ACD, and AOD), our study found multiple nonpupillary block factors such as higher lens vault and thinner and more anteriorly placed ciliary body to be associated with APAC.

Key words: Acute primary angle closure, anterior segment OCT, axial length, ocular biometric parameters, retinochoroidal thickness, ultrasound biomicroscopy
purpose of our study was to compare the anterior and posterior ocular biometric parameters in APAC eyes and the fellow eyes prior to laser (LPI) or surgical intervention and to study the relationship between ciliary body and choroid in APAC in a South Indian population.

Methods

This was a cross-sectional, observational study conducted between September 2019 and December 2020 after approval by the institutional review board (IRB2019008CII) and adhered to the tenets of the declaration of Helsinki. All the participants provided informed written consent for participation in the study. Patients presenting with unilateral APAC attacks and their fellow eyes with either PACS or PAC were recruited to participate in the study. We excluded patients with current use of topical or systemic medications that could affect the angle or pupillary reflex-like topical pilocarpine in the past 5 days, those who had recent Nd:YAG laser treatment in the affected eye or cataract surgery in the fellow eye, and poor quality AS-OCT and UBM images. We also excluded patients with any of the following ocular findings: high myopia with a spherical equivalent of more than −6 D or high hypermetropia of more than +3 D, angle closure secondary to lens or tumor, recent history of trauma, retinal or choroidal disease, systemic diseases such as uncontrolled diabetes and hypertension, and inability to tolerate examination or not willing to participate in the study.

APAC was defined based on the following criteria: (1) presence of at least two of the following symptoms: ocular pain, periocular pain, or headache; (2) nausea and/or vomiting; (3) a previous history of intermittent blurred vision or halos around light; (4) raised IOP of at least 25 mm Hg; and (5) presence of at least three of the following signs: conjunctival injection, corneal epithelial edema, mid-dilated nonreactive pupil and/or a shallow anterior chamber. PACS was defined as an iridotrabecular contact of 180 degrees or more under noncompressive gonioscopy with normal IOP (<21 mm Hg) and without peripheral anterior synechiae or glaucomatous neuropathy. PAC was defined as an iridotrabecular contact of 180 degrees or more under noncompressive gonioscopy with elevated IOP (>21 mm Hg) or peripheral anterior synechiae without glaucomatous optic neuropathy.[15]

All the recruited patients underwent detailed ocular examination including best-corrected visual acuity by Snellen chart, anterior segment examination, IOP by Goldmann applanation tonometry, gonioscopy by Goldmann 2-mirror, undilated fundus examination of the fellow eyes with 90-D lens, measurement of anterior biometric parameters using AS-OCT (Heidelberg Spectralis, Heidelberg engineering, Heidelberg, Germany) [Fig. 1a and b], ciliary body parameters by ultrasound biomicroscopy (UBM) [Fig. 2a and b], axial length measurement by A-scan, and retinocchoroidal thickness by B-mode USG (4 Sight Accutome by Keeler plus, USA- has separate probes for UBM, A-scan and B-scan). All the imaging examinations were performed by a single experienced physician before any laser (Nd:YAG PL, Argon laser iridoplasty) or surgical intervention (surgical iridectomy or trabeculectomy).

We ensured that the patients were medically treated for APAC and were asymptomatic prior to all investigations. The quantitative data acquired from AS-OCT, UBM, A-scan, and B-scan images of the APAC and fellow eyes of APAC patients were consolidated and comparatively analyzed.

Statistical methods

Statistical analyses were performed using STATA software version 14.1 (Texas USA). The continuous variables are presented as mean (standard deviation), and categorical variables are presented as frequency and percentage. The normality of the data was checked using Shapiro–Wilk’s test. The variance between the APAC eyes and their fellow eyes are similar, and paired t test/Wilcoxon sign rank test was used to detect the differences between the two groups. Two sample t test/Mann–Whitney U test was used for the between-group comparison. Univariate and multivariate linear regression was used to determine the relationship between the RCS and CBTmax with other parameters in APAC eyes and fellow eyes. P < 0.05 was considered significant.

Results

A total of 32 consecutive patients who presented with unilateral APAC were enrolled, of which five patients were excluded due to poor patient cooperation and persistent corneal edema leading to poor quality ASOCT and UBM images. Twenty-seven patients (54 eyes) with unilateral APAC
and fellow eyes defined as PACS/PAC were analyzed. Out of 27 patients, 19 patients had PACS and eight patients had PAC in fellow eyes.

Table 1 shows the demographic and baseline characteristics of patients. The mean age (SD) of the study patients was 55.66 (7.23) years. The mean (SD) IOP at presentation in the affected eye was 54.74 (11.67) mm Hg and in the fellow eye was 18.7 (11.67) mm Hg. The median (IQR) baseline presenting logMAR visual acuity in the affected eye was 0.78 (0.48–1.08).

Table 2 shows the comparison of baseline biometric data between APAC and fellow eyes. The average values of these parameters (ACA, AC depth, AOD 500, AOD700, CBTmax, CBT0, APCB, and AL) were higher in the fellow eyes as compared to the APAC eyes. Also, the other parameters such as LV, APCB, axial length, and IOP were higher for the APAC eyes. These differences were statistically significant ($P < 0.05$) between the APAC and fellow eyes except for the RCS thickness.

Table 3 shows the univariate and multivariate linear regression for the association between RCS and CBTmax with respect to other parameters in APAC eyes. CBTmax is the only variable which had a negative correlation ($\beta = -0.421$, $P = 0.034$) with RCS thickness in the univariate analysis for APAC eyes. It suggests that the CBTmax value increases by 1 unit if the RCS value decreases by 0.421 units. However, none of the other biometric factors were significant in the multivariate analysis. Similarly, there was a significant correlation between CBT0 ($P < 0.0001$), APCB ($P = 0.039$) with CBTmax value, when the CBT0 value increases by 1 unit, the CBTmax value also increases by 0.894 units. Further, the CBTmax value is inversely related to APCB, where it decreases by 0.351 units for every 1 unit increase in APCB, which is also significant ($P = 0.016$) in the multivariate analysis.

Table 4 shows the univariate and multivariate linear regression for association between RCS and CBTmax with other parameters in fellow eyes. APCB parameter alone was negatively correlated ($\beta = -0.557$, $P = 0.041$) with RCS in the univariate analysis and baseline IOP alone was negatively correlated ($\beta = -0.0166$, $P = 0.044$) with RCS in multivariate analysis in fellow eyes. Similarly, in the fellow eyes, CBT0 was alone positively correlated ($\beta = 0.9$, $P < 0.0001$) in the univariate analysis and ACA ($\beta = 0.031$, $P = 0.006$), CBT0 ($\beta = 0.88$, $P < 0.0001$)

Figure 2: (a and b) Determination of ciliary body parameters on ultrasound biomicroscopy. The figure is showing the measurement of ciliary body thickness at the point of the scleral spur (CBT0), maximum ciliary body thickness (CBTmax), and anterior placement of the ciliary body (APCB)

Figure 3: Scatter plot for RCS thickness with CBTmax in APAC eyes

Table 1: Demographic and baseline characteristics of the patients

| Characteristic                    | n (%)          |
|----------------------------------|----------------|
| N patients (N eyes)              | 27 (27)        |
| Mean age (SD) in years           | 55.66 (7.23)   |
| Sex, Male/Female                 | 6/21           |
| Laterality of APAC eye, Right/Left| 19/8           |
| Presenting IOP, mmHg, APAC eye (SD) | 54.74 (11.67) |
| Presenting IOP, mmHg, fellow eye (SD) | 18.7 (11.67) |
| Presenting VA, Logmar, APAC eye | 0.78 (6/36)    |

Table 2: Comparing the baseline data and biometric data of APAC eyes and fellow eyes

| Parameters   | APAC eyes (n=27) | Fellow eyes (n=27) | P     |
|--------------|------------------|--------------------|-------|
| ACA (degrees)| 5.48 (3.14)      | 12.88 (4.97)       | <0.0001* |
| AOD 500      | 98.14 (57.46)    | 212.37 (93.35)     | <0.0001* |
| AOD 700      | 149.25 (80.58)   | 277.71 (141.42)    | <0.0001* |
| ACD (mm)     | 1.4 (0.19)       | 1.68 (0.21)        | <0.0001* |
| LV (micron m)| 1370.37 (403.36) | 1125.77 (338.73)   |        |
| CBTmax (mm)  | 1.03 (0.13)      | 1.12 (0.18)        | 0.0023* |
| CBT0 (mm)    | 0.82 (0.103)     | 0.88 (0.14)        | 0.0323* |
| APCB (mm)    | 0.92 (0.15)      | 0.79 (0.13)        | <0.0001* |
| Axial length (mm) | 22.29 (8.88) | 21.87 (6.65)       | <0.0009* |
| RCS (mm)     | 1.54 (0.13)      | 1.52 (0.19)        | 0.7282* |
| IOP (mmHg)   | 54.74 (11.67)    | 18.7 (6.1)         | <0.0001* |

W- Wilcoxon Sign Rank test; P-Paired t test
Table 3: Univariate and multivariate linear regression for the association between RCS and CBTmax with other parameters of APAC eyes

| Parameters | Univariate | Multivariate |
|------------|------------|--------------|
|            | β (95% CI) | P            | β (95% CI) | P            |
| RCS        |            |              |            |              |
| ACA        | 0.0002 (−0.017 to 0.018) | 0.974 | −0.033 (−0.081 to 0.013) | 0.153 |
| AOD 500    | 0.00016 (−0.00079 to 0.0012) | 0.701 | 0.0011 (−0.0013 to 0.0003) | 0.362 |
| AOD 700    | 0.000189 (−0.00005 to 0.00008) | 0.581 | 0.00007 (−0.00006 to 0.00022) | 0.255 |
| LV         | −0.000091 (−0.0004 to 0.00023) | 0.566 | −0.0002 (−0.00007 to 0.00002) | 0.340 |
| CBT0       | −0.3676 (−0.894 to 0.159) | 0.163 | 0.0856 (−0.865 to 1.03) | 0.851 |
| CBTmax     | −0.421 (−0.806 to−0.035) | 0.034 * | −0.288 (−1.06 to 0.491) | 0.444 |
| APCB       | 0.297 (−0.053 to 0.648) | 0.094 | 0.454 (−0.142 to 1.05) | 0.126 |
| ACD        | −0.048 (−0.345 to 0.247) | 0.737 | −0.203 (−0.56 to 0.152) | 0.244 |
| AL         | −0.028 (−0.091 to 0.034) | 0.361 | 0.007 (−0.071 to 0.085) | 0.845 |
| IOP        | 0.0013 (−0.003 to 0.006) | 0.562 | 0.0018 (−0.003 to 0.007) | 0.458 |

Table 4: Univariate and multivariate linear regression for the association between RCS and CBTmax with other parameters of fellow eyes

| Parameters | Univariate | Multivariate |
|------------|------------|--------------|
|            | β (95% CI) | P            | β (95% CI) | P            |
| RCS        |            |              |            |              |
| ACA        | −0.005 (−0.021 to 0.010) | 0.500 | −0.018 (−0.063 to 0.027) | 0.413 |
| AOD 500    | −0.0004 (−0.0012 to 0.00004) | 0.313 | 0.0001 (−0.0007 to 0.0003) | 0.177 |
| AOD 700    | −0.0002 (−0.0008 to 0.00002) | 0.324 | −0.0007 (−0.0019 to 0.00004) | 0.207 |
| LV         | −0.00012 (−0.0007 to 0.00004) | 0.694 | −0.0001 (−0.0008 to 0.00005) | 0.617 |
| CBT0       | 0.008 (−0.056 to 0.57) | 0.975 | −0.166 (−1.177 to 0.843) | 0.731 |
| CBTmax     | −0.102 (−0.323 to−0.52) | 0.49 | 0.48 (−0.388 to 1.35) | 0.257 |
| APCB       | −0.557 (−1.09 to−0.024) | 0.041 * | −0.568 (−1.31 to 0.17) | 0.125 |
| ACD        | −0.078 (−0.46 to 0.302) | 0.674 | −0.413 (−0.86 to 0.039) | 0.071 |
| AL         | −0.004 (−0.125 to 0.117) | 0.944 | −0.017 (−0.157 to 0.122) | 0.794 |
| IOP        | −0.009 (−0.0221 to 0.0025) | 0.116 | −0.0166 (−0.032 to−0.005) | 0.044 * |

Table 3: Univariate and multivariate linear regression for the association between RCS and CBTmax with other parameters of APAC eyes

| Parameters | Univariate | Multivariate |
|------------|------------|--------------|
|            | β (95% CI) | P            | β (95% CI) | P            |
| RCS        |            |              |            |              |
| ACA        |              |              |            |              |
| AOD 500    | 0.0016 (−0.00079 to 0.0012) | 0.701 | 0.0011 (−0.0013 to 0.0003) | 0.362 |
| AOD 700    | 0.000189 (−0.00005 to 0.00008) | 0.581 | 0.00007 (−0.00006 to 0.00022) | 0.255 |
| LV         | −0.000091 (−0.0004 to 0.00023) | 0.566 | −0.0002 (−0.00007 to 0.00002) | 0.340 |
| CBT0       | −0.3676 (−0.894 to 0.159) | 0.163 | 0.0856 (−0.865 to 1.03) | 0.851 |
| CBTmax     | −0.421 (−0.806 to−0.035) | 0.034 * | −0.288 (−1.06 to 0.491) | 0.444 |
| APCB       | 0.297 (−0.053 to 0.648) | 0.094 | 0.454 (−0.142 to 1.05) | 0.126 |
| ACD        | −0.048 (−0.345 to 0.247) | 0.737 | −0.203 (−0.56 to 0.152) | 0.244 |
| AL         | −0.028 (−0.091 to 0.034) | 0.361 | 0.007 (−0.071 to 0.085) | 0.845 |
| IOP        | 0.0013 (−0.003 to 0.006) | 0.562 | 0.0018 (−0.003 to 0.007) | 0.458 |

*P<0.05 – significant, CI- Confidence Interval
and baseline IOP ($\beta = 0.009, P = 0.033$) were all positively correlated with CBTmax in the multivariate analysis.

Fig. 3 is the scatter plot for RCS thickness with CBTmax in the APAC eyes; it shows that CBTmax is negatively correlated ($\beta = -0.421, P = 0.034$) to RCS thickness.

Fig. 4 is the scatter plot for CBT0 with CBTmax in the APAC eyes; it shows that they both are directly proportional with $\beta = 0.89, P < 0.0001$.

Fig. 5 is the scatter plot for CBTmax with APCB in the APAC eyes; it shows that CBTmax is inversely proportional ($\beta = -0.35, P = 0.039$) to APCB.

**Discussion**

APAC is a sight-threatening ocular emergency and hence understanding the pathophysiologic mechanisms is very crucial as multiple biometric factors may have a contributory role.$^{[8]}$ Previously published studies have demonstrated significant anatomical differences in the ocular biometric parameters such as iris thickness, iris volume and lens vault, and relative lens position of APAC eyes compared to the fellow eyes.$^{[6,11]}$ To the best of our knowledge, this is the first study in Indian eyes to provide a simultaneous quantification of both anterior chamber angle parameters (including the AC angle, lens, and ciliary body) and retinochoroidal thickness in APAC eyes and fellow eyes before any laser or surgical intervention. Our observations of shallower ACD, narrower angle parameters, higher LV, decreased CBT, and more anteriorly placed ciliary body of APAC eyes compared to fellow eyes are supported by previous published studies.$^{[6,11,16,17]}$

Smaller anterior segment dimensions (ACD, AOD, and ACA) are known risk factors for angle closure.$^{[11]}$ Our study results also revealed that eyes with APAC had significantly narrower anterior biometric parameters than the fellow eyes. Literature reports using UBM have shown that a thicker iris and ciliary body have a significant odds of developing angle closure compared to normal controls.$^{[18,19]}$ However, there exists a paucity of information on differences in ciliary body parameters between APAC eyes and fellow eyes. Our study results demonstrated a thinner and more anteriorly placed ciliary body in APAC eyes compared to fellow eyes as reported by Wang$^{[20]}$ and He et al.$^{[20]}$ Both CBT0 and CBTmax was significantly thinner in our cohort of APAC eyes than the fellow eyes, in contrast to Li et al.$^{[11]}$ who reported only CBT0 to be thinner in APAC eyes. The proposed mechanism of angle closure here is believed to be due to the thinner ciliary body, which could have caused laxity of zonules and thus a more variable forward positioning of the lens.$^{[20]}$ However, further longitudinal studies are needed to understand whether a thinner and anteriorly placed ciliary body is a cause or a result of APAC.

Lan et al.$^{[21]}$ concluded that relative lens size represented by lens/axial length factor (LAF) and relative lens position play a major role in development of APAC attack. The extent of lens located anterior to the chamber angles can be quantified by LV, which has better performance than other parameters of lens, such as lens position and relative lens position.$^{[20]}$ Our patients had higher lens vault in the APAC eyes than the fellow eyes. We speculate that the higher LV may increase the iris lens contact distance by pushing the iris anteriorly and aggravate the pupillary block and angle crowding.

In a retrospective study by Niu et al.$^{[22]}$ in the Chinese population, where the ocular biometric parameters of eyes with APAC were compared with fellow eyes as well as with normal eyes, there was no difference in axial length between the APAC and fellow eyes, whereas APAC eyes had shorter axial length compared to the normal individuals. Similarly, Li et al.$^{[11]}$ in their prospective study found no difference between APAC and fellow eyes. In contrast, we noticed a borderline increase in axial length in the APAC eyes than the fellow eyes. Eyes of Indian ethnic origin may behave differently, and our study group included patients with recent-onset angle closure attack. Several previous studies have quantified the change in axial length when IOP was modified. Short-term elevation in IOP in healthy subjects may result in the increase in axial length by exerting negative pressure to the globe.$^{[23]}$ Also, earlier studies have supported this by showing an increase in IOP by darkroom prone provocative test, which is perhaps associated with eye elongation in eyes with angle closure.$^{[24]}$

Knowledge of the effects of acute primary angle closure on the choroid is important because the choroidal expansion is hypothesized to play a crucial role in these eyes.$^{[7,8]}$ In a previous study, a slightly greater thickness of choroid in APAC eyes than fellow eyes was observed.$^{[11]}$ In contrast, our patients...
had only marginal increase in RCS thickness in affected eyes than in fellow eyes. We presume greater choroidal thickness in APAC eyes than in the fellow eyes before the APAC attack and a drastic rise in IOP during the APAC attack could have decreased the uveal blood flow leading to decrease in choroidal thickness, thus explaining our study results. Hata et al.\(^5\) and Song et al.\(^6\) proved that increased IOP causes choroidal hypoperfusion in primary angle closure glaucoma eyes. Kumar et al.\(^6\) reported 25% of APAC eyes of Asian population presenting with uveal effusion that might have manifested as increased RCS thickness. However, in our study, none of the patients presented with uveal effusion.

Taking all the anatomic factors into account, in logistic regression analysis, we found that decreased CBTmax and CBT0 and anteriorly placed ciliary body were significantly associated with the APAC attacks. Anteriorly positioned ciliary body is associated with the nonpupillary block mechanism of angle closure, which could be explained by choroidal expansion hypothesis.\(^9\) The choroidal expansion associated with APAC attack would have pushed the ciliary body forward. Thus, we speculate that choroidal expansion may affect the ciliary body size and location. These dynamic changes may push the lens anteriorly, aggravating the pupillary block mechanism. However, further longitudinal studies are needed to evaluate these dynamic changes in APAC eyes.

Our study had a few limitations. First, the sample size was limited. Second, this cross-sectional study made it difficult to establish temporal or causal relationships between the measured ocular biometric parameters and acute angle closure. Thus, a prospective longitudinal study is needed to explore the cause-and-effect relationship between the dynamic changes of different parameters of the uvea. Third, iris parameters were not included in our study due to a lack of standardized measurement protocols. Additionally, IOP measurements at the time of investigations after institution of medical management to reverse AAC are not available. It is plausible that alterations in IOP could have influenced several ocular biometric parameters, including axial length and RCS thickness. Spherical equivalent and corneal curvature were not measured as many eyes had corneal edema at the time of measurements of ocular biometric parameters. Another major limitation of our study is the influence of diurnal fluctuation in choroidal thickness. Some studies have used spectral-domain optical coherence tomography to demonstrate the diurnal variation of choroidal thickness.\(^{17,26}\) This is likely to influence the correlation of choroidal thickness with the anterior placement of the ciliary body and ciliary body thickness. The studies were conducted in a South Indian population, and given the ethnic differences in the ocular biometric parameters predisposing to angle closure disease, results from our study may not be generalizable. Finally, limitations associated with capturing AS-OCT and UBM images were unavoidable.

A major strength of our study is that ocular biometric parameters were measured prior to intervention for AAC in contrast to many of the published studies, which obtained these measurements retrospectively after LPI and reversal of pupillary block and normalization of IOP. Both the anterior and posterior ocular biometric parameters were assessed in this study in APAC eyes, and the possible association between the ciliary body and choroid was analyzed. Our study significantly adds to the existing literature on ocular biometric parameters in eyes with acute angle closure. To the best knowledge of the authors, this is the first study to compare the ocular biometric parameters of APAC eyes with their fellow eyes in a population of Indian ethnic origin.

**Conclusion**

To conclude, our study is the first to use AS-OCT, UBM, A-scan, and B-scan for the concurrent measurement of anterior and posterior biometric parameters of the uvea in eyes with APAC. Compared to the fellow eyes, APAC eyes had narrower anterior biometric parameters, higher lens vault, longer axial length, thinner ciliary body, and more anteriorly placed ciliary body. We observed significant changes in different parts of the uvea and lens during APAC attacks and found that several nonpupillary block factors such as anteriorly placed ciliary body and decreased thickness of the ciliary body may be associated with APAC. In addition to the known pupillary block phenomenon as a cause for APAC, our study revealed a mixed mechanism with multiple nonpupillary block factors contributing to the occurrence and progression of APAC. However, this needs to be further investigated in prospective and longitudinal studies.

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**Conflicts of interest**

There are no conflicts of interest.

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