Original Article

Primary congenital glaucoma: An iridotrabeculodysgenesis?

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Purpose: To analyze primary congenital glaucoma (PCG) anterior chamber and angle anomalies over 360° as possible biomarkers of severity and prognosis. **Methods:** A cross-sectional observational study was conducted analyzing anterior segment anomalies of PCG patients over 4 years of age who underwent trabeculectomy combined with trabeculotomy and age-matched controls using anterior segment optical coherence tomography (ASOCT), CASIA-2. Anterior iridotrabecular adhesions or anterior iris insertion was identified and quantified from the scleral spur using the iridotrabecular contact (ITC) index parameter as a surrogate. **Results:** There was a variable but significantly increased anterior iridotrabecular adhesion on ITC index, ITC area, corneal volume, anterior chamber volume, iris volume, anterior chamber depth, and small/absent trabecular meshwork in PCG eyes compared to control eyes. In PCG eyes, anterior iridotrabecular adhesion had a positive correlation with pre-operative central corneal thickness (CCT) (r = 0.53, P = 0.02), review iris thickness (r = 0.4, P = 0.04), and ITC area (r = 0.85, P < 0.001). Review iris thickness had a negative correlation with pre-operative vertical cup-disc ratio (r = -0.51, P = 0.008). Iris hypoplasia with fewer or absent folds, collarette, pupillary ruff, and pupillary ruff to collarette distance was significantly different from controls. **Conclusion:** ASOCT in PCG eyes has shown that they have variable anterior iridotrabecular tissue adhesions, anomalous tissue/membranes in the angle, and iris hypoplasia correlating with pre-operative cup-disc ratio. These features could be used as gonioscopic and clinical biomarkers to assess the severity and prognosis of the disease. The presence of abnormal iris morphology and iridotrabecular tissue anomalies in PCG suggests that it is more than just isolated trabeculodysgenesis and is probably best considered as part of the anterior segment dysgenesis spectrum.

Key words: ASOCT, iridotrabeculodysgenesis, PCG

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Primary congenital glaucoma (PCG) contributes 30 to 40% of all childhood glaucomas[1,2] and is defined as having trabecular dysgenesis alone. Cranial neural crest cells undergo mesenchymal transition and form parts of the cornea, iris, sclera, ciliary body, and trabecular outflow channels. Trabecular meshwork and Schlemm's canal are the last structures to be differentiated during development at the iridocorneal angle.[3,4] An altered interaction between cells of the surface epithelium with neural crest cells leads to anterior segment dysgenesis, involving the cornea, angle, and iris.[5] Arrested development of tissues of the neural crest origin in the third trimester results in immature angle appearance in congenital glaucoma, which is also likely to affect the iris, ciliary body, and cornea.[6,7] The severity of these abnormalities varies with the extent and the stage at which developmental arrest has occurred.

PCG is not included in the anterior segment dysgenesis so far because clinically recorded anterior segment abnormalities were thought to be restricted to the trabecular meshwork, even though a recent study revealed that CYP1B1-associated PCG had iris abnormalities.[8] Histopathology of the trabecular meshwork in PCG eyes has shown fused trabecular beams, abnormal membranes, higher iris insertion, enlarged trabeculae with diminished inter-trabecular spaces, and a normal/anomalous Schlemm's canal.[7,9]

Anterior segment optical coherence tomography (ASOCT, has better sensitivity in diagnosing angle anomalies compared to gonioscopy) and ultrasound biomicroscopy (UBM) have been used to study angle dysgenesis in eyes with developmental glaucomas, reported as abnormal tissues in angle, hyperreflective membranes, or the absence of Schlemm's canal and ciliary body thinning.[10–14]

No study has analyzed all anterior segment structures over 360°in PCG eyes; therefore, this study aimed to analyze cornea, iris, ciliary body face, angle details, and extent of anomalous trabecular adhesions in primary congenital glaucoma using CASIA-2 ASOCT (Tomey Corporation, Japan) and correlate them with clinical parameters at baseline and on review. Evaluation of factors responsible for the common occurrence of varying severities of glaucoma at a similar age could help identify possible biomarkers.

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Methods

A cross-sectional observational study was conducted after obtaining our Institute's ethical committee approval. Patients with PCG of an age more than 4 years regularly reviewing at the glaucoma services after undergoing combined trabeculotomy with trabeculectomy were recruited. PCG was diagnosed based on the presentation in infancy/early childhood (neonatal PCG <1 month, infantile PCG 1 month to 24 months, late-onset PCG >2 years) with photophobia, tearing, intra-ocular pressure (IOP) >21 mmHg, or signs of IOP-driven ocular anatomical changes: Haab striae, corneal diameter >11 mm in newborn, >12 mm in infants, >13 mm at any age, glaucomatous optic disc cupping, and in the absence of other ocular or systemic defects. Other criteria included progressive myopia/myopic shift coupled with an abnormal increase in ocular dimensions and reproducible visual field defects consistent with glaucoma, with no other reason contributing to the same.[1] Age-matched controls without any ocular abnormality visiting for routine ocular examination were recruited. Participants not cooperative for slit-lamp/ASOCT examination or having other ocular diseases except refractive error or those not willing to give consent for the study were excluded. The study was conducted according to the tenets of the Declaration of Henski. Informed written consent was obtained from all participants/parents/guardians as applicable.

Participants' age, sex, pre-operative baseline IOP, cup-disk ratio (CDR), corneal diameter, and central corneal thickness (CCT), together with the last review IOP, baseline anterior segment examination details on slit lamp, and CASIA-2 ASOCT parameters, were noted. The presence or absence of Haab's striae and other corneal abnormalities were noted. The iris was carefully examined to document the number and extent of concentric furrows, classified as absent, 1 to 2, 3 to 4, and >5, and circumferential extent was classified as absent, <90 °, 90 to 180°, 180 to 270°, and >270 °. The maximum number of iris radial folds in one quadrant was noted and was classified as absent, 1 to 2, 3 to 4, and >5. The prominence of iris radial folds was noted and classified as absent, subtle, and prominent. The number of iris crypts was noted and classified as absent, <3, 3 to 5, and >5. Iris collarette was classified as absent, subtle, and prominent. Pupillary ruff was classified as absent, subtle, and prominent, and the collarette to pupil distance was noted (reduced/normal). The slit-lamp findings were noted by a single experienced ophthalmologist (KM).

CASIA-2 ASOCT scans were obtained by a single experienced ophthalmic technician (AKM). This study objectively recorded abnormalities of the trabecular meshwork and iris using the ASOCT. Any anterior iris insertion was quantified using the iridotrabecular contact (ITC) index as a surrogate as this is a measure of peripheral iris contact to the angle anterior to the scleral spur.[14] This iris 'contact' anterior to scleral spur in PCG eyes with a deep anterior chamber would be due to anterior iris insertion due to developmental anomalies, as against peripheral anterior synechiae or iridotrabecular contact due to a convex iris in angle-closure eyes. ITC is defined on CASIA software as any contact between the iris and angle wall anterior to the scleral spur.[15] To obtain the ITC index, scleral spurs were marked in all 128 frames as the point of change in the corneoscleral interface. ITC area was taken into account only in the eyes where more than 80% of the angle had a good quality scan. The presence and extent of iris anomalies were correlated with PCG severity. The iris thickness was measured 2 mm from the pupillary margin. The length of the trabecular meshwork anterior to iris insertion was also noted.

Other parameters noted on ASOCT were Schwalbe's line morphology, central corneal thickness/any corneal abnormality, anterior chamber depth (ACD), corneal volume, iris volume, anterior chamber volume, and anterior chamber width (ACW). The trabecular meshwork was identified and classified according to its size and shape: normal elongated ellipse, small, flat, or absent. Iris surface patterns were classified as flat, subtle ridges, and prominent ridges.

Statistical analysis

Data were entered in Excel version 16.6.5, and IBM SPSS Statistics version 3 (SPSS, Inc., Chicago, IL) was used for analysis. Normality of data was tested with Kolmogorov–Smirnov test. Variables were expressed as mean ± standard deviation (SD). For continuous parametric data, independent *t*-test and paired *t*-test were used accordingly. For continuous non-parametric data, the Mann–Whitney U test was used. For categorical variables, Pearson's Chi-squared test/Fisher's exact test was used. As both eyes of a patient were taken for analysis, the generalized estimating equation method was used to correct for bias. Among PCG eyes further, sub-analysis was done with median cut-offs of ITC index 25.3%, ITC area 3 mm^2, ACW 13 mm, and iris thickness 430 µm. A P value < 0.05 was considered significant.

Results

Thirty-nine eyes of 29 participants met all criteria and were analyzed, that is, 28 PCG eyes (18 patients) and 11 control eyes (11 participants). Four PCG patients were uncooperative for ASOCT. There was no significant difference in age between PCG patients, 8.6 ± 3.5 years, and controls, 7.7 ± 2.4 years, $P = 0.4$. The male: female ratio of PCG (2:1) and controls (1.75:1) was also comparable, ($P = 0.38$). The median age at presentation of PCG patients was 3 months (inter-quartile range: 1–4 months). Ten eyes had neonatal PCG, 15 eyes had infantile PCG, and 3 eyes had late onset PCG. The presenting symptoms were cloudy cornea in 50% (9), enlarged eye in 44.4% (8), tearing in 27.8% (5), and photophobia in 22.2% (4). The pre-operative corneal diameter was 12.9 ± 0.9 mm, the central corneal thickness was 576 ± 63.5 µm, and the vertical cup-disk ratio was 0.65 ± 0.2: 1. Haab's striae were seen in 42.8% (12) of the eyes at review. The mean number of surgeries done in PCG eyes was 1.2 ± 0.4. There was a significant reduction in IOP baseline from 25 ± 3.8 mmHg to 11.7 ± 3.1 mmHg on the last review (<0.001).

Quantitative analysis of Casia 2 ASOCT data of PCG and controls showed a significantly increased extent of anterior iris insertion recorded as ITC index, ITC area, corneal volume, anterior chamber (AC) volume, iris volume, and anterior chamber depth (ACD) in PCG eyes compared to control eyes [Figs. 1 and 2]. The mean ITC index in control eyes was 4.1 ± 2.5%. The length of the exposed trabecular meshwork anterior to anomalous iridotrabecular adhesion and iris thickness was significantly smaller in PCG eyes compared to controls [Table 1].

Correlating parameters in PCG eyes, extent of anterior iris insertion recorded as ITC index had a positive correlation with pre-operative CCT (r = 0.53, $P = 0.02$), review iris thickness (r = 0.4, $P = 0.04$), and ITC area (r = 0.85, $P < 0.001$). Iris thickness at review had a negative correlation with

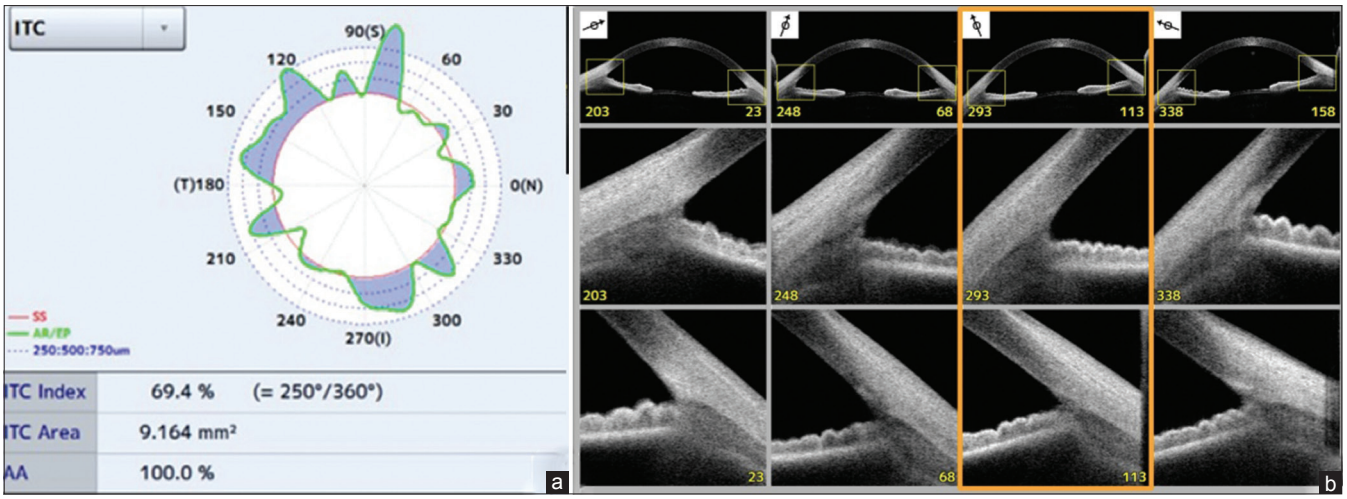

Figure 1: (a and b) CASIA-2 ASOCT showing sectoral differences in TM structure and anomalous uveotrabecular tissue adhesions in PCG

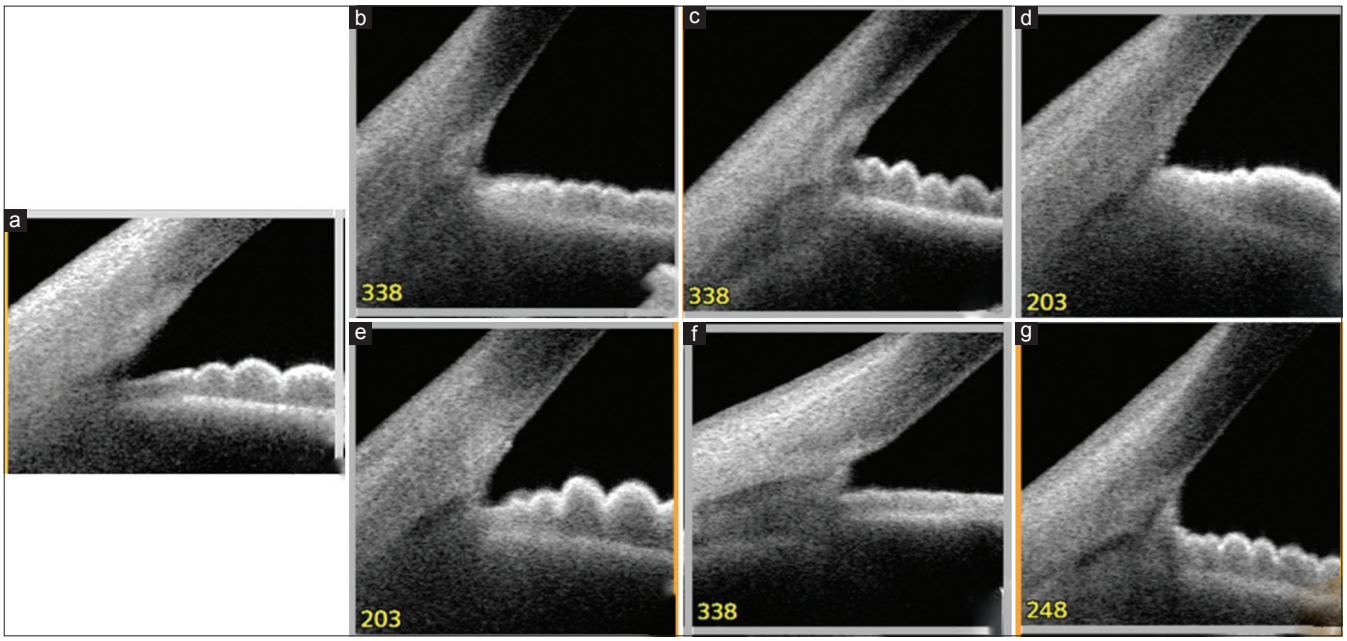

Figure 2: (a) CASIA-2 ASOCT of a control eye, (b-g) uveotrabecular anomalies of different PCG eyes: (b-d) abnormal insertion onto posterior, middle, and anterior TM, (e) abnormal membrane, (f) ciliary body adhesion to TM, (g) abnormal tissue from CB covering the TM

pre-operative vertical CDR [r = -0.51, *P* = 0.008, Fig. 3e]. Pre-operative IOP showed a significant correlation with anterior chamber volume (r = 0.47, *P* = 0.03). ACW had an inverse correlation with CCT (r = -0.53, *P* = 0.04) and a positive correlation with iris volume (r = 0.63, *P* = 0.002), AC volume (r = 0.92, *P* < 0.001), and ACD (r = 0.78, *P* < 0.001).

Sub-group analysis among PCG eyes using median values showed that those with greater extent of anterior iris insertion recorded as ITC index >25.3% had Haab striae in a significantly higher percentage of eyes compared to eyes with less extent of anterior iris insertion recorded, 62.5% versus 16.7%, *P* = 0.02. Eyes with ACW >13 mm on the last review had a significantly increased iris volume (*P* = 0.05) and a higher pre-operative corneal diameter (*P* = 0.04) compared to eyes with a lesser ACW. 56.2% of PCG eyes with a thin iris (<430 μm) had abnormal tissue adhesion/membrane in the angle, while only 33.3% of eyes with a greater iris thickness had abnormal tissue adhesion/membrane in the angle (*P* = 0.41). PCG eyes with a thin iris, <430 μm, showed a significant correlation with pre-operative vertical cup: disc ratio (r = -0.51, *P* = 0.008).

The iris pattern characteristics of PCG eyes clinically, such as number and extent of concentric furrows, presence of pupillary ruff, and pupillary ruff to collarette distance, were significantly different from controls [Table 1, Fig. 3f and g]. An absent or less prominent iris surface pattern was present in 67.2% of PCG eyes as compared to 27.3% of controls on clinical examination.

Qualitative 3D evaluation of the angle on ASOCT showed gross circumferential variability in the extent and height of anomalous iridotrabecular adhesions, abnormal membranes or tissues in the angle, and any trabecular abnormality within the same PCG eye and between PCG eyes, as compared to controls [Fig. 3a]. Some iridotrabecular adhesions went

Table 1: Anterior segment features of PCG and control eyes

Parameters	PCG (28 eyes)	Controls (11 eyes)	*P**
Concentric furrows:			0.03
Absent	10 (35.7%)	0	
1-2	6 (21.4%)	2 (18.2%)	
3-4	12 (42.9%)	9 (81.8%)	
Concentric furrows extent:			0.001
Absent	10 (35.7%)	0	
<90°	1 (3.6%)	0	
90-180°	4 (14.3%)	6 (54.5%)	
180-270°	6 (21.4%)	5 (41.7%)	
>270°	7 (25%)		
Iris radial folds (max no. In 1 quadrant)			0.13
Absent	10 (35.7%)	3 (27.3%)	
1-2	3 (10.7%)	4 (36.4%)	
3-4	7 (25%)	4 (36.4%)	
5-6	8 (28.6%)	0	
Iris crypts number			0.27
Absent	7 (25%)	7 (63.6%)	
<3	3 (10.7%)	0	
3-5	4 (14.3%)	1 (9.1%)	
>5	14 (50%)	3 (27.3%)	
Collarette			
Absent	9 (32.1%)	1 (9.1%)	0.13
Subtle	9 (32.1%)	3 (27.3%)	
Prominent	10 (35.7%)	7 (63.6%)	
Pupillary ruff			<0.001
Absent	2 (7.1%)	0	
Subtle	15 (53.6%)	0	
Prominent	11 (39.3%)	11 (100%)	
Collarette to pupillary ruff distance			0.008
No collarette	9 (32.1%)	1 (9.1%)	
Reduced	11 (39.3%)	2 (18.2%)	
Normal	8 (28.6%)	8 (72.7%)	
Cornea volume (mm^3)	113.3±11.6	92.2±6.9	<0.001
CCT (μm)	510.4±70.5	526.8±31.1	<0.001
ACD (mm)	3.6±0.5	2.9±0.2	<0.001
ACW (mm)	13.3±0.8	12±0.4	<0.001
AC volume (mm^3)	259.6±62.3	167.9±28.6	<0.001
Extent of anterior iridotrabecular adhesion recorded as ITC index (percentage)	30.5±14.7	4.1±2.5	<0.001
ITC area (mm^2)	2.9±1.9	0.18±0.2	<0.001
Iris volume (mm^3)	40.8±5.9	32.5±3.7	<0.001
Iris surface appearance in ASOCT			0.02
Flat	3 (10.7%)	0	
Subtle ridges	16 (57.2%)	3 (27.3%)	
Prominent ridges	9 (32.1%)	8 (72.7%)	
Trabecular meshwork in ASOCT	(*n*=25)	(*n*=11)	<0.001
Absent/small/flat	23 (92%)	0	
Normal	2 (8%)	11 (100%)	
Iris insertion	(*n*=26)	(*n*=11)	<0.001
Ciliary body	0	11 (100%)	
Mid trabecular meshwork	19 (73.1%)	0	
Anterior trabecular meshwork	7 (26.9%)	0	
Length of trabecular meshwork anterior to iris insertion (μm)	458.6±118.7	676.1±65.2	<0.001
Iris thickness (μm, at 500 μm from pupil)	374.1±100	546.3±89	<0.001
ASOCT angle	(*n*=26)	(*n*=11)	
Abnormal adhesions/tissue	9 (34.6%)	0	0.02
Abnormal membrane	5 (19.2%)	0	0.16

Continuous variables are mentioned as mean ± standard deviation. Categorical variables are measured as numbers (percentage). CCT central corneal thickness; ACD anterior chamber depth; ACW anterior chamber width; AC anterior chamber; ITC, iridotrabecular contact; ASOCT, anterior segment optical coherence tomography. *Adjusted for presence of clustering by using generalized estimating equation method.

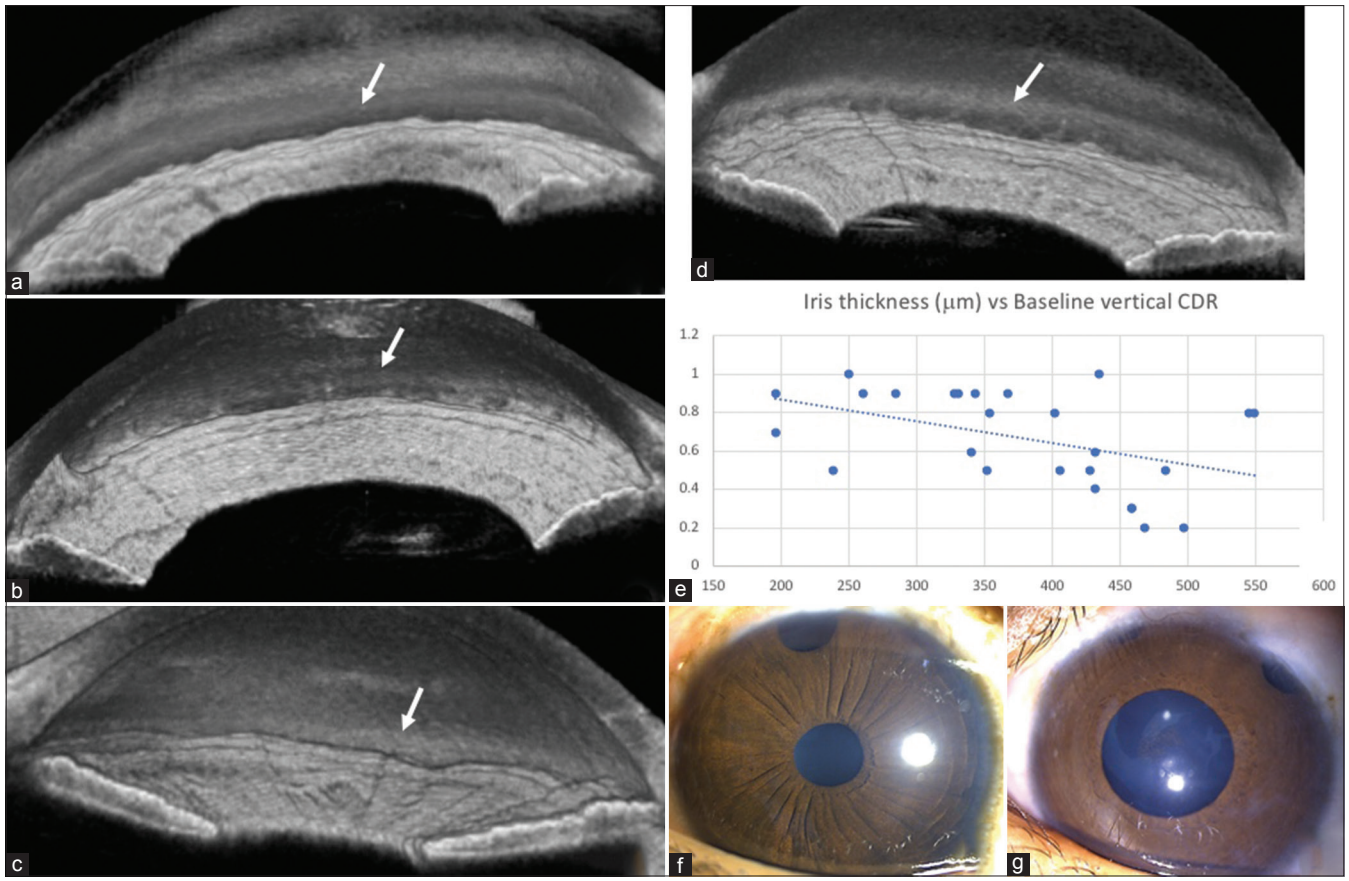

Figure 3: (a-d) CASIA-2 ASOCT (Tomey Corporation, Japan) 3D image showing gross variability in the extent and height of anomalous iridotrabecular or ciliotrabecular tissue adhesions, abnormal membranes or tissues in the angle, and a trabecular meshwork structure over the circumference. (a) normal child's eye, (b-d) PCG eyes. (e) scatter plot showing the relationship between iris thickness with baseline cup-disc-ratio. (f and g) slit-lamp clinical picture of PCG showing different iris patterns: absent/subtle pupillary ruff, a reduced distance between collarette and pupillary ruff (g), absent/subtle radial folds, and concentric furrows (f)

up to Schwalbe's line, while in other sectors of the same eye, the trabecular area could be seen [Fig. 3b-d]. ASOCT angle recording in the area of trabeculectomy combined with trabeculotomy surgery showed a trabeculectomy scleral ostium. This was flanked by a linear cleft in the iridotrabecular tissue of approximately 60–70º on either side due to trabeculotomy, which appeared anatomically open to the anterior chamber [Fig. 4]. The cornea in the eyes with Haab's striae showed a thickening of the stroma and Descemet's membrane in all cases. Wider Haab's striae had rolled edges of the Descemet's on either side, while at the tapering narrower ends, the Descemet's appeared to have been anatomically restored with only an increased stromal density around it.

Discussion

Primary congenital glaucoma has been defined as having isolated trabeculodysgenesis with an abnormality in iris insertion, that is, anomalous iridotrabecular tissue adhesion.[16,17] The angle changes described are fused trabecular beams, thicker trabecular beams, anterior iris insertion, abnormal or hyperreflective membrane in the angle, and absent or anomalous Schlemm's canal.[9,11,12,18,19] Gupta *et al*.[7] have shown an anomalous ciliary body on UBM, thin and stretched. These reports were based upon snapshots of small areas on histopathology, UBM, and ASOCT.

Our study has specifically documented circumferential differences in the type and extent of anterior chamber angle dysgenesis and associated iris. On qualitative 3D-ASOCT analysis, a varying circumferential and anterior extent of anomalous iridotrabecular tissue adhesions and abnormal membranes or tissues in the angle, over the circumference, were seen in all PCG eyes as compared to controls. A small or absent trabecular meshwork was seen in 92% of PCG eyes as compared to none in controls. Similarly, an absent or less prominent iris surface pattern and iris hypoplasia were present in 67.9% of PCG eyes, clinically and on ASOCT as compared to 27.3% in controls.

Anomalous iridotrabecular tissue adhesion anterior to the scleral spur was objectively evaluated for the first time in PCG eyes. This was found to be significantly higher in PCG eyes, 30.5 ± 14%, compared to controls 4.1 ± 2.5%. The extent of anterior iris insertion recorded as ITC index was found to correlate significantly with pre-operative CCT, presence of Haab's striae, and a higher percentage of eyes with a pre-operative corneal diameter >12.5 mm. As a trabeculectomy combined with trabeculotomy was done in all eyes, around 120 degrees of the angle showed a trabecular cleft and scleral ostium; therefore, the extent of anterior iris insertion was probably more in each eye. The greater extent of anomalous iridotrabecular adhesions decreasing aqueous outflow would have led to a raised IOP stretching the cornea and causing Haab's striae

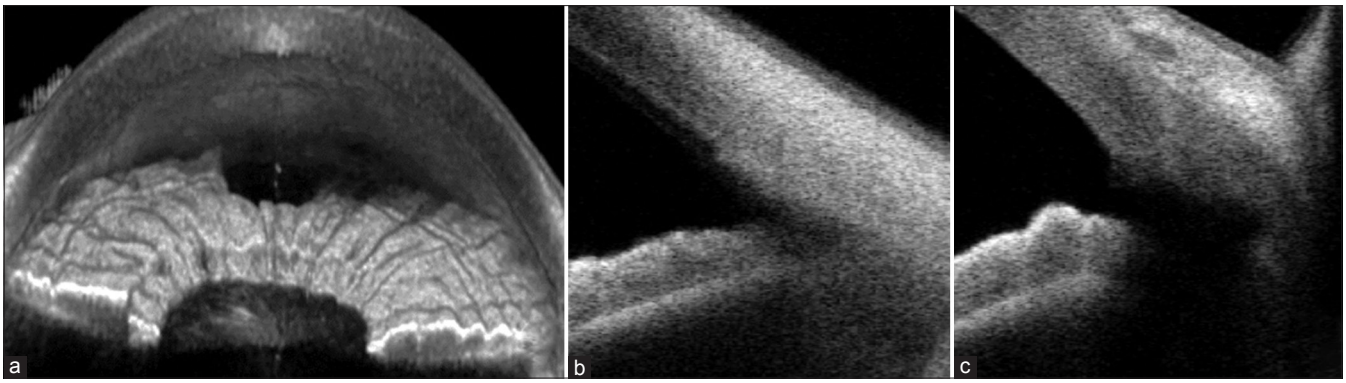

Figure 4: (a) CASIA 2 ASOCT 3D angle recording in the area of trabeculectomy combined with trabeculotomy surgery showing trabeculectomy scleral ostium, flanked by a linear cleft in iridotrabecular tissue of approximately 60 to 70 degrees on either side due to trabeculotomy, (b) 2D image of an angle showing the area of trabeculotomy with a cleft in trabecular tissues, and (c) image showing the area of trabeculectomy with an iridectomy, scleral ostium, and the edge of the filtering bleb

with an increased CCT recorded at baseline on UBM.[20,21] Many studies have shown an increased corneal thickness in PCG eyes which had a positive correlation with increased IOP.[22–25] Our study recorded an anomalous uveotrabecular tissue adhesion in all PCG eyes, a mid trabecular meshwork in 73.1%, and anterior in 26.9%, with only a small part of the trabecular meshwork open to aqueous. Hussein *et al*.[25] noted that 56% of PCG eyes had anterior iris insertion by using UBM. On the contrary, Pilat *et al*.[11] examined a few meridia on hand-held ASOCT and found only 12% of PCG eyes showed an anterior iris insertion. The many correlations of the extent of anterior iris insertion seen in PCG eyes indicate that this is associated with dysgenesis of the outflow channels and therefore the severity of the disease. It could be used as a biomarker of disease severity even at a later stage, when baseline details of the eyes may be unknown.

Our study also showed that the area of iridotrabecular adhesions and angle anomalies varied across the circumference of any PCG eye, affecting the posterior TM in some places and more anterior elsewhere and also having an overlying membrane or abnormal tissue in other areas of the same eye. Hamanaka *et al*.[26] described the formation of sections of the Schlemm's canal at 28 weeks of gestation, with a complete canalogenesis only at 40 weeks, suggesting that the variegated angle anomalies seen in this study on ASOCT could reflect sectors of different degrees of canalogenesis or angle development. Differences in outflow malformations across the circumference and between eyes may also explain the disparity in onset and severity of ocular changes seen among PCG eyes. It is therefore important to assess gonioscopy over the entire 360 degrees pre-operatively to help determine appropriate surgery and the best areas for angle surgeries such as goniotomy or trabeculotomy.

This study found a thin iris or iris hypoplasia in 75% of PCG eyes compared to 18.1% in control eyes. Eyes with a thin iris had a higher baseline vertical cup-disk ratio and more frequent angle abnormalities, showing that PCG eyes had both angle and iris dysgenesis coexisting. In our study, PCG eyes had fewer and less extensive concentric anterior iris furrows, recorded as a flat iris or one with subtle ridges on ASOCT. The collarette was either absent or subtle in 64.2% of eyes with PCG and more than half of the eyes with a collarette had a reduced collarette to pupil distance. The pupillary ruff was either absent or subtle in 60.7% of the eyes. Pilat *et al*.[11] reported that PCG eyes had significant flattening of the anterior limiting layer of the iris and hypothesized that the flattening of the iris may not be due to stretching of the eye occurring as a result of increased IOP. Previous studies using UBM in PCG also identified abnormal iris configuration and a thinner iris compared to controls.[7,25,27] As the angle structures and iris stroma both originate from neural crest cell-derived periocular mesenchyme, anomalies of both could occur together. Classical studies have described three waves of periocular mesenchyme derived from neural crest cells in the anterior segment, the second forming iris stroma and the third the trabecular meshwork. It is therefore entirely possible that developmental defects could occur in both iris stroma and outflow channels, and PCG eyes with an abnormal iris pattern may be a subset of the anterior segment dysgenesis spectrum. Further substantiating the inclusion of PCG in the ASD spectrum, Siggs *et al*.[28] conducted a genetic analysis in 131 patients with suspected PCG and found that 6.1% were having Axenfeld-Rieger syndrome. Gould and John have shown that mutations in ASD genes sometimes cause PCG and mutations reported with PCG can cause obvious ASD.[29] Our study has shown that it is important to differentiate PCG eyes with iris anomalies as they had more severe pre-operative glaucomatous changes, and this can be done easily by clinical examination of the anterior segment or ASOCT evaluation where available.

In our study, the trabecular meshwork was absent/flat/small in 92% of PCG eyes, with various forms of trabecular dysgenesis as reported earlier.[6,9,18] Either anomalous tissue, 34.6%, or a membrane, 19.2%, was seen in the angle of 46.1% of PCG eyes. Shi *et al*.[30] recorded abnormal tissues in angle in 27.5% of PCG using a high-frequency UBM. Bradfeild *et al.* identified abnormal tissues over angle or Schlemms's canal in 8 (of 13) PCG eyes using ASOCT.[31] Hussein *et al*.[25] used UBM and observed abnormal tissue membranes in the angle of 12% of PCG eyes. Gupta *et al*.[12] showed that an abnormal tissue or hyperreflective membrane was seen in the angle of all eyes of PCG. The discrepancy in frequency could be due to only sectors being evaluated earlier, as compared to 360 degrees in this study.

The limitations include a small sample size (due to poor fixation/uncooperative children) and ASOCT performed at an older age, years after surgery. It would have been best if the ASOCT evaluation was done at the presentation on untreated eyes. Since our hospital was a referral center, most of the patients

were already on glaucoma medications (with/without correct IOP documentation) before we see the patient. So, the baseline IOP might not be accurate. This might be a cause for poor correlation of many of the anterior chamber angle changes with pre-operative IOP. Due to prior surgery, ITC over approximately 100–120 degrees, the extent of trabeculotomy, and the scleral ostium were absent, but this was seen in all eyes. Correlation with UBM could have helped correlate ciliary abnormalities.

Conclusion

In conclusion, Casia ASOCT in PCG eyes has shown that they have variable anterior iridotrabecular tissue adhesion, anomalous tissues/membranes in the angle, and iris hypoplasia correlating with pre-operative cup-disc ratio and Haab's striae. These features could be used as gonioscopic and clinical biomarkers to assess the severity and prognosis of the disease. The presence of abnormal iris morphology and iridotrabecular tissue anomalies in PCG suggests that it is more than just isolated trabeculodygenesis and is probably best considered as part of the anterior segment dysgenesis spectrum.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author KM.

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Conflicts of interest: There are no conflicts of interest.

References

1. Hoguet A, Grajewski A, Hodapp E, Chang TCP. A retrospective survey of childhood glaucoma prevalence according to Childhood Glaucoma Research Network classification. Indian J Ophthalmol 2016;64:118–23.
2. Senthil S, Badakere S, Ganesh J, Krishnamurthy R, Dikshit S, Choudhari N, *et al*. Profile of childhood glaucoma at a tertiary center in South India. Indian J Ophthalmol 2019;67:358–65.
3. Remé C, d'Epinay SL. Periods of development of the normal human chamber angle. Doc Ophthalmol 1981;51:241–68.
4. Smith RS, Zabaleta A, Savinova OV, John SW. The mouse anterior chamber angle and trabecular meshwork develop without cell death. BMC Dev Biol 2001;1:3.
5. Cvekl A, Tamm ER. Anterior eye development and ocular mesenchyme. Bioessays 2004;26:374–86.
6. Ko F, Papadopoulos M, Khaw PT. Primary congenital glaucoma. Prog Brain Res 2015;221:177–89.
7. Gupta V, Jha R, Srinivasan G, Dada T, Sihota R. Ultrasound biomicroscopic characteristics of the anterior segment in primary congenital glaucoma. J AAPOS 2007;11:546–50.
8. Gupta V, Panigrahi A, Mahalingam K, Singh A, Somarajan BI, Gupta S. Expanding the phenotypic spectrum of CYP1B1 associated primary congenital glaucoma. Clin Exp Ophthalmol 2022;50:1112–5.
9. Rojas B, Ramírez AI, de-Hoz R, Salazar JJ, Remírez JM, Triviño A. [Structural changes of the anterior chamber angle in primary congenital glaucoma with respect to normal development]. Arch Soc Esp Oftalmol 2006;81:65–71.
10. Gupta V, Chaurasia AK, Gupta S, Gorimanipalli B, Sharma A, Gupta A. *In Vivo* analysis of angle dysgenesis in primary congenital, juvenile, and adult-onset open angle Glaucoma. Invest Ophthalmol Vis Sci 2017;58:6000–5.
11. Pilat AV, Proudlock FA, Shah S, Sheth V, Purohit R, Abbot J, *et al*. Assessment of the anterior segment of patients with primary congenital glaucoma using handheld optical coherence tomography. Eye 2019;33:1232–9.
12. Gupta V, Singh A, Pandya I, Sofi R, Sen S, Somarajan BI, *et al*. Differences in outflow channels between two eyes of unilateral primary congenital glaucoma. Acta Ophthalmol 2021;99:187-94.
13. Kobayashi H, Ono H, Kiryu J, Kobayashi K, Kondo T. Ultrasound biomicroscopic measurement of development of anterior chamber angle. Br J Ophthalmol 1999;83:559–62.
14. Nolan WP, See JL, Chew PTK, Friedman DS, Smith SD, Radhakrishnan S, *et al*. Detection of primary angle closure using anterior segment optical coherence tomography in Asian eyes. Ophthalmology 2007;114:33–9.
15. Angmo D, Nongpiur ME, Sharma R, Sidhu T, Sihota R, Dada T. Clinical utility of anterior segment swept-source optical coherence tomography in glaucoma. Oman J Ophthalmol 2016;9:3–10.
16. Hoskins HD Jr, Shaffer RN, Hetherington J. Anatomical classification of the developmental glaucomas. Arch Ophthalmol 1984;102:1331–6.
17. Maumenee AE. The Pathogenesis of congenital glaucoma*: A new theory. American J Ophthalmol 1959;47:827–59.
18. Agarwal R, Sen S, Kashyap S, Dada T, Nag TC, Gupta V, *et al*. Correlation of histopathology of trabecular meshwork with clinical features in primary congenital glaucoma. Br J Ophthalmol 2022;106:60-4.
19. Anderson DR. The development of the trabecular meshwork and its abnormality in primary infantile glaucoma. Trans Am Ophthalmol Soc 1981;79:458–85.
20. Costagliola C, Romano V, Forbice E, Angi M, Pascotto A, Boccia T, *et al*. Corneal oedema and its medical treatment. Clin Exp Optom 2013;96:529–35.
21. Li X, Zhang Z, Ye L, Meng J, Zhao Z, Liu Z, *et al*. Acute ocular hypertension disrupts barrier integrity and pump function in rat corneal endothelial cells. Sci Rep 2017;7:6951.
22. Cronemberger S, Calixto N, Avellar Milhomens TG, Gama PO, Milhomens EG, Rolim H, *et al*. Effect of intraocular pressure control on central corneal thickness, horizontal corneal diameter, and axial length in primary congenital glaucoma. J AAPOS 2014;18:433–6.
23. Amini H, Fakhraie G, Abolmaali S, Amini N, Daneshvar R. Central corneal thickness in iranian congenital glaucoma patients. Middle East Afr J Ophthalmol 2012;19:194–8.
24. Oberacher-Velten I, Prasser C, Lorenz B. Evolution of central corneal thickness in children with congenital glaucoma requiring glaucoma surgery. Graefes Arch Clin Exp Ophthalmol 2008;246:397–403.
25. Hussein TR, Shalaby SM, Elbakary MA, Elseht RM, Gad RE. Ultrasound biomicroscopy as a diagnostic tool in infants with primary congenital glaucoma. Clin Ophthalmol 2014;8:1725–30.
26. Hamanaka T, Bill A, Ichinohasama R, Ishida T. Aspects of the development of Schlemm's canal. Exp Eye Res 1992;55:479–88.
27. Alexander JL, Wei L, Palmer J, Darras A, Levin MR, Berry JL, *et al*. A systematic review of ultrasound biomicroscopy use in pediatric ophthalmology. Eye 2021;35:265–76.
28. Siggs OM, Souzeau E, Pasutto F, Dubowsky A, Smith JEH, Taranath D, *et al*. Prevalence of FOXC1 variants in individuals with a suspected diagnosis of primary congenital glaucoma. JAMA Ophthalmol 2019;137:348–55.
29. Gould DB, John SWM. Anterior segment dysgenesis and the developmental glaucomas are complex traits. Hum Mol Genet 2002;11:1185–93.
30. Shi Y, Han Y, Xin C, Hu M, Oatts J, Cao K, *et al*. Disease-related and age-related changes of anterior chamber angle structures in patients with primary congenital glaucoma: An *in vivo* high-frequency ultrasound biomicroscopy-based study. PLoS One 2020;15:e0227602.
31. Bradfield Y, Barbosa T, Blodi B, Tompson SW, McLellan GJ, Struck M, *et al*. Comparative intraoperative anterior segment OCT findings in pediatric patients with and without glaucoma. Ophthalmol Glaucoma 2019;2:232–9.