Journal of Health, Wellness and Community Research
ISSN: 3007, 0570

OPEN ACCESS

JHWCR

Type: Review Article
Published: 29 October 2025
Volume: III, **Issue:** XV
DOI: https://doi.org/10.61919/c5g1qn63

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Received 11, 09, 25
Accepted 18, 10, 2025

Authors' Contributions
Concept: TJ; Design: SL; Data Collection: FA, AT, IB, RUA; Analysis: TJ, SL; Drafting: TJ, FA.

Declarations
No funding was received for this study. The authors declare no conflict of interest. The study received ethical approval. All participants provided informed consent.

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Comparison of Visual and Corneal Parameters Before and After Corneal Cross-Linking Therapy in Patients with Keratoconus

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ABSTRACT

Background: Keratoconus is a progressive ectatic corneal disorder leading to irregular astigmatism and reduced visual acuity, and corneal collagen cross-linking (CXL) is used to improve biomechanical stability and delay progression. Objective: To compare visual acuity and corneal parameters before and six months after epithelium-on accelerated CXL in patients with keratoconus. Methods: A quasi-experimental before–after study was conducted on 30 keratoconic eyes from patients aged 10–30 years attending Mayo Hospital, Lahore. Uncorrected and corrected distance visual acuity (logMAR), keratometry (K1, K2, mean K), and pachymetry (central and thinnest) were recorded preoperatively and at six months postoperatively using Galilei G4. Normality was assessed using Shapiro–Wilk test, and comparisons were performed using paired-sample t-test or Wilcoxon signed-rank test as appropriate (p≤0.05). Results: Mean age was 21.19±6.31 years. UDVA improved from 1.00±0.76 to 0.64±0.30 logMAR (mean improvement 0.36; p=0.005) and CDVA improved from 0.51±0.48 to 0.28±0.26 logMAR (mean improvement 0.23; p=0.001). K1, K2, and mean K increased significantly (p=0.001 for all). Central and mean pachymetry remained stable (p>0.05), with a borderline non-significant reduction in thinnest pachymetry (p=0.056). Conclusion: Epithelium-on accelerated CXL resulted in significant visual improvement with pachymetric stability at six months, while keratometric indices increased, warranting structured tomographic monitoring over longer follow-up.

Keywords

Keratoconus; corneal collagen cross-linking; visual acuity; keratometry; pachymetry; Galilei G4.

INTRODUCTION

Keratoconus is a progressive, non-inflammatory corneal ectasia characterized by localized stromal thinning, corneal protrusion, and irregular astigmatism, resulting in deterioration of both uncorrected and corrected vision and reduced quality of life (1). It commonly presents during adolescence or early adulthood and may show accelerated progression in younger patients, making timely diagnosis and stabilization particularly important in this age group (2). Although the exact etiology remains multifactorial, several clinical and environmental associations—including ocular allergy and habitual eye rubbing—have been consistently implicated, and local evidence from Pakistan has also reinforced the contribution of allergic eye disease and mechanical factors as important correlates of keratoconus in clinical practice (3). With the increasing availability of corneal tomography and topographic imaging, earlier detection of keratoconus and monitoring of progression have become feasible, allowing clinicians to intervene at a stage where vision may still be preserved and structural deterioration prevented.

Management of keratoconus is typically staged according to severity and progression. Early disease may be managed with spectacles or soft contact lenses, while moderate disease often requires rigid gas-permeable or scleral lenses, and advanced stages may necessitate surgical interventions including keratoplasty in the presence of scarring or contact lens intolerance (4). Among the current therapeutic approaches, corneal collagen cross-linking (CXL) is the only intervention that targets the biomechanical instability underlying ectasia by inducing additional covalent bonds within the corneal stroma through riboflavin-mediated photochemical activation with ultraviolet-A light, thereby slowing or halting progression and reducing the need for corneal transplantation Over the last two decades, variations of CXL—including accelerated protocols and epithelium-on ("transepithelial") techniques—have been explored to improve comfort, reduce healing complications, and enhance feasibility in broader clinical settings Systematic evidence comparing epithelium-on versus epithelium-off approaches indicates differences in riboflavin penetration and epithelial integrity, highlighting an ongoing clinical need to balance efficacy with safety and patient tolerance (5). Furthermore, long-term follow-up studies in adolescent populations suggest that accelerated CXL can stabilize keratometric parameters and improve best-corrected vision, though outcomes may vary depending on protocol and baseline disease characteristics (6).

Despite the extensive global literature on CXL, there remains limited structured evidence from local clinical settings evaluating short-term outcomes using standardized objective corneal parameters and visual acuity metrics, particularly using modern imaging platforms such as the Galilei G4. In addition, short-term follow-up at six months is clinically relevant because early post-treatment remodeling, stabilization trends, and safety signals—particularly corneal thickness behavior—can be detected during this phase and may guide follow-up planning and counseling (7). Therefore, this study was designed to evaluate changes in visual acuity and corneal parameters before and six months after epithelium-on accelerated CXL in patients with keratoconus (8).The study aimed to compare uncorrected and corrected visual acuity (logMAR), keratometric

indices (K1, K2, and mean K), and pachymetric measures (central and thinnest corneal thickness) before and after treatment to assess functional and structural outcomes within six months of therapy (9).

MATERIALS AND METHODS

A quasi-experimental before–after study was conducted among patients diagnosed with keratoconus who attended the outpatient services of the Eye Ward, Mayo Hospital, King Edward Medical University (KEMU), Lahore, Pakistan, after obtaining ethical approval from the Institutional Review Board (IRB/ERB: 46/RC/KEMU). Non-probability convenience sampling was used. Patients aged 10–30 years of either sex with clinically and tomographically confirmed mild, moderate, or advanced keratoconus were eligible for inclusion, while those with severe keratoconus were excluded. Diagnosis and clinical eligibility were established using clinical assessment and corneal imaging (Orbscan-based evaluation), followed by corneal tomography and pachymetry using the Galilei G4 system. After eligibility confirmation, patients who opted for corneal collagen cross-linking (CXL) were enrolled following written informed consent, in accordance with the principles of the Declaration of Helsinki.

The unit of analysis for this study was the eye. A total of 30 keratoconic eyes were included in the final analysis. Baseline participant characteristics including age and sex were recorded at enrollment. Visual and corneal outcomes were assessed at two standardized time points: immediately before the CXL procedure (preoperative baseline) and six months after the intervention (postoperative follow-up). Visual acuity was measured using a logMAR chart, and both uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA) were documented following subjective refraction. Corneal parameters were obtained using Galilei G4 tomography, including keratometry readings (K1, K2, and mean keratometry) and pachymetry measures (central corneal thickness and thinnest pachymetry). Refraction variables (sphere, cylinder, and axis) were also recorded pre- and post-treatment as secondary visual parameters.

Corneal collagen cross-linking was performed following an epithelium-on accelerated protocol. Riboflavin was instilled into the treated eye at one-minute intervals for 30 minutes, followed by ultraviolet-A irradiation using an irradiance of 9 mW/cm² for 10 minutes (total energy dose 5.4 J/cm²), with the epithelium maintained intact. A bandage contact lens was applied at the completion of the procedure. Patients were followed routinely and were reassessed at six months for repeat refraction, visual acuity measurement, and Galilei G4 tomography.

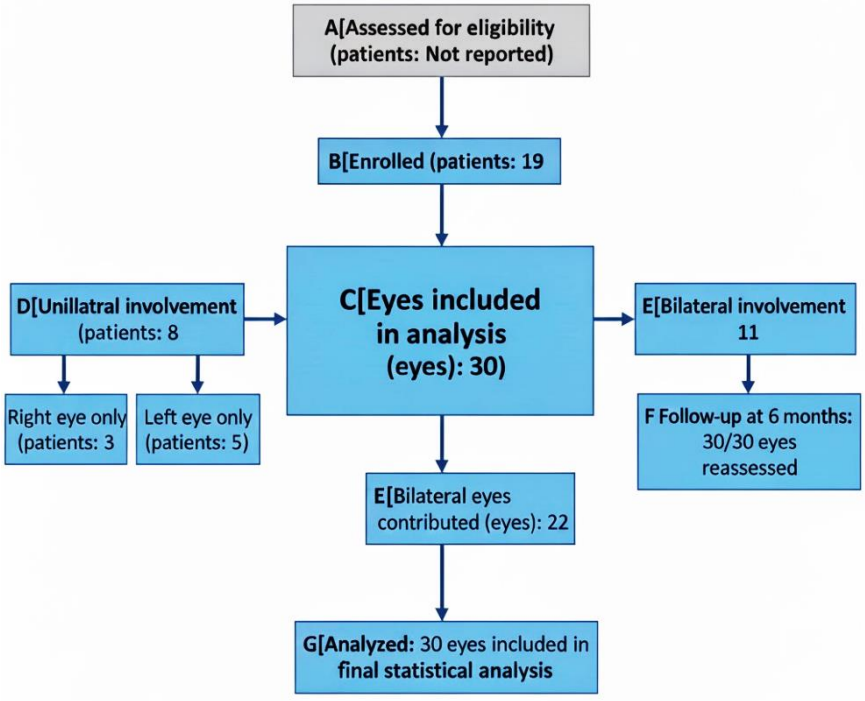

Figure 1 CONSORT Flowchart

Sample size was estimated using a significance level of 5% and power of 90%, based on expected pre- and post-operative mean keratometric readings reported in previous work (10). Data were entered and analyzed using IBM SPSS Statistics version 26. Continuous variables were summarized as mean ± standard deviation (SD), and categorical variables were presented as frequencies and percentages. Normality of continuous outcomes was assessed using the Shapiro–Wilk test. For outcomes that were normally distributed, pre- and post-treatment comparisons were performed using the paired-sample t-test. For non-normally distributed outcomes, the Wilcoxon signed-rank test was used. A two-sided p-value of ≤0.05 was considered statistically significant.

RESULTS

A total of 30 keratoconic eyes were analyzed. The mean age of participants was 21.19 ± 6.31 years, and males comprised 73.33% (n=22) of the sample. Based on laterality at the patient level (n=19), unilateral keratoconus involvement was present in 3 right eyes (15.79%) and 5 left eyes (26.32%), while bilateral involvement was noted in 11 patients (57.89%), yielding the 30-eye analytical dataset. With respect to disease stage, 3 eyes (10.0%) were classified as mild keratoconus, 15 eyes (50.0%) as moderate, and 12 eyes (40.0%) as advanced keratoconus.

At six months after epithelium-on accelerated corneal collagen cross-linking, visual outcomes showed statistically significant improvement. Uncorrected visual acuity improved from 1.00 ± 0.76 logMAR preoperatively to 0.64 ± 0.30 logMAR postoperatively, corresponding to a mean improvement of 0.36 logMAR (p=0.005). Corrected visual acuity also improved significantly from 0.51 ± 0.48 logMAR to 0.28 ± 0.26 logMAR, reflecting a mean improvement of 0.23 logMAR (p=0.001). In contrast, refractive variables did not demonstrate statistically significant changes;

sphere shifted from −1.30 ± 1.68 D to −1.76 ± 2.37 D (p=0.232), cylinder changed from −2.77 ± 1.54 D to −2.32 ± 1.88 D (p=0.280), and axis increased from 80.58 ± 55.78 degrees to 93.71 ± 53.53 degrees without statistical significance (p=0.156).

Table 1. Baseline and Demographic Characteristics of Participants (n = 19 patients; 30 eyes)

Variable	Frequency (n)	Percentage (%)
Gender (patients)		
Male	22	73.33
Female	8	26.67
Age (years)	Mean ± SD	21.19 ± 6.31
10–15	8	26.67
16–20	6	20.00
21–25	7	23.33
26–30	9	30.00
Laterality (patients; n=19)		
Right eye only	3	15.79
Left eye only	5	26.32
Both eyes	11	57.89
Keratoconus severity (eyes; n=30)		
Mild	3	10.00
Moderate	15	50.00
Advanced	12	40.00

Table 2. Pre- vs Post-CXL Corneal Parameters (Parametric Comparison: Paired t-test)

Outcome (Diopters/µm)	Pre-CXL Mean ± SD	Post-CXL Mean ± SD	Mean Change (Post − Pre)	p-value
K1 (D)	44.77 ± 3.50	46.41 ± 3.44	+1.64 D	0.001
K2 (D)	49.42 ± 4.57	52.03 ± 5.11	+2.61 D	0.001
Mean K (D)	47.09 ± 3.91	49.22 ± 4.09	+2.13 D	0.001
Central pachymetry (µm)	483.60 ± 54.54	482.67 ± 55.24	−0.93 µm	0.753
Thinnest pachymetry (µm)	461.62 ± 55.09	453.48 ± 54.62	−8.14 µm	0.056
Mean pachymetry (µm)	473.50 ± 52.72	468.94 ± 53.29	−4.56 µm	0.082

Table 3. Pre- vs Post-CXL Visual and Refraction Parameters (Non-parametric Comparison: Wilcoxon Signed-Rank Test)

Outcome	Pre-CXL Mean ± SD	Post-CXL Mean ± SD	Mean Change (Pre − Post)	p-value
Uncorrected VA (logMAR)	1.00 ± 0.76	0.64 ± 0.30	0.36 improvement	0.005
Corrected VA (logMAR)	0.51 ± 0.48	0.28 ± 0.26	0.23 improvement	0.001
Sphere (D)	−1.30 ± 1.68	−1.76 ± 2.37	+0.46	0.232
Cylinder (D)	−2.77 ± 1.54	−2.32 ± 1.88	−0.45	0.280
Axis (degrees)	80.58 ± 55.78	93.71 ± 53.53	−13.13	0.156

Corneal curvature parameters demonstrated statistically significant changes at six months. K1 increased from 44.77 ± 3.50 D to 46.41 ± 3.44 D, representing a mean change of +1.64 D (p=0.001). Similarly, K2 increased from 49.42 ± 4.57 D to 52.03 ± 5.11 D, with a mean change of +2.61 D (p=0.001). Mean keratometry increased from 47.09 ± 3.91 D to 49.22 ± 4.09 D, corresponding to a mean increase of +2.13 D (p=0.001). Pachymetric outcomes remained statistically stable over six months. Central pachymetry showed minimal change from 483.60 ± 54.54 µm to 482.67 ± 55.24 µm (p=0.753). Although thinnest pachymetry decreased from 461.62 ± 55.09 µm to 453.48 ± 54.62 µm (mean change −8.14 µm), this did not reach statistical significance (p=0.056). Mean pachymetry also remained stable (473.50 ± 52.72 µm vs 468.94 ± 53.29 µm; p=0.082). Collectively, these findings indicate significant functional visual improvement at six months with pachymetric stability, while keratometric indices exhibited statistically significant increases over the same interval.

DISCUSSION

This quasi-experimental before–after study evaluated short-term functional and tomographic outcomes six months after epithelium-on accelerated corneal collagen cross-linking (CXL) in a young keratoconus cohort. The key findings were (i) statistically significant improvement in both uncorrected and corrected visual acuity and (ii) pachymetric stability of central and mean corneal thickness, while (iii) keratometric indices (K1, K2, and mean K) demonstrated statistically significant increases. Collectively, these results suggest that early functional improvement can occur following CXL even when keratometric parameters do not show the classic flattening response that is often emphasized in the literature.

The observed improvement in visual acuity is consistent with the broader evidence supporting CXL as a biomechanical stabilization therapy that can translate into better optical performance, particularly when progression is halted and irregular astigmatism becomes less visually disruptive over time (4). In the present study, UDVA improved by 0.36 logMAR and CDVA improved by 0.23 logMAR at six months, which aligns directionally with reports showing that accelerated CXL—especially when applied early in disease—may improve visual function and reduce dependence on high-order correction (6,10,11). Although some long-term studies report a more pronounced gain in best-corrected acuity in adolescents and pediatric populations over 1–10 years, these improvements are not always immediate and may evolve with ongoing remodeling (6,11). Therefore, the magnitude and timing of improvement in this cohort, assessed at six months, is clinically meaningful and supports the functional benefit of CXL as a progression-modifying treatment rather than as a refractive procedure (4,12).

DOI: https://doi.org/10.61919/c5g1qn63

Pachymetric parameters in this study remained statistically stable at six months, with no significant change in central or mean pachymetry, and only a borderline reduction in thinnest pachymetry that did not reach statistical significance. This finding is clinically important because corneal thinning after CXL has been reported in some cohorts—particularly with epithelium-off protocols or longer follow-up intervals—and is often interpreted as part of post-treatment stromal remodeling (11,13). In contrast, prospective evidence suggests that ocular surface parameters and topographic indices may remain largely unchanged after CXL, particularly when assessed over shorter follow-up windows and when modern protocols are used (14). Additionally, systematic evidence comparing epithelium-on versus epithelium-off CXL indicates that transepithelial techniques may offer improved safety and comfort while potentially preserving epithelial integrity and reducing early postoperative complications, which may contribute to more stable pachymetry in the short term (5,15). The pachymetric stability observed here supports the procedural safety profile of epithelium-on accelerated CXL in this cohort, although it should be interpreted in the context of small sample size and the absence of long-term serial thickness mapping.

A central interpretive challenge in this manuscript is the statistically significant increase in keratometric indices after CXL. Classical CXL literature frequently reports corneal flattening (reduced keratometry) or stabilization of keratometric progression, particularly when Kmax is included as the principal curvature marker (4,16). However, not all studies demonstrate consistent early flattening, and in certain subgroups—such as advanced keratoconus, younger corneas with aggressive ectasia, or short follow-up windows—keratometric responses may be variable and can include transient steepening or delayed flattening trajectories (6,10,11). Methodological explanations should also be considered: keratometry derived from different platforms (e.g., simulated keratometry versus total corneal refractive power) may yield different trends, and measurement repeatability can be affected by tear film instability, corneal irregularity, or postoperative epithelial remodeling (8,14). Moreover, in accelerated protocols, the depth and uniformity of cross-linking and the extent of biomechanical stiffening may differ from standard Dresden techniques, potentially influencing curvature behavior in the early months (10,11). These considerations emphasize that keratometry alone—particularly without Kmax, posterior curvature indices, or ABCD progression tracking—may not fully capture stability or progression, and the integration of structured staging parameters is recommended when evaluating ectatic change over time (8).

The present findings should be interpreted as demonstrating meaningful visual improvement with pachymetric stability at six months after epithelium-on accelerated CXL, while keratometric behavior warrants cautious interpretation and more robust monitoring. From a clinical perspective, this pattern may still represent beneficial disease control, particularly if the curvature increase reflects measurement differences, short-term remodeling, or inclusion of a sizable proportion of advanced keratoconus eyes, where corneal biomechanics are substantially compromised and early stability may not manifest as flattening (2,6,11). Evidence from long-term cohorts suggests that while many patients remain stable, a proportion—particularly younger patients—may show progression or require repeat intervention, highlighting the importance of structured follow-up and progression criteria (11,15). The American Academy of Ophthalmology technology assessment supports the overall safety and efficacy of CXL in delaying progression but also underscores that outcomes can vary by protocol and baseline disease severity (16). Therefore, future work in local populations should include longer follow-up, standardized progression endpoints (e.g., ABCD staging, Kmax trends, posterior elevation indices), and statistical methods that account for potential bilateral-eye correlation to strengthen causal inference and clinical generalizability (8,16).

Several limitations should be acknowledged. The study used non-probability sampling with a modest sample size and a short follow-up period of six months, which limits detection of longer-term stabilization and refractive remodeling. The analysis was performed at the eye level; when bilateral cases are included, intra-subject correlation can influence variance estimates and may affect p-values if not modeled appropriately. Additionally, the absence of higher-order tomography indices (e.g., Kmax, posterior curvature progression, elevation maps, corneal haze grading) limits mechanistic interpretation of why keratometric indices increased despite improved vision. Nonetheless, the study contributes clinically relevant local evidence demonstrating short-term visual gains and pachymetric safety following epithelium-on accelerated CXL in keratoconus patients managed in a tertiary care setting, supporting the integration of accessible CXL services and structured follow-up pathways (4,16).

CONCLUSION

At six months following epithelium-on accelerated corneal collagen cross-linking, keratoconus patients demonstrated statistically significant improvement in both uncorrected and corrected visual acuity with overall pachymetric stability, while keratometric indices (K1, K2, and mean K) showed statistically significant increases. These findings support short-term functional benefit and corneal thickness safety of the applied protocol, but the atypical keratometric trend highlights the need for structured progression monitoring using comprehensive tomographic endpoints and longer follow-up to confirm true stabilization and to clarify curvature behavior after CXL in this population.

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