• Clinical Research •

Ocular development in children with unilateral congenital cataract and persistent fetal vasculature

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Abstract

● **AIM:** To investigate the ocular development of patients who had unilateral congenital cataract (CC) combined with persistent fetal vasculature (PFV).

● **METHODS:** This cross-sectional, observational study included patients who had unilateral CC and PFV and those with isolated unilateral CC. Axial length (AL), keratometry, anterior chamber depth (ACD), lens thickness, and vitreous length were obtained. The ocular biometric parameters of the affected eyes of patients with CC and PFV were compared with the fellow eyes and with the affected eyes of patients with isolated CC.

● **RESULTS:** A total of 110 patients were included and divided into 4 groups: group 1 (18 patients with CC and PFV, <24mo), group 2 (22 patients with CC and PFV, ≥24mo), group 3 (35 patients with CC, <24mo), and group 4 (35 patients with CC, ≥24mo). The ALs of the affected eyes were shorter than those of the fellow eyes in group 1 (20.02±1.06 *vs* 20.66±0.63 mm, *P*=0.025). While the ALs of the affected eyes were longer than those of the fellow eyes in group 2 (23.18±2.00 *vs* 22.31±1.06 mm, *P*=0.044) and group 4 (22.64±1.80 *vs* 22.02±1.01 mm, *P*=0.033). The keratometries of the affected eyes were steeper than those of the fellow eyes in group 2 (44.78±1.66 *vs* 43.83±1.38 D, *P*=0.041) and group 4 (43.76±1.91 *vs* 43.34±1.46 D, *P*=0.043). No difference of ACDs between two eyes was found in all groups (all *P*>0.05).

● **CONCLUSION:** Compared with the fellow eyes, the ALs of the eyes with unilateral CC and PFV are shorter in patients younger than 24mo and longer in those older than 24mo; the keratometries of the eyes with unilateral CC and PFV are steeper in patients older than 24mo and similar with those younger than 24mo. These findings provide further understanding of ocular development in patients with both CC and PFV.

● **KEYWORDS:** ocular development; congenital cataract; persistent fetal vasculature; axial length; keratometry
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INTRODUCTION

Normal ocular growth is vital for the development of the visual system in infants and young children[1]. The ocular development could be affected by various congenital factors[2]. Congenital cataract (CC) is one of the leading causes of childhood blindness[3], and persistent fetal vasculature (PFV) is one of the most common ocular abnormalities that combined with unilateral CC, including three types: anterior, posterior and combined, with 90%[4] being in unilateral cases and its incidence rate up to 45%[5]. The form deprivation caused by CC that occurs in the critical period of visual development may lead to excessive ocular elongation[6]. While the hyaloid stalk from optic disc to the posterior capsule due to the failure of the embryonic hyaloid vasculature regression, namely PFV, could restrict ocular growth[7]. However, the ocular growth of unilateral patients who have both CC and PFV remains unclear, and these patients still exhibit poor visual outcomes[8-12]. Researchers and ophthalmologists have directed extensive efforts toward understanding the ocular development of patients with both unilateral CC and PFV. However, due to the limited number of cases with this complex ocular condition, previous reports regarding ocular development included both unilateral and bilateral patients with CC or without CC and

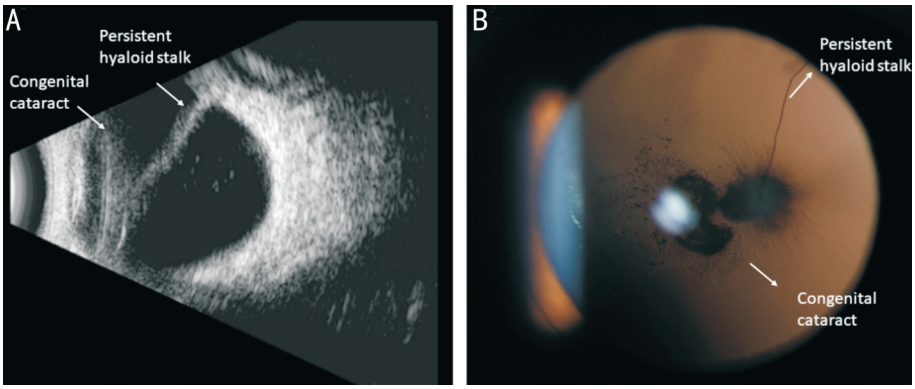

Figure 1 Characteristics of patients with CC and PFV in this study A: Ultrasonography showing congenital cataract combined with a persistent hyaloid stalk extending from the optic disc attached to posterior capsule; B: Slit-lamp image showing congenital cataract combined with a persistent hyaloid stalk.

manifested as different types of PFV, some of which did not have a hyaloid stalk, or lens opacity that affected the ocular growth[9,13].

The current study aimed to investigate the ocular development of unilateral patients with both CC and PFV (focusing on only one type of PFV that has hyaloid stalk from the optic disc attached to the posterior capsular of the lens without retinal disorders) at different visual development stages (before and after 24mo) by analysing their ocular biometric parameters, including axial length (AL), keratometry, anterior chamber depth (ACD), lens thickness (LT), and vitreous length. This study could provide a deeper understanding of ocular development in patients with both CC and PFV, which is significant for the further treatment strategy and visual function improvement.

SUBJECTS AND METHODS

Ethical Approval The study was approved by the Human Research Ethics Committee of the Zhongshan Ophthalmic Center (ZOC) at Sun Yat-sen University and conformed to the tenets of the Declaration of Helsinki. Informed written consent was obtained from at least one parent of each patient.

Patients under the age of 10 years diagnosed as unilateral CC with PFV (opacity of the lens and combined with a hyaloid stalk from the optic disc attached to the lens posterior without retinal disorder) and isolated unilateral CC (opacity of the lens) were included. All of them were referred to Cataract Department in the ZOC due to white pupil or poor visual acuity and enrolled in Children Cataract Program of the Chinese Ministry of Health[14] between February 2015 and August 2021.

The patients with CC and PFV were diagnosed by the slit-lamp and B-ultrasound examinations (Figure 1): lens opacity, a hyaloid stalk from the optic disc attached to posterior capsule with or without a retrolental membrane, and elongated ciliary process. The age-matched isolated unilateral CC patients were included as controls. Patients with ocular traumas, ocular infection, anterior segment dysplasia such as microphthalmia, congenital glaucoma, retinal disorders such as retina detachment or retina folds and posterior disease such as Lowe syndrome, prematurity, trisomy 13, Norrie disease, and maternal rubella syndrome were excluded.

Because ALs increase mostly during the first two years[15-16], patients were separated into four groups: group 1 (patients with CC and PFV, <24mo), group 2 (patients with CC and PFV, ≥24mo), group 3 (patients with CC, <24mo) and group 4 (patients with CC, ≥24mo).

Ocular Examinations All patients underwent comprehensive bilateral ocular examinations. Best corrected visual acuity (BCVA, Teller acuity card test, Snellen tests, or Symbols tests according to ages) and intraocular pressure (Icare; TAO1i, Icare Finland Oy, Tonopen; Reicher Inc., Seefeld, Germany or non-contact tonometer; Nidek NT-530, Japan depending on age) were assessed. Visual acuity measurements were converted to logMAR units[17]. Slit-lamp examinations (BX900; HAAG-STREIT AG, Bern, Switzerland) were performed through dilated pupils. ALs were obtained by the contact A-scan (B-SCAN-Vplus/ BIOVISION, Quantel Medical, France), and ACDs and LTs were obtained in the same way. The vitreous length was calculated as the AL minus the sum of ACD and the LT. Keratometries were measured by the handheld keratometer (HandyRef-K, Nidek Co., Ltd., Japan) and the average keratometry power was calculated as the mean of the flat keratometry and the steep keratometry readings. A B-mode ultrasound scan was performed in all eyes to evaluate the vitreous and retinal conditions. Patients who could not cooperate with the examinations were sedated by chloral hydrate (0.8 mL/kg, oral or rectal administration)[18].

Statistical Analysis Statistical analysis was performed using SPSS (SPSS ver. 19.0, Chicago, IL, USA). The patients' ages, ALs, keratometries, ACDs, LTs, and vitreous lengths were

Table 1 Characteristics of patients in 4 groups

Characteristics	Group 1 (CC+PFV, <24mo)	Group 2 (CC+PFV, ≥24mo)	Group 3 (CC, <24mo)	Group 4 (CC, ≥24mo)
Patients	18	22	35	35
Gender (M:F)	7:11	14:8	19:16	18:17
Age at examination (mo)				
Mean±SD	12.33±5.51	55.04±20.72	11.87±5.95	53.44±22.04
Range	3.65, 22.29	27.65, 109.81	3.81, 23.57	24.30, 114.51
Affected eyes, *n* (%)				
Right	10 (52.38)	13 (59.09)	14 (40.00)	16 (45.71)
Left	18 (47.62)	9 (40.91)	21 (60.00)	19 (54.29)
BCVA				
Affected eyes	NA	1.37±0.77	NA	1.20±0.63
Fellow eyes	NA	0.15±0.19	NA	0.19±0.24
IOP (mm Hg)				
Affected eyes	12.67±1.89	14.64±2.82	12.71±3.46	13.83±2.78
Fellow eyes	11.67±0.47	13.28±3.90	13.19±3.01	14.28±3.13

BCVA: Best-corrected visual acuity; NA: Non available; IOP: Intraocular pressure.

evaluated. The normality of data distribution was assessed with the Shapiro-Wilk test. ALs, keratometries, ACDs, LTs and vitreous lengths of the affected eyes and fellow eyes within the patients with CC and PFV were compared using paired *t* tests (or Wilcoxon signed rank test when the distribution was non-Gaussian), and those of the affected eyes between the patients with CC and PFV and the patients with CC were compared using independent-samples *t* test (or Wilcoxon Mann-Whitney when the distribution was non-Gaussian). All the statistical tests were two-tailed and a *P* value below 0.05 was considered statistically significant.

RESULTS

Patient and Baseline Characteristics Forty patients with CC and PFV and 70 patients with CC were included. Among patients with isolated CC, there were two main types of cataract, with 23 patients (32.86%) manifested as posterior capsular or posterior polar cataract, and 47 patients (61.43%) manifested as complete cortex or nuclear cataract. All patients were separated into 4 groups: 18 in group 1, 22 in group 2, 35 in group 3 and 35 in group 4. The mean age at examinations was similar between group 1 and group 3 (*P*=0.787), as well as group 2 and group 4 (*P*=0.640). Due to uncooperation or young age, all patients in group 1 and group 3, 13 patients in group 2 and 17 patients in group 4 failed to obtain BCVA, and 15 patients in group 1, 3 patients in group 2, 21 patients in group 3, 9 patients in group 4 failed to obtain intraocular pressure. The baseline characteristics of four groups were showed in Table 1.

Comparisons of Ocular Biometric Parameters Between Affected Eyes and Fellow Eyes Compared with the fellow eyes, the ALs of the eyes with unilateral CC and PFV were shorter (20.02±1.06 *vs* 20.66±0.63 mm, *P*=0.025) in group 1, but longer (23.18±2.00 *vs* 22.31±1.06 mm, *P*=0.044) in group 2. No difference was found in the ALs between the two eyes in group 3, while the ALs of the affected eyes were longer than those of the fellow eyes in group 4 (22.64±1.80 *vs* 22.02±1.01 mm, *P*=0.033).

The keratometries of the affected eyes were steeper than those of the fellow eyes in group 2 (44.78±1.66 *vs* 43.83±1.38 D, *P*=0.041) and group 4 (43.76±1.91 *vs* 43.34±1.46 D, *P*=0.043), and there was no difference in the keratometries between two eyes in group 1 and group 3. The ACDs of the affected eyes and those of the fellow eyes were similar in all groups (Table 2).

The LTs, vitreous lengths, and the ratios of vitreous length to AL failed to obtain in group 1 and group 3, due to uncooperative to the examinations or young age. The affected eyes and the fellow eyes were similar in both groups 2 and 4 (Table 3).

Comparisons of Ocular Biometric Parameters Between Eyes with Congenital Cataract and Persistent Fetal Vasculature and those with Congenital Cataract In the comparison of the affected eyes between group 1 and group 3, no difference was found regarding ALs, keratometries and ACDs (*P*=0.193, *P*=0.680, and *P*=0.137). In the comparison of the affected eyes between group 2 and group 4, no difference was found regarding ALs, and ACDs (*P*=0.295 and *P*=0.446). However, the keratometries of the affected eyes in group 2 were steeper than those in group 4 (44.78±1.66 *vs* 43.76±1.91 D, *P*=0.046; Table 2).

DISCUSSION

To our knowledge, this is the first study to explore the ocular development of patients with CC and PFV at different ages (younger or older than 24mo), which are affected by both form deprivation and hyaloid stalk traction. We found that compared with the fellow eyes, the ALs of the eyes with CC and PFV

Table 2 Distribution of axial length, keratometry and anterior chamber depth in 4 groups mean±SD

Parameters	Group 1 (CC+PFV, <24mo)	Group 2 (CC+PFV, ≥24mo)	Group 3 (CC, <24mo)	Group 4 (CC, ≥24mo)
Axial length				
Affected eyes (mm)	20.02±1.06	23.18±2.00	20.65±1.69	22.64±1.80
Fellow eyes (mm)	20.66±0.63	22.31±1.06	20.56±0.99	22.02±1.01
P	0.025[a]	0.044[a]	0.654	0.033[a]
Keratometry				
Affected eyes (D)	44.21±2.02	44.78±1.66	44.18±2.05	43.76±1.91
Fellow eyes (D)	43.44±1.33	43.83±1.38	43.52±1.57	43.34±1.46
P	0.073	0.041[a]	0.112	0.043[a]
Anterior chamber depth				
Affected eyes (mm)	2.16±0.45	3.20±0.58	2.43±0.51	3.26±0.43
Fellow eyes (mm)	2.31±0.40	3.10±0.67	2.59±0.46	3.16±0.33
P	0.168	0.255	0.301	0.089

[a]*P*<0.05 between affected eyes and fellow eyes.

Table 3 Lens thickness, vitreous length, the ratio of ACD to AL and vitreous length to AL in groups 2 and 4 mean±SD

Parameters	Group 2 (CC+PFV, ≥24mo)	Group 4 (CC, ≥24mo)
Lens thickness		
Affected eyes (mm)	3.65±0.32	3.47±0.33
Fellow eyes (mm)	3.57±0.21	3.62±0.34
P	0.188	0.126
Vitreous length		
Affected eyes (mm)	16.01±2.24	15.85±1.64
Fellow eyes (mm)	15.76±0.83	15.51±1.24
P	0.753	0.577
Ratio of ACD to AL		
Affected eyes	0.14±0.02	0.15±0.02
Fellow eyes	0.14±0.02	0.14±0.01
P	0.963	0.355
Ratio of vitreous length to AL		
Affected eyes	0.69±0.03	0.70±0.02
Fellow eyes	0.69±0.01	0.69±0.02
P	0.730	0.514

ACD: Anterior chamber depth; AL: Axial length.

were shorter in patients younger than 24mo but longer in those older than 24mo. As all we know, the ALs increase mostly in the first two years of life[15-16]. The mechanical traction caused by hyaloid stalk between optic disc and lens posterior capsule may restrict the ocular growth in this rapid eyeball development stage. A typical example is that in 18 patients with combined PFV (a hyaloid stalk) at a median age of 5.5mo, the ALs of the affected eye were shorter than those of the fellow healthy eyes[19]. Furthermore, Khokhar *et al*[13] included 21 patients with a mean age of 6.17mo with unilateral CC and anterior, posterior, or combined PFV, and Shen *et al*[20] evaluated 8 patients with a mean age of 13.7mo with unilateral anterior, posterior, or combined PFV with or without CC. Both of them found that the ALs of the affected eyes were shorter than those of the fellow eyes, which was similar with our findings. After two years of age, the development of the eyeball slowed down[21]. In addition to the mechanical traction by the hyaloid stalk in vitreous cavity, the eyeball development of patients with both CC and PFV is also affected by the form deprivation[22-24]. The patients with unilateral CC and PFV in this study were those referred to the Cataract Department of the ZOC with relatively mild symptoms of PFV younger or older than 24mo: presented a narrow hyaloid stalk from the optic disc attached to the lens posterior capsule without retinal disorder. The long-term accumulated effects of form deprivation were greater than the mild mechanical traction and eventually led to eyeball elongations in older patients. Furthermore, among patients with CC and PFV older than 24mo, the ratios of ACD to AL and the ratios of vitreous length to AL of the affected eyes were comparable to those of the fellow eyes, indicating that anterior and posterior segment of the eyeball between the two eyes grew in a similar pattern.

The keratometries of the affected eyes were found steeper than those of the fellow eyes in patients older than 24mo, while no difference was found between the two eyes in patients younger than 24mo. Asbell *et al*[25] evaluated 11 eyes with PFV and found that the affected eyes had steeper corneas than those of the fellow eyes at any given age. Khokhar *et al*[13] also obtained similar outcomes by evaluating 21 cases with PFV. However, these studies included both PFV patients with or without CC, which may explain the difference in results. In the current study, we only focused on patients with CC and PFV, with impairments of both anterior and posterior segments, and compared with patients with isolated CC. Among patients with CC and PFV, compared with the affected eyes in those younger than 24mo, those older than 24mo had steeper keratometries, which might be due to the ocular development of the older

patients being affected by the disease for a longer period. Furthermore, no difference of the keratometries in the affected eyes was found between the age-matched patients with CC and PFV and those with isolated CC at a younger age (<24mo); however, the keratometries of the affected eyes were steeper in patients with CC and PFV at age of older than 24mo, indicating that the PFV might have additional influences on ocular development over time.

ALs and keratometries play important roles in refractive status, with the AL elongation and cornea flattening allowing the refractive error to remain relatively constant during the ocular development[26]. In this study, in patients older than 24mo, the ALs and keratometries were longer and steeper in the affected eyes than the fellow eyes among both patients with unilateral CC and PFV and those with unilateral CC. Specifically, the keratometries of the affected eyes were steeper in patients with CC and PFV than those in age-matched patients with CC, indicating that patients with CC and PFV might be more likely to suffer from myopia over time. Therefore, for patients with CC and PFV, close attention and timely treatment should be considered not only for hyaloid stalk traction but also for the high risk of myopia.

This study has limitations. First, most patients included were younger than 4 years old and their visual acuity could not be accurately evaluated and were not included in the current study. Besides, although this study is the largest cohort of patients with CC and PFV reported to date, the number of patients remains relatively small, which is due to both CC and PFV being rare diseases. Further studies are warranted to verify and expand the clinical significance of the findings from this study.

In summary, in the patients with CC and mild PFV, the mechanical traction caused by hyaloid stalk may restrict the ocular growth in the first two years of life of rapid ocular development stage. However, the long-term accumulated effects of form deprivation caused by CC might be greater than the mild mechanical traction and eventually lead to eyeball elongations with age. Furthermore, in patients older than 24mo, the keratometries of the eyes with both CC and PFV were steeper than those of the fellow eyes and those of the eyes with isolated CC, indicating that PFV might have additional influences on ocular development. Therefore, the patients older than 24mo, with longer ALs and steeper keratometries, might be more likely to suffer from myopia. These findings could be useful in understanding the ocular development in patients with both CC and PFV, which is significant for the further treatment strategy and visual function improvement.

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