Original Article

# Accelerated Corneal Collagen Cross-Linking in Pediatric Keratoconus

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## Abstract

**Purpose:** To evaluate the visual, refractive, and topographic outcomes of accelerated corneal collagen cross-linking (CXL) in the pediatric age group.

**Methods:** In this retrospective case series study, 89 eyes of 56 patients with progressive keratoconus (KCN) who were under or equal to 18 years old at the time of surgery were included. All patients underwent accelerated corneal CXL. A thorough baseline and follow-up ophthalmic examination including uncorrected distance visual acuity, best corrected visual acuity (BCVA), slit-lamp and fundus examination, and corneal tomography by Scheimpflg camera Pentacam (Oculus, Wetzlar, Germany) were performed.

**Results:** The mean age of patients was 16.2 ± 1.8 years. Mean follow-up was 16.46 ± 11.6 months (range, 6–40 months). The mean BCVA improved significantly from 0.26 ± 0.26 to 0.16 ± 0.19 (logMAR) after accelerated CXL ($P < 0.001$). The mean corneal astigmatism based on refraction decreased from 3.69 ± 2.12 to 3.15 ± 1.86 after the intervention ($P = 0.016$). The mean maximum keratometry ($K_{max}$) reduced significantly from 53.23 ± 6.07 diopter (D) to 52.23 ± 6.33 D ($P = 0.047$). The mean flat keratometry ($K_1$) reduced from 46.37 ± 3.69 to 45.95 ± 3.65 after the intervention ($P = 0.119$).

**Conclusion:** Our study shows that accelerated CXL increases visual acuity and stabilizes or improves keratometric indices in pediatric patients with progressive KCN without any serious complication for a mean follow-up time of 16 months.

**Keywords:** Accelerated corneal collagen cross-linking, Keratoconus, Pediatric ophthalmology

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## Introduction

Keratoconus (KCN) is a degenerative, bilateral, and often asymmetric corneal disease. It is characterized by conical shape of the cornea and progressive stromal thinning.[1] KCN is usually diagnosed in the second decade of life and can progress until the third or fourth decade.[2] In some cases, the onset is earlier, and unfortunately in these cases, the disease shows a more aggressive course. Compared to adults, KCN in children progresses more rapidly and is usually more severe at the time diagnosis. Hence, prompt management to halt the progression of the disease and enhance visual performance is crucial.[3]

The incidence of KCN is estimated about 1 in 2000 participants, and the prevalence is about 54.5 in 100,000 participants.[2,4] Patients with KCN generally have reduced visual acuity due to optical aberrations caused by irregular astigmatism. Visual rehabilitation can be done by prescribing proper spectacles, rigid gas-permeable contact lenses, and intracorneal ring segments in mild-to-moderate cases.[5,6] Compared to adults, children are often less tolerant and/or not eligible for these modalities.[3]

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The incidence of KCN in children is higher in males and patients with allergic diseases and chronically eye rubbers.[5] The management of KCN in children and teenagers is very difficult because of the more severe and more progressive nature of the disease in this age group.[7,8] Children may not cooperate to perform topography or tomography and frequently refuse abstinence of eye rubbing.[9]

The only way that has shown to cease progression of the ectasia is corneal collagen cross-linking (CXL).[10] CXL causes cross-linking of the stromal collagen by using a photo sensitizer (riboflavin, Vitamin $B_2$) and ultraviolet A (UVA) radiation on a bare stroma (epi-off) or epithelium (epi-off). This process increases the rigidity of corneal stroma and delays or stops the progression.[11,12]

Some newer preparations of riboflavin and surgical techniques have facilitated the procedure without shaving the epithelium, which is called epi-on. This method did not show similar efficacy as compared to the classic epi-off Dresden standard method in most studies.[13,14] Recently, accelerated protocols with shorter time and similar efficacy have been used for CXL in adults.[15,16]

KCN usually presents as more severe and more progressive in patients who are equal or under the age of 18 years in comparison to adult subjects,[8] so many practitioners prefer the standard 30 min Dresden protocol for children.[11] Considering the exhausting time which is uncomfortable for the pediatric age group, accelerated protocol seems like an attractive alternative if it shows reasonably comparable results.

In this study, we reported the visual, refractive, and topographic outcomes of accelerated CXL in the pediatric age group. Furthermore, we compared the impact of intervention based on the participants' age (≤15 and >15 years old) and follow-up time (≤12 and >12 months) to evaluate outcome stability.

## Methods

This retrospective case series study reports the results of accelerated CXL in the pediatric age group which was performed at the Farabi Eye Hospital, Department of Ophthalmology, Tehran University of Medical Sciences, Tehran, Iran, from 2010 to 2017. The study was approved by the Ethics Committee of Tehran University of Medical Sciences (Ethics approval code: IR.TUMS.VCR.REC.1395.1957) and adhered to the tenets of the Declaration of Helsinki. At the time of planning for surgery, written informed consent for the procedure and potential future use of the data for research purposes was obtained from all participants and/or their legal guardians after explanation of the potential options and their *pros and cons*.

Medical records of all patients with KCN who were under or equal to 18 years of age at the time of CXL treatment who underwent CXL by a cornea subspecialty ophthalmologist (F. A.) were retrospectively evaluated.

The diagnosis of KCN in these patients was based on the topographic imaging. Progressive KCN was defined as increasing maximum keratometry ($K_{max}$) (1 diopter [D] or more), increasing corneal astigmatism (1 D or more) in 2 separate examination with a minimum 3 months interval.

All patients underwent corneal tomography by Scheimpflug camera Pentacam (Oculus, Wetzlar, Germany). Corneal thickness was measured by Scheimpflug camera and confirmed by ultrasound pachymetry in cases with borderline thickness on pachymetry Pentacam map. The imaging was done by a well-trained optometrist.

Patients who had <450 μm thickness in the thinnest location of the cornea, central or paracentral scarring, ocular surface inflammation (severe meibomian gland dysfunction, allergic conjunctivitis, and dry eye), coexisting ocular pathology, and history of systemic disease were excluded from the study. Patients with follow-up duration <6 months were not included in the study. None of the patients had a history of using contact lens.

All patients underwent a thorough baseline and follow-up ophthalmic examination by the same cornea subspecialist ophthalmologist (F. A.) including uncorrected distance visual acuity (UDVA), best corrected visual acuity (BCVA), slit-lamp examination, intraocular pressure measurement, and fundus examination. Visual acuity was measured using the E metric charts and transformed into logMAR for further statistical analysis.

### Cross-linking technique

One of the parents accompanied the child during the procedure. Under sterile conditions, after instillation of topical tetracaine and sufficient anesthesia, the central 8 mm of epithelium was removed by a blunt spatula. This step was followed by the application of topical 0.1% riboflavin (Sina Daru, Iran) every 3 min for 30 min to ensure saturation of corneal stroma with riboflavin. Then, the corneal surface was washed with normal saline. A solid-state UVA light source (Collages; LightMed, San Clemente, CA, USA) with a wavelength of 365 nm and an irradiance of 9 mW/cm$^2$ was used to irradiate the central cornea for 10 min. At the end of the procedure, the eye was again washed with normal saline, and a silicone hydrogel bandage contact lens was applied on the cornea. The bandage contact lens was removed 1 week after the procedure.

Topical betamethasone (Betamethasone 0.1%; Daroupakhsh Co., Iran) every 2 h in a tapering method for 1 month, topical Oftaquix (Levofloxacin; Santen, UK) every 6 h for 1 week, and frequent lubrication with nonpreserved artificial tears were prescribed for the patients.

We analyzed the parameters before and after intervention in all participants and in two different subgroups (divided by age and follow-up duration). The descriptive analysis presented by frequency with percentage in categorical variable and mean with standard deviation (SD) and median with interquartile range in nominal variable. We used the statistical (Kolmogorov–Smirnov test) and graphical approaches (Q-Q and histogram plot) for the assessment of normality assumption. Because we entered two

eyes of some patients, for the test of score change in indices after intervention, compared with before, we used the robust generalized estimating equations with exchangeable correlation between the two eyes. $P$ <0.05 was considered statistically significant. All of the analysis was conducted with Stata statistical software: Release 14.2 College Station, TX, USA: StataCorp LP.

## Results

Eighty-nine eyes of 56 patients (34 bilateral and 17 unilateral) were included in this study. In total, 89 eyes were analyzed, 50.6% of which were right eyes. Thirty-three (61.1%) of the participants were male. Study participants were 10–18 years old with a mean age of 16.2 ± 1.8 years. Mean follow-up was 16.46 ± 11.6 months (range, 6–40 months).

The final visual acuity score was improved after the intervention. The mean BCVA improved from 0.26 ± 0.26 to 0.16 ± 0.19 ($P$ < 0.001) [Table 1].

The mean corneal astigmatism based on refraction decreased after the intervention (From − 3.69 ± 2.12 to − 3.15 ± 1.86), and this difference was statistically significant ($P$ = 0.016).

The mean $K_{max}$ score decreased after the intervention and changed from 53.23 ± 6.07 D to 52.23 ± 6.33 D ($P$ = 0.047). The flat keratometry ($K_1$) mean score decreased after the intervention (from 46.37 to 45.95; $P$ = 0.119), and mean astigmatism score decreased after the intervention (From 3.79 to 3.47; $P$ = 0.091) [Table 2]. Furthermore, steep keratometry ($K_2$), minimum keratometry ($K_{min}$), and sphere scores showed no significant difference after the intervention.

The impact of intervention was compared between two age groups (≤15 and >15 years old). Twenty-seven eyes were included in the ≤15 years old subgroup and 62 eyes with the >15 years old subgroup. The final visual acuity score showed statistically significant improvement after the intervention in both age groups ($P$ = 0.026 and $P$ < 0.001, respectively). The $K_{max}$ and $k_{min}$ were decreased significantly in the >15 years old age group ($P$ = 0.049, $P$ = 0.022, respectively). Furthermore, corneal astigmatism based on the topographic image and subjective refraction only showed statistically significant improvement in the >15 years old age group ($P$ = 0.048, $P$ = 0.003, respectively). $K_1$ and $k_2$ indices improvement were not significant in the ≤15 years old or >15 years old age groups [Table 3].

The impact of intervention was assessed at two follow-up times (≤12 and >12 months). The BCVA logMAR significantly improved in both follow-up duration groups (≤12 and >12 months) ($P$ = 0.001, $P$ = 0.001, respectively). The $K_{max}$ improvement after intervention was significant in the ≤12-month follow-up time group ($P$ = 0.046). Corneal astigmatism changes based on the topographic image and subjective refraction were not significant [Table 4].

Preoperative pachymetry was 434.64 ± 37.84 μm and remained stable at mean follow-up time of 16 months with 430.09 ± 54.26 μm ($P$ = 0.30).

No significant side effects (permanent corneal haze, corneal keratitis, and endothelial damage) were observed. Postoperative transient pain and mild-moderate transient haze were the most common side effects. Only three eyes from our patients showed a decline of more than one Snellen lines in either UDVA or CDVA.

**Table 1: Visual outcome and refractive error baseline and after cross-linking**

| Parameter | Mean±SD | | Mean differences* (95% CI) | Median (IQR) | | *P** |
|---|---|---|---|---|---|---|
| | Baseline | Final | | Baseline | Final | |
| UCVA logMAR | 0.46±0.37 | 0.41±0.32 | −0.05 (−0.13, 0.03) | 0.39 (0.54) | 0.30 (0.46) | 0.248 |
| BCVA logMAR | 0.26±0.26 | 0.16±0.19 | −0.11 (−0.14, −0.07) | 0.22 (0.27) | 0.15 (0.22) | <0.001 |
| Sphere | −2.22±2.84 | −1.90±2.26 | 0.29 (−0.26, 0.84) | −1.00 (2.38) | −1.25 (2.00) | 0.297 |
| Astigmatism | −3.69±2.12 | −3.15±1.86 | 0.49 (0.09, 0.89) | −3.50 (3.00) | −3.00 (3.00) | 0.016 |

*Based on GEE. SD: Standard deviation, IQR: Inter-quartile range, CI: Confidence interval, UCVA: Uncorrected visual acuity, BCVA: Best corrected visual acuity, GEE: Generalized estimating equations

**Table 2: Topographic parameters: baseline and after cross-linking**

| Parameter | Mean±SD | | Mean differences* (95% CI) | Median (IQR) | | *P** |
|---|---|---|---|---|---|---|
| | Baseline | Final | | Baseline | Final | |
| $K_1$ | 46.37±3.69 | 45.95±3.65 | −0.37 (−0.83, 0.09) | 45.40 (3.70) | 45.40 (4.30) | 0.119 |
| $K_2$ | 50.01±4.56 | 49.59±4.52 | −0.41 (−0.96, 0.13) | 49.30 (6.04) | 48.90 (5.90) | 0.139 |
| $K_{min}$ | 48.43±3.96 | 48.05±3.81 | −0.39 (−0.98, 0.21) | 47.45 (5.28) | 46.83 (5.28) | 0.201 |
| $K_{max}$ | 53.23±6.07 | 52.23±6.33 | −0.85 (−1.68, −0.01) | 53.00 (9.00) | 52.55 (9.45) | 0.047 |
| Astigmatism | −3.79±2.17 | −3.47±1.97 | 0.31 (−0.5, 0.67) | −3.70 (3.15) | −3.50 (3.23) | 0.091 |

*Based on GEE. SD: Standard deviation, IQR: Inter-quartile range, CI: Confidence interval, $K_1$: Flat keratometry, $K_2$: Steep keratometry, $K_{min}$: Minimum keratometry, $K_{max}$: Maximum keratometry, GEE: Generalized estimating equations

**Table 3: Visual and topographic outcome before and after cross-linking by age group**

| | ≤15 years old | | | >15 years old | | |
|---|---|---|---|---|---|---|
| | Before intervention | After intervention | *P* | Before intervention | After intervention | *P* |
| UCVA logMAR | | | | | | |
| Mean±SD | 0.37±0.27 | 0.35±0.31 | 0.447 | 0.49±0.40 | 0.43±0.32 | 0.648 |
| Median (IQR) | 0.30 (0.37) | 0.30 (0.40) | | 0.39 (0.52) | 0.35 (0.52) | |
| BCVA logMAR | | | | | | |
| Mean±SD | 0.29±0.34 | 0.18±0.26 | 0.026 | 0.25±0.21 | 0.15±0.16 | <0.001 |
| Median (IQR) | 0.15 (0.22) | 0.15 (0.27) | | 0.22 (0.31) | 0.12 (0.22) | |
| Sphere | | | | | | |
| Mean±SD | −1.65±2.17 | −1.61±1.91 | 0.947 | −2.43±3.04 | −2.00±2.39 | 0.248 |
| Median (IQR) | −0.75 (2.88) | −1.25 (1.00) | | −1.50 (2.50) | −1.50 (2.50) | |
| UCVA logMAR | | | | | | |
| Mean±SD | 0.37±0.27 | 0.35±0.31 | 0.485 | −2.43±3.04 | −2.00±2.39 | 0.265 |
| Median (IQR) | 0.30 (0.37) | 0.30 (0.40) | | −1.50 (2.50) | −1.50 (2.50) | |
| Astigmatism | | | | | | |
| Mean±SD | −3.35±1.69 | −3.29±1.80 | 0.820 | −3.83±2.28 | −3.09±1.89 | 0.003 |
| Median (IQR) | −3.50 (3.13) | −3.75 (2.38) | | −3.50 (3.00) | −3.00 (3.50) | |
| $K_1$ | | | | | | |
| Mean±SD | 46.15±4.19 | 45.56±4.17 | 0.109 | 46.67±3.50 | 46.11±3.45 | 0.367 |
| Median (IQR) | 45.20 (3.18) | 45.40 (3.13) | | 45.40 (4.40) | 45.50 (5.00) | |
| $K_2$ | | | | | | |
| Mean±SD | 48.90±4.10 | 48.00±4.75 | 0.109 | 50.25±4.64 | 49.92±4.47 | 0.393 |
| Median (IQR) | 48.30 (4.95) | 48.10 (6.40) | | 49.60 (6.50) | 49.00 (6.40) | |
| $K_{min}$ | | | | | | |
| Mean±SD | 47.56±3.91 | 47.86±5.13 | 0.682 | 50.25±4.64 | 49.92±4.47 | 0.022 |
| Median (IQR) | 46.20 (3.43) | 46.13 (5.58) | | 49.60 (6.50) | 49.00 (6.40) | |
| $K_{max}$ | | | | | | |
| Mean±SD | 50.66±4.27 | 49.56±5.58 | 0.217 | 48.72±3.98 | 48.11±3.33 | 0.049 |
| Median (IQR) | 48.80 (7.70) | 46.80 (9.10) | | 48.20 (5.60) | 47.40 (5.10) | |
| Astigmatism | | | | | | |
| Mean±SD | −3.39±1.86 | −3.17±2.15 | 0.712 | 54.10±6.39 | 53.15±6.38 | 0.048 |
| Median (IQR) | −3.60 (3.43) | −2.40 (3.85) | | 53.80 (8.50) | 53.20 (8.10) | |

Based on GEE. UCVA: Uncorrected visual acuity, BCVA: Best corrected visual acuity, SD: Standard deviation, IQR: Inter-quartile range, $K_1$: Flat keratometry, $K_2$: Steep keratometry, $K_{min}$: Minimum keratometry, $K_{max}$: Maximum keratometry, GEE: Generalized estimating equations

## Discussion

Cross-linking has an important role in the treatment of pediatric patients with progressive KCN. Previously, some studies reported the outcome of standard CXL in pediatric patients.[8,9,17-29] Chatzis and Hafezi proposed to perform CXL when KCN diagnose has been made, even before progression was documented.[8]

They are different modification of standard CXL to use in pediatric patients because they are not as cooperative as adults. Few studies used epithelium on technique for pediatric progressive KCN to decrease pain and need for anesthesia. The results are controversial. Caporrosi showed unfavorable results after epi-off CXL in pediatric KCN after 24 months follow-up; hence, 50% of patients need to retreat with epi-off CXL.[25] Magli *et al*. reported epi-on CXL provided similar efficacy and lower complications compared to epi-off CXL in pediatric patients with progressive KCN at 12 months' follow-up.[26] It seems that this technique needs to be evaluated more in future studies.

In our study, we used accelerated CXL as another modification of standard CXL, and we found it safe and effective. Standard CXL is defined as irradiation of 3 mW/cm$^2$ for 30 min. Accelerated CXL compared to standard protocol shows a greater amount of UVA and lower exposure time.[30,31] Few studies reported the outcome of accelerated CXL in pediatric patients with progressive KCN.[32,33] Shetty *et al*. evaluated accelerated CXL in thirty eyes of 18 patients below 14 years with progressive KCN. They used irradiation of 9 mW/cm$^2$ for 10 min. Ozugurhan *et al*. reported an outcome of accelerated CXL in 44 eyes of pediatric patients with progressive KCN. Accelerated CXL was done with setting of 30 mW/cm$^2$ for 4 min.[33] Badawi studied the impact of accelerated CXL with irradiance of 10 mW/cm$^2$ for 9 min in pediatric KCN.[34] Henriquez *et al*. compared accelerated transepithelial (A-epi-on) CXL with standard CXL (epi-off) for children with progressive KCN, and they did not find a significant difference.[35] Agca *et al*. evaluated results of two different accelerated CXL protocols (4 min of 30 mW/cm$^2$ versus 5 min of 18 mW/cm$^2$).[36] In our study, we used accelerated CXL technique with 9 mW/cm$^2$ irradiation to the cornea for

**Table 4: Visual and topographic parameters before and after cross-linking by follow-up duration**

| | ≤12 months | | | >12 months | | |
|---|---|---|---|---|---|---|
| | Before intervention | After intervention | *P* | Before intervention | After intervention | *P** |
| UCVA logMAR | | | | | | |
| Mean±SD | 0.40±0.31 | 0.37±0.31 | 0.849 | 0.47±0.42 | 0.38±0.30 | 0.492 |
| Median (IQR) | 0.30 (0.37) | 0.30 (0.56) | | 0.46 (0.54) | 0.30 (0.37) | |
| BCVA logMAR | | | | | | |
| Mean±SD | 0.30±0.24 | 0.18±0.18 | <0.001 | 0.23±0.27 | 0.15±0.21 | 0.001 |
| Median (IQR) | 0.26 (0.40) | 0.15 (0.30) | | 0.15 (0.26) | 0.09 (0.22) | |
| Sphere | | | | | | |
| Mean±SD | −2.02±2.51 | −1.67±2.09 | 0.276 | −2.14±2.94 | −1.94±2.30 | 0.844 |
| Median (IQR) | −1.00 (2.88) | −1.00 (1.88) | | −1.25 (2.25) | −1.50 (2.25) | |
| Astigmatism | | | | | | |
| Mean±SD | −3.29±1.75 | −2.92±1.67 | 0.095 | −3.85±2.52 | −3.58±2.31 | 0.356 |
| Median (IQR) | −3.40 (2.39) | −2.80 (2.40) | | −4.30 (3.55) | −4.00 (3.25) | |
| $K_1$ | | | | | | |
| Mean±SD | 46.22±3.25 | 46.40±3.76 | 0.601 | 46.15±3.76 | 45.73±3.43 | 0.110 |
| Median (IQR) | 45.96 (4.30) | 45.50 (5.00) | | 45.15 (2.93) | 44.95 (3.08) | |
| $K_2$ | | | | | | |
| Mean±SD | 49.51±3.95 | 49.63±4.62 | 0.900 | 49.80±4.96 | 49.32±4.36 | 0.211 |
| Median (IQR) | 48.90 (6.40) | 48.50 (5.50) | | 49.55 (5.75) | 48.90 (5.40) | |
| $K_{min}$ | | | | | | |
| Mean±SD | 48.20±3.70 | 47.95±3.59 | 0.697 | 48.02±3.95 | 48.21±3.82 | 0.850 |
| Median (IQR) | 47.80 (5.85) | 47.05 (4.85) | | 46.88 (3.98) | 46.75 (5.40) | |
| $K_{max}$ | | | | | | |
| Mean±SD | 52.72±7.70 | 51.92±7.60 | 0.046 | 53.23±5.18 | 52.18±5.45 | 0.746 |
| Median (IQR) | 52.80 (11.28) | 51.60 (11.83) | | 53.10 (8.10) | 52.70 (7.90) | |
| Astigmatism | | | | | | |
| Mean±SD | 3.29±1.75 | 2.92±1.67 | 0.095 | 3.85±2.52 | 3.58±2.31 | 0.356 |
| Median (IQR) | 3.40 (2.39) | 2.80 (2.40) | | 4.30 (3.55) | 4.00 (3.25) | |

*Based on GEE. UCVA: Uncorrected visual acuity, BCVA: Best corrected visual acuity, SD: Standard deviation, IQR: Inter-quartile range, $K_1$: Flat keratometry, $K_2$: Steep keratometry, $K_{min}$: Minimum keratometry, $K_{max}$: Maximum keratometry. GEE: Generalized estimating equations

10 min, and we have more patients (89 eyes of 56 patients) compared to several previous studies.

In our study, the mean BCVA improved from 0.26 ± 0.26 to 0.16 ± 0.19 (logMAR) after accelerated CXL, and the difference was statistically significant ($P < 0.001$). The UCVA improved from 0.46 ± 0.37 to 0.41 ± 0.32 (logMAR) after intervention, although this difference did not show statistically significant value ($P = 0.248$). The mean corneal astigmatism based on refraction decreased after the intervention, and this difference was statistically significant ($P = 0.016$). Several studies reported visual acuity improvement after standard CXL in pediatric age with KCN.[19-23] Previous studies reported BCVA improvement after accelerated CXL, the same as our study.[32-36] Visual acuity improvement could be a result of refractive and keratometric index improvement. Reduction of astigmatisms helps pediatric patients have better vision with eyeglasses.

The mean $K_{max}$ score decreased after the intervention, which was statistically significant ($P = 0.047$). However, $K_1$ and astigmatism score changes were insignificant. These results are consistent with studies about standard CXL and accelerated CXL in pediatric KCN studies. CXL seems to improve keratometric index.

We compared impact of intervention between two age groups (≤15 and >15-year-old). The final visual acuity score showed statistically significant improvement after the intervention in both age groups. The $K_{max}$ and $k_{min}$ were decreased significantly in the >15-year-old age group). Furthermore, corneal astigmatism based on the topographic image and subjective refraction only showed statistically significant improvement in the >15 years old age group ($P < 0.05$). This result is consistent with Shetty *et al*.'s study which evaluated patients under 14 years with progressive KCN.[32]

Mean follow-up time after intervention was 16.70 month (SD = 11.16). The impact of intervention was assessed at two follow-up times (≤12 and >12 month). The BCVA (logMAR) significantly improved in both follow-up duration group ($P < 0.05$). The $K_{max}$ score improvement after intervention was significant in the ≤12-month follow-up time group ($P < 0.05$). Hence, $K_{max}$ improvement was not significant in the >12-month follow-up time group. CXL would improve keratometric indices more significantly in early 12 months, and after that, the impact will decrease and remain stable.

This study has several limitations. Our study has a limited samples size and does not include a control group due to

its retrospective nature. Another drawback of the study is the follow-up duration and incomplete medical records. A randomized, prospective study with longer follow-up duration is required.

Our study shows that accelerated CXL increases visual acuity and stabilizes or improves keratometric indices in pediatric patients with progressive KCN without any serious complication for mean follow-up time of 16 months.

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### *Conflicts of interest*
There are no conflicts of interest.

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