Open Access

Original Article

Topographic Changes after Cxl in Keratoconus Patients at 3- and 6-Months Follow-Up

Asma Anwar, Abdul Moqeet Khan, Maimona Khalid, Tehreem Tanveer

Department of Ophthalmology, Al-Shifa Trust Eye Hospital, Rawalpindi Pakistan

ABSTRACT

Objective: To measure the mean change in keratometry after corneal collagen cross-linking (CXL) in keratoconus patients at 3- and 6-month follow-up.

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of Ophthalmology, Al-Shifa Trust Eye Hospital, Rawalpindi Pakistan, from May to Dec 2025.

Methodology: After obtaining approval from the ethical committee, we collected a sample of sixty patients suffering from progressive keratoconus between the ages of 18–30 years. All patients underwent corneal collagen cross-linking (CXL) and were followed up at three- and six-month intervals. The primary outcomes were mean flat and steep keratometry measured with the help of a Dual Scheimpflug analyzer (Galilei™ G4; Ziemer, Switzerland). Comparisons were made between pre-operative and post-operative readings.

Results: The primary outcome parameter was keratometry (flat and steep). The pre-operative flat simulated keratometry (K1) was 47.47±1.17 Diopters (D), steep simulated keratometry (K2) was 53.09±1.39 Diopters, and mean average keratometry (Km) was 50.58±0.97 D. The Km was 47.12±0.95 D after three months of CXL, K1 was 46.21±1.40 D, and K2 was 48.04±1.34 D, which showed a statistically significant difference compared to pre-operative values through paired t-test with p-value less than 0.001. The mean average keratometry (Km) was 45.92±0.94 D after six months of CXL, K1 was 43.67±1.31 D, and K2 was 47.22±1.39 D, with *p*-value <0.001. When keratometry values were compared at three- and six-month intervals, there was a significant difference with *p*-value <0.001.

Conclusion: We concluded that corneal topography, astigmatism, and visual acuity improved significantly in three and six months.

Keywords: Cornea, keratoconus, and visual acuity.

How to Cite This Article: *Anwar A, Khan AM, Khalid M, Tanveer T. Topographic Changes after Cxl in Keratoconus Patients at 3- and 6-Months Follow-Up. Pak Armed Forces Med J 2026; 76(Suppl-8): S1363-S1367. DOI: https://doi.org/10.51253/pafmj.v76iSUPPL-8.14009*

INTRODUCTION

Keratoconus is a corneal disease characterized by cone-shaped protrusion of the anterior corneal surface due to asymmetric, progressive, and non-inflammatory ectasia caused by advancing loss of stromal structural integrity and thinning. These alterations lead to irregular astigmatism and myopia, which ultimately result in a decline in visual acuity.[1] Progressive keratoconus is usually established at the onset of puberty as it rapidly progresses through adolescence, halts in the third or fourth decade of life, and stabilizes with aging.[2] Keratoconus is found in all ethnicities, although the incidence and prevalence are more than four times higher in Asians than in White people. It shows gender predominance, being more common in men than in women among both Asians and Whites (Asians: 60% vs 40%; Whites: 65% vs 35%).[3] In Pakistan, its incidence is almost 8% with male predominance.[4] Early forms of keratoconus used to go unnoticed when only slit-lamp examination was performed; however, with advancements in technology, corneal topography helps in screening and has become the gold standard for the diagnosis of keratoconus.[5]

The precise cause of keratoconus is still not known; however, eye rubbing due to allergy is often a primary predisposing factor for the development and progression of keratoconus.[6] In Pakistan, various studies have been performed to determine the incidence of keratoconus. According to Akbar *et al.*, transepithelial corneal collagen cross-linking (CXL) is not a substitute for the conventional epithelium-off technique. Nevertheless, they advocated that patients with thin corneas might benefit from transepithelial CXL. There is significant gap in literature after their work and no study has been conducted to assess the topographic changes after CXL, which is a relatively newer modality in Pakistan.[7] Therefore, the aim of our study was to measure morphological parameters, especially keratometry, at three and six months after

Correspondence: Dr Asma Anwar, Department of Ophthalmology, Al-Shifa Trust Eye Hospital, Rawalpindi Pakistan

Received: 31 Oct 2025; revision received: 07 Apr 2026; accepted: 08 Apr 2026

corneal collagen cross-linking (CXL) to determine its effectiveness and improvement in visual acuity.

METHODOLOGY

Permission from the hospital ethical board was obtained before initiation of the study (IERB number ERC-25/AST-25 dated 14-05-2025). The study was performed in the Ophthalmology Department of Al-Shifa Trust Eye Hospital Rawalpindi, Pakistan from May to December 2025. The duration of the study was eight months. The sample size was estimated with the help of the WHO sample size calculator by keeping the confidence level at 95%, absolute precision (d) at 0.05, anticipated improvement in average keratometry (Km) at three months (P1) to be 1 diopter,[8] and anticipated improvement at six months (P2) to be 3 diopters.[8] The sample size calculated was 60. Non-probability consecutive sampling was employed to collect 68 eyes over eight months, considering the incidence of keratoconus in Pakistan (8.01%).

Inclusion Criteria: Patients aged 18–30 years suffering from progressive keratoconus[9] who were subjected to corneal collagen cross-linking (CXL) were included.

Exclusion Criteria: Patients with corneal scars (central or paracentral), active inflammation, xerophthalmia, or previous ocular surgeries were excluded. Pregnant or lactating women were also excluded.

Patients were booked through the outpatient department for CXL after detailed medical history and ophthalmic examination. Corneal collagen cross-linking (CXL) was performed in all patients by the same surgeon to prevent bias. For the first twenty minutes, topical anesthetic (0.5% proparacaine hydrochloride) was applied, the epithelium in the central 7–8 mm of the cornea was removed with a beaver knife, and riboflavin (0.1%), without dextran, was applied every two minutes. Patients were examined under slit-lamp light to confirm the presence of riboflavin in the anterior chamber. For the next ten minutes, UV-A irradiation was carried out while riboflavin 0.1% (1 drop/2 minutes) continued to be applied. Pachymetry was performed before and after epithelial removal, after 20 minutes of riboflavin administration, and after UV-A exposure to measure corneal thickness at each stage. Balanced Salt Solution (BSS) was used to irrigate the cornea, and a bandage contact lens (BCL) was applied. A sterile eye pad was applied afterward. On the following day, antibiotic and steroid drops were started (tobramycin-dexamethasone 0.1% for the first month, followed by fluorometholone 0.1% in the second month), along with artificial tears for two months. On the fifth postoperative day, the BCL was removed. Each eye was thoroughly examined on the first postoperative day and after the first week for any complications. Patients were followed up at the third and sixth months after CXL, and keratometry measurements were obtained using corneal topography with a Dual Scheimpflug analyzer (Galilei™ G4; Ziemer, Switzerland). To reduce bias, a single experienced ophthalmologist performed corneal topography on each eye. The following parameters were measured preoperatively and postoperatively (three and six months): flat simulated keratometry (K1), steep simulated keratometry (K2), average keratometry (Kav), astigmatism, and logMAR (Logarithm of the Minimum Angle of Resolution) visual acuity. Demographic details included age, gender, and eye involved.

Data was analyzed using the Statistical Package for the Social Sciences (SPSS). Normality of data was assessed using the Shapiro–Wilk and Kolmogorov–Smirnov tests. For non-normal data, median and interquartile range were calculated. For normal data, quantitative measurements were analyzed using mean and standard deviation. For qualitative variables, frequency and percentage were calculated. Paired samples t-test was used to determine statistical significance for quantitative variables. Wilcoxon Signed Rank Test was used to compare LogMAR Visual acuity. The *p*-value of ≤0.05 was considered statistically significant. The different phases of study are shown in the Figure.

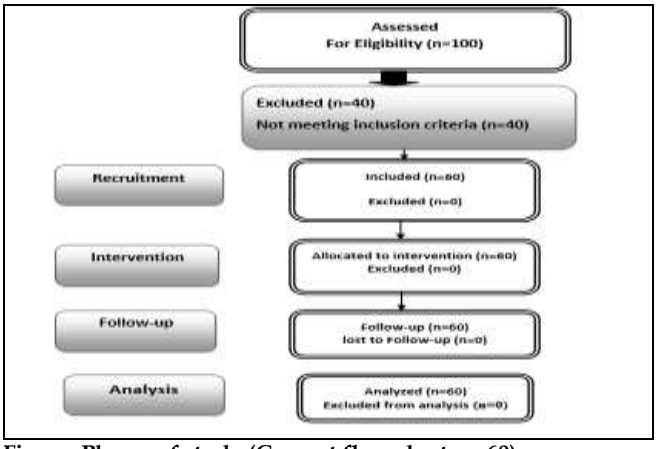

Figure: Phases of study (Consort flow chart, n=60)

RESULTS

A cohort of 60 eyes diagnosed with keratoconus were included in the study. The mean age of the patients

was 23.10±2.50 years, with male predominance. The median age was 23.00 years (IQR 21.00–25.00). There were 46(76.7%) males and 14(23.3%) females in the study. Thirty-eight (63.3%) right eyes were involved, and twenty-two (36.7%) left eyes were involved (Table-I).

Table-I: Demographic Features of Study Group (n=60)

Attributes		Mean±SD
Mean Age (years)		23.10±2.50
		Frequency (%)
Gender	Male	46(76.7%)
	Female	14(23.3%)
Eye involved	Right	38(63.3%)
	Left	22(36.7%)

The primary outcome parameter was keratometry (flat and steep). The pre-operative flat simulated keratometry (K1) was 47.47±1.17 Diopters (D), steep simulated keratometry (K2) was 53.09±1.39 Diopters, and mean average keratometry (Km) was 50.58±0.97 D. The Km was 47.12±0.95 D after three months of CXL, K1 was 46.21±1.40 D, and K2 was 48.04±1.34 D, which showed a statistically significant difference compared to pre-operative values through paired t-test with *p*-value less than 0.001. The mean average keratometry (Km) was 45.92±0.94 D after six months of CXL, K1 was 43.67±1.31 D, and K2 was 47.72±1.42 D, with *p*-value <0.001. When keratometry values were compared at three- and six-month intervals, there was a significant difference with *p*-value <0.001.

Table-II: Topographic Changes before and after Corneal Collagen Cross-Linking (CXL) (n=60)

Outcome variables	Pre-operative Mean±SD	Post-operative		*p*-value
		3 months Mean±SD	6 months Mean±SD	
Mean Average keratometry (Km) D**	50.58±0.97	47.12±0.95	45.92±0.97	<0.001
Mean Flat keratometry (k1) D	47.78±1.17	46.21±1.40	43.67±1.31	<0.001
Mean Steep keratometry (K2) D	53.09±1.39	48.04±1.34	47.72±1.42	<0.001
Mean Astigmatism (D)	4.25±0.05	3.46±0.39	3.13±0.40	<0.001
LogMAR Visual acuity*	0.53 (IQR 0.52-0.55)	0.31 (IQR 0.29-0.33)	0.14 (IQR 0.12-0.18)	<0.001

** LogMar-Logarithm of the Minimum Angle of Resolution*
*** D-Diopters*

The mean preoperative astigmatism of 4.25±0.05 Diopters improved to 3.36±0.39 D in three months and 3.13±0.40 D at six months. The distribution of uncorrected logMAR visual acuity showed a non-normal distribution. The preoperative median logMAR visual acuity was 0.53 (IQR 0.52–0.55). At three months, the median logMAR visual acuity was 0.31 (IQR 0.29–0.33), and at six months, it was 0.14 (IQR 0.12–0.18). There was significant improvement in visual acuity at three and six months compared to preoperative values (p<0.001), as well as when visual acuity was compared between three and six months (Table-II).

DISCUSSION

The corneal topography showed a substantial improvement after corneal collagen cross-linking (CXL). We also measured visual acuity to ascertain whether the improvement in topography led to better visual outcomes or not. Nevertheless, our primary focus was topographic changes, which mainly included keratometric measurements. We used dual Scheimpflug and Placido disc (Galilei), which, in addition to providing precise curvature and topographic examination of the cornea, offers more dependable pachymetry data. The Galilei dual Scheimpflug analyzer is a more recent non-invasive technique for pachymetry that uses Placido imaging in conjunction with two spinning Scheimpflug cameras 180° apart.[10]

Emilia Felter *et al.*, conducted longitudinal study of keratoconic eyes (n=200) and assessed biomechanical and tomographic changes up to four years after corneal collagen cross-linking (CXL). According to them, early follow-up showed a significant reduction in biomechanical indices and a transient increase in tomographic deviation, indicating stromal remodeling. Over time, keratometry values decreased steadily, indicating sustained corneal flattening. Although corneal thickness remained reduced, visual acuity improved. Overall, their findings support early postoperative fluctuations followed by long-term corneal stabilization after CXL.[11] Our study showed that corneal thickness reduced substantially in three months (K average = 48.04±1.34 D) and showed further reduction at six months (K average = 47.22±1.39 D) follow-up which was in alignment with their findings.

Growing research evidence has advocated and demonstrated the effectiveness of CXL treatment, which uses UV-A radiation and the photosensitizer riboflavin to stop the progression of keratoconus and corneal ectasia following refractive surgery. The exact method by which CXL enhances or modifies eyesight is unknown, but it is proposed that it could result from improvements in defined topographic indices as well as a decrease in astigmatism, corneal steepness, and refractive error.[12] It has been postulated that physiological age-related collagen cross-linking

happens naturally, resulting in a lifetime increase in corneal collagen fibrils, providing protection against keratoconus. Glycosylation-related collagen cross-linking is seen in diabetic individuals, which imparts immunity against keratoconus. This led to the idea that materialized in the form of a method for chemical CXL in corneas that are biomechanically weaker using ultraviolet (UV-A) light and riboflavin. Crosslinks are created through an intricate photochemical mechanism that involves both aerobic and anaerobic stages.[13]

It is a well-established fact that CXL nearly always causes some central anterior corneal flattening. Our study showed that enhanced topographic regularity led to improved visual acuity. We demonstrated that keratoconus stopped progressing from three to six months. We did not follow up for 12 months, as the topography at six and 12 months is almost the same, as proposed by Tian *et al*.[14] They demonstrated that corneal thickness reduced after one month; after six and twelve months of follow-up, no discernible change was seen.

Our results are consistent with prior clinical reports that suggest CXL stops ectasia from progressing and enhances corneal keratometry and refractive status.[15] There are a few case reports that have documented side effects ranging from non-infectious corneal melting and minor stromal haze to sight-threatening infectious keratitis.[16] In our study, we did not encounter any side effects, possibly because an experienced surgeon performed all the surgeries.

When riboflavin, a B-complex vitamin, is applied to the cornea of keratoconus patients, the cornea is exposed to UVA light, which causes the collagen fibers to cross-link, or cling to one another. Collagen is the main protein found in the body's connective tissues. The surgery helps the cornea regain its proper curvature and structure. According to earlier reports of CXL, pachymetry reaches its narrowest point, roughly three months after surgery. These findings are consistent with our study.[17]

Alex C. Fredi *et al.*, provided the most extensive long-term CXL study to date, with 162 eyes at 5 years and 976 eyes at 1 year. Their results were analogous to data retrieved from randomized controlled trials based on routine clinical practice outcomes of CXL in Australia, New Zealand, Italy, France, and Spain. They concluded that total visual acuity improves gradually over a 5-year period following CXL and that the cornea flattens dramatically at the 1-year mark and then stabilizes. They also demonstrated that a subset of patients did not respond well to CXL, and four percent of eyes did not stabilize even after five years. Clinically severe haze, scarring, persistent epithelial abnormalities, and recurrent erosions were among the few adverse events that occurred in their patients in the long run.[18] Despite their rarity, these adverse effects are crucial for patients and physicians; however, our patients did not develop any side effects until their last follow-up.

According to Badawi *et al.*, corneal astigmatism considerably improved in adolescents with keratoconus, which was also observed in our patients. After surgery, we observed a decrease in corneal astigmatism at three and six months, respectively.[19] They followed patients for one year, whereas we followed them for six months.

LIMITATION OF STUDY

This study was conducted at a single center with a relatively small sample size and a short follow-up duration of six months, which may limit the generalizability of the findings and the ability to assess long-term stability and late complications after corneal collagen cross-linking. Additionally, the absence of a control group restricts direct comparison with the natural progression of keratoconus or alternative treatment modalities

ACKNOWLEDGEMENT

We are thankful to our departmental colleagues for their help and support.

CONCLUSION

We concluded that corneal topography, astigmatism, and visual acuity improved significantly at three and six months after corneal collagen cross-linking (CXL).

Conflict of Interest: None.
Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AA & AMK: Data acquisition, data analysis, critical review, approval of the final version to be published.

MK & TT: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Singh RB, Koh S, Sharma N, Woreta FA, Hafezi F, Dua HS, et al. Keratoconus. Nat Rev Dis Primers 2024; 10(1): 81. https://doi.org/10.1038/s41572-024-00565-3

2. Joshi V, Chaudhary S. Keratoconus in Children. InKeratoconus: Diagnosis and Treatment. Springer 2022; 89-104. https://doi.org/10.1007/978-981-19-4262-48
3. Niazi S, Gatzioufas Z, Doroodgar F, Findl O, Baradaran-Rafii A, Liechty J, et al. Keratoconus: exploring fundamentals and future perspectives–a comprehensive systematic review. Ther Adv Ophthalmol 2024; 16: e25158414241232258. https://doi.org/10.1177/25158414241232258
4. Badar F, Mahmood S. Cancer in Lahore, Pakistan, 2010–2019: an incidence study. BMJ Open 2023; 11(8): e047049. https://doi.org/10.1136/bmjopen-2020-047049
5. Nicula CA, Bulboacă AE, Nicula D, Nicula AP, Horvath KU, Bolboacă SD. Performances of corneal topography and tomography in the diagnosis of subclinical and clinical keratoconus. Front Med 2022; 9: 904604. https://doi.org/10.3389/fmed.2022.904604
6. Singh RB, Koh S, Sharma N, Woreta FA, Hafezi F, Dua HS. Keratoconus. Nat Rev Dis Primers 2024; 10(1): 81. https://doi.org/10.1038/s41572-024-00565-3
7. Akbar B, Intisar-ul-Haq R, Ishaq M, Fawad A, Arzoo S, Siddique K. Comparison of transepithelial corneal crosslinking with epithelium-off crosslinking (epithelium-off CXL) in adult Pakistani population with progressive keratoconus. Taiwan J Ophthalmol 2017; 7(4): 185-190. https://doi.org/10.4103/tjo.tjo_38_17
8. Pedrotti E, Caldarella G, Fasolo A, Bonacci E, Gennaro N, De Gregorio A, et al. Topographic and biomechanical changes after application of corneal cross-linking in recurrent keratoconus. Int J Environ Res Public Health 2024; 16(20): 3872. https://doi.org/10.3390/ijerph16203872
9. Ulutas HG, Ozkaya G, Hamidi NA. Comparison of central corneal thickness measured by ultrasound pachymetry, corneal topography, spectral domain-optical coherence tomography, and non-contact specular microscopy. Photo diagnosis Photodyn Ther 2023; 42: 103527. https://doi.org/10.1016/j.pdpdt.2023.103527
10. Lee Y, Oh JY, Choi HJ, Kim MK, Yoon CH. Agreement in anterior segment measurements between swept-source optical coherence and dual Scheimpflug tomography devices in keratoconus eyes. Sci Rep 2024; 14: 24368. https://doi.org/10.1038/s41598-024-76031-7
11. Felter E, Khoramnia R, Friedrich M, Son HS, Auffarth GU, Augustin VA. Biomechanical changes following corneal crosslinking in keratoconus patients. Graefes Arch Clin Exp Ophthalmol 2024; 262(11): 3635-3642. https://doi.org/10.1007/s00417-024-06549-z
12. Razmjoo H, Nasrollahi AP, Salam H, Karbasi N, Najarzadegan MR. Topographic corneal changes after collagen cross-linking in patients with corneal keratoconus. J Res Med Sci 2013; 18(10): 882-886.
13. Vaidya NS, Daneshmand A, Epstein RJ, Majmudar PA, Belin MW, Parsons EC, et al. Pachymetric Assessment After EpiSmart® Epithelium-on Cross-Linking for Keratoconus and Post-Surgical Ectasia. Clin Ophthalmol 2022; 16: 1829-1835. https://doi.org/1: 10.2147/OPTH.S359710
14. Tian M, Jian W, Zhang X, Sun L, Shen Y, Zhou X. Predictive factors of the accelerated transepithelial corneal cross-linking outcomes in keratoconus. BMC Ophthalmol 2022; 22(1): 7. https://doi.org/110.1186/s12886-021-02235-4
15. Deshmukh R, Ong ZZ, Rampat R, Alió JL, Barua A. Management of keratoconus: an updated review. Front Med 2023; 10: 1212314. https://doi.org/110.3389/fmed.2023.1212314
16. Tiveron MC Jr, Pena CRK, Hida RY, Moreira LB, Branco FRE, Kara-Junior N. Topographic outcomes after corneal collagen crosslinking in progressive keratoconus: 1-year follow-up. Arq Bras Oftalmol 2017; 80(2): 93-96. https://doi.org/10.5935/0004-2749.20170023
17. Ryu S, Yoon SH, Jun I, Seo KY, Kim EK, Kim TI. Anterior Ocular Biometrics Using Placido-scanning-slit System, Rotating Scheimpflug Tomography, and Swept-source Optical Coherence Tomography. Korean J Ophthalmol 2022; 36(3): 264-273. https://doi.org/110.3341/kjo.2021.0120
18. Ferdi AC, Kandel H, Nguyen V, Tan J, Arnalich-Montiel F, Abbondanza M, et al. Five-year corneal cross-linking outcomes: A Save Sight Keratoconus Registry Study. Clin Exp Ophthalmol 2023; 51(1): 9-18. https://doi.org/1 10.1111/ceo.14177
19. Preethi B, Kumar KK, Babu GS, Sridhar S, Srinivasa KH. Outcomes of accelerated collagen cross linking in progressive paediatric keratoconus. Indian J Ophthalmol 2023; 71(5): 1889-1893. https://doi.org/10.4103/ijo.IJO146922

.....