Original Article

Visual and keratometric outcomes following corneal collagen cross-linking in keratoconus: an experience from Nepal

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ABSTRACT

Background: Keratoconus is a progressive corneal ectasia causing visual impairment, often initially managed using spectacles or rigid gas permeable contact lenses, which do not halt disease progression. Corneal collagen cross-linking (CXL) is the only treatment proven to stabilize the condition. Although its efficacy is well documented globally, data from Nepal are limited. This study evaluated visual and keratometric parameters before and after CXL in Nepali patients with varying severities of keratoconus.

Methods: This retrospective, hospital-based study analyzed visual acuity and keratometric outcomes in patients with keratoconus who underwent epithelium-off CXL at Biratnagar Eye Hospital, Biratnagar, Nepal, between January 2019 and March 2023. Secondary data were extracted from medical records. Only eyes with minimum corneal thickness ≥ 400 µm were included. Patients were classified into Amsler–Krumeich stages I–IV. Pre- and 1-month post-CXL assessments included uncorrected and best-corrected distance visual acuity (UCDVA and BCDVA, respectively) both recorded in logarithm of the minimum angle of resolution, keratometry, slit-lamp biomicroscopy, corneal topography, and fundus evaluation.

Results: A total of 195 eyes from 106 patients with keratoconus were analyzed; 84.0% (n = 89) underwent bilateral CXL. The mean (standard deviation [SD]) age was 19.4 (4.9) years, with most (n = 43, 40.6%) aged 16–20 years. Male patients comprised 71.7% (n = 76) of the cohort. The mean (SD) follow-up duration after CXL was 7.5 (2.6) months. Following CXL, overall BCDVA improved, with statistically significant gains in stages I and IV (both $P < 0.05$). UCDVA significantly improved in stage II ($P < 0.05$). In stage I and II eyes, the average keratometry became flatter by –0.4 D and –0.2 D, respectively (both $P < 0.05$). The mean average keratometry remained comparable to baseline in stage III and IV eyes (both $P > 0.05$).

Conclusions: CXL is effective in stabilizing keratoconus in Nepali patients, particularly in early stages. Significant improvements in BCDVA, as well as keratometric flattening, were observed in stage I and IV and in stage I and II eyes, respectively. Although advanced-stage eyes (III and IV) showed keratometric stability without significant flattening, the results suggest that CXL can slow or halt disease progression even in later stages. These findings highlight the importance of early diagnosis and timely intervention. Further prospective, multicenter studies are warranted to optimize treatment protocols and expand the understanding of CXL outcomes in this patient population.

KEYWORDS

keratoconus, corneal collagen cross-linking, ultraviolet therapies, ultraviolet A, vitamin B2, corneal topographies, visual acuities

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INTRODUCTION

Keratoconus is a progressive, non-inflammatory, ectatic disorder of the cornea featuring localized stromal thinning and conical protrusion, leading to irregular astigmatism and progressive visual impairment [1-3]. The condition typically presents during the second decade of life [1, 4] and progresses variably depending on individual risk factors and environmental influences [3, 4].

Globally, the reported prevalence of keratoconus is approximately 50–230 per 100 000 individuals, although newer diagnostic modalities suggest higher rates, with incidence estimates ranging from 2530–3333 per 100 000 in certain populations [5-9]. Prevalence also varies significantly across geographical regions and ethnic groups, with higher rates reported in South Asian, Middle Eastern, and Black populations [6-8].

Initial management of keratoconus often involves spectacles to correct refractive error; however, as the disease progresses and irregular astigmatism increases, rigid gas permeable (RGP) contact lenses are frequently required to achieve acceptable visual acuity [3, 10, 11]. Although RGP lenses improve vision by masking corneal irregularities, they do not alter the underlying biomechanical instability or halt disease progression [10, 11].

In recent years, corneal collagen cross-linking (CXL) has emerged as the only evidence-based intervention shown to slow or halt the progression of keratoconus [12, 13]. This minimally invasive procedure involves the application of riboflavin (vitamin B2) eye drops to the corneal stroma followed by controlled exposure to ultraviolet-A (UVA) light. The resulting photochemical reaction strengthens the corneal collagen matrix by forming additional covalent bonds between collagen fibers, thereby enhancing corneal biomechanical rigidity and stability [14].

Numerous international studies have demonstrated the efficacy of CXL in stabilizing keratoconus, with improvements in visual acuity and corneal topographic parameters [15, 16]. However, there remains a paucity of region-specific data, particularly from low- and middle-income countries such as Nepal [17], where ethnic, environmental, and healthcare system variables may influence disease presentation and treatment outcomes.

Therefore, we evaluated the efficacy of CXL in Nepali patients with varying severities of keratoconus by comparing pre- and post-treatment visual acuity and keratometric parameters at a tertiary eye care center.

METHODS

This hospital-based retrospective study evaluated pre- and post-CXL visual acuity and keratometric parameters in patients with keratoconus who underwent CXL between January 2019 and March 2023 at Biratnagar Eye Hospital, Biratnagar, Nepal. Ethical approval was obtained from the Institutional Review Committee of Biratnagar Eye Hospital (BEH-IRC-81/A). The study adhered to the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants prior to inclusion, and strict confidentiality was maintained throughout the study. No physical or psychological harm was inflicted on any participant.

This study employed a quantitative approach using secondary data extracted from hospital records maintained by the Contact Lens and Cornea Department of Biratnagar Eye Hospital. A non-probability convenience sampling method was used to identify eligible cases [18]. Patients were included if they had been diagnosed with keratoconus , had undergone CXL, had complete pre- (Figure 1) and post-treatment (Figure 2) data available in the hospital records, and were attending follow-up visits for contact lens evaluation after CXL. Additionally, only patients with a minimum corneal thickness of ≥ 400 μm at the thinnest point were included. Patients who had undergone any ocular surgery other than CXL or had coexisting corneal pathologies (e.g., herpes simplex keratitis) were excluded.

Medical records of patients meeting the inclusion criteria were reviewed, and demographic information, laterality of the eye that underwent CXL, visual acuities, and average keratometry readings before and after CXL were recorded for each treated eye. Patients were stratified into five age groups: 10–15 years, 16–20 years, 21–25 years, 26–30 years, and over 30 years, with the number of patients in each group recorded. Visual acuity assessments included uncorrected distance visual acuity (UCDVA) and best-corrected distance visual acuity (BCDVA), both recorded in logarithm of the minimum angle of resolution (logMAR) notation. Manifest refraction was performed using objective retinoscopy (Heine Beta-200 Streak Retinoscope; Heine Optotechnik, Herrsching, Germany) and refined subjectively. A detailed anterior segment evaluation was conducted using a slit-lamp biomicroscope (SL 800; Carl Zeiss Meditec, Dublin, CA, USA). A detailed fundus examination was performed under the slit lamp with a 90 diopter (D) non-contact lens (Volk Optical, Inc., Mentor, OH, USA). Corneal topography was performed using the Sirius Scheimpflug camera–Placido disc topography system (CSO Costruzione Strumenti Oftalmici Srl, Scandicci, Florence, Italy).

All eyes underwent epithelium-off CXL using a standard protocol, performed by a single experienced specialist to ensure procedural consistency [19-22]. A single postoperative medication regimen was administered to all patients, following established protocols [19-22].

Keratoconus severity was classified using the Amsler–Krumeich classification system, which stratifies the disease into four clinical stages (I–IV) based on topographic, refractive, pachymetric, and slit-lamp findings [23]. Stage I is characterized by eccentric corneal steepening, induced myopia and/or astigmatism < 5 D, mean keratometry ≤ 48 D, presence of Vogt's striae, and absence of corneal scarring. Stage II includes eyes with induced myopia and/or astigmatism between 5 D and 8 D, mean keratometry ≤ 53 D, no central scarring, and minimum corneal thickness ≥ 400 μm. Stage III is defined as induced

myopia and/or astigmatism between 8 D and 10 D, mean keratometry > 53 D, no central scarring, and corneal thickness ranging from 200–400 μm. Stage IV, the most advanced stage, includes eyes in which refraction is not measurable, mean keratometry exceeds 55 D, central scarring or corneal perforation is present, and corneal thickness is < 200 μm [23]. This staging system was applied to categorize patients prior to CXL and to facilitate evaluation of treatment outcomes in relation to disease severity.

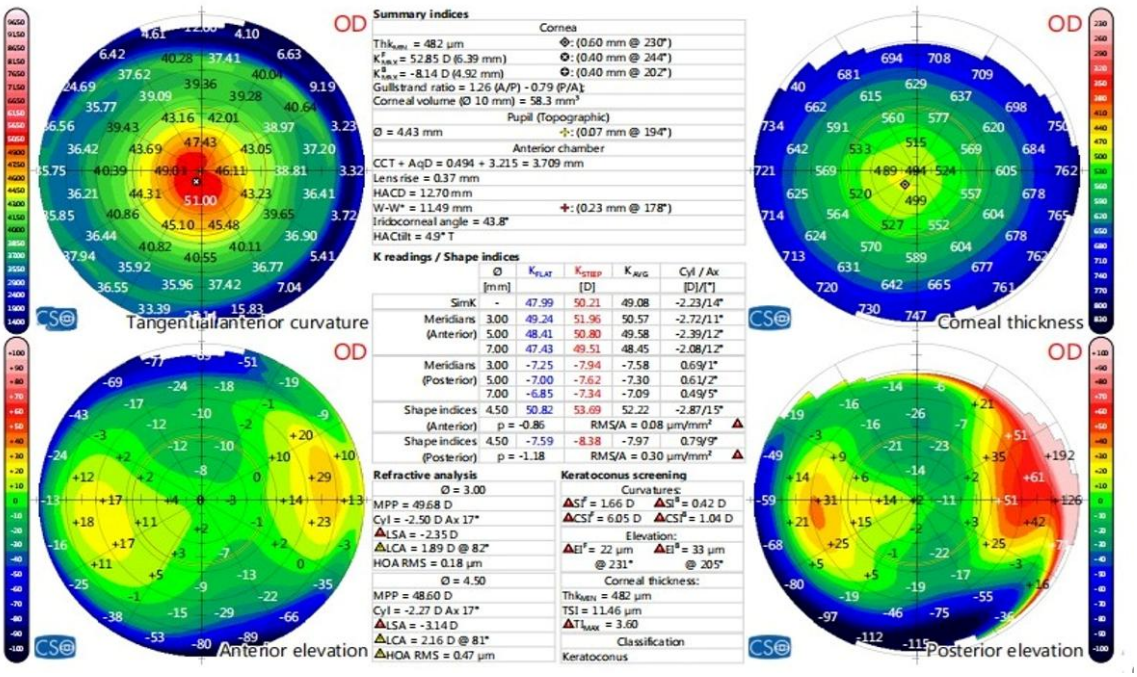

Figure 1. Pre-corneal collagen cross-linking (CXL) corneal topography of a representative eye with keratoconus captured using the Sirius Scheimpflug camera–Placido disc topography system (CSO, Florence, Italy). Elevation and pachymetry maps confirm corneal ectasia with minimum corneal thickness exceeding 400 μm, meeting the minimum safety criteria for CXL.

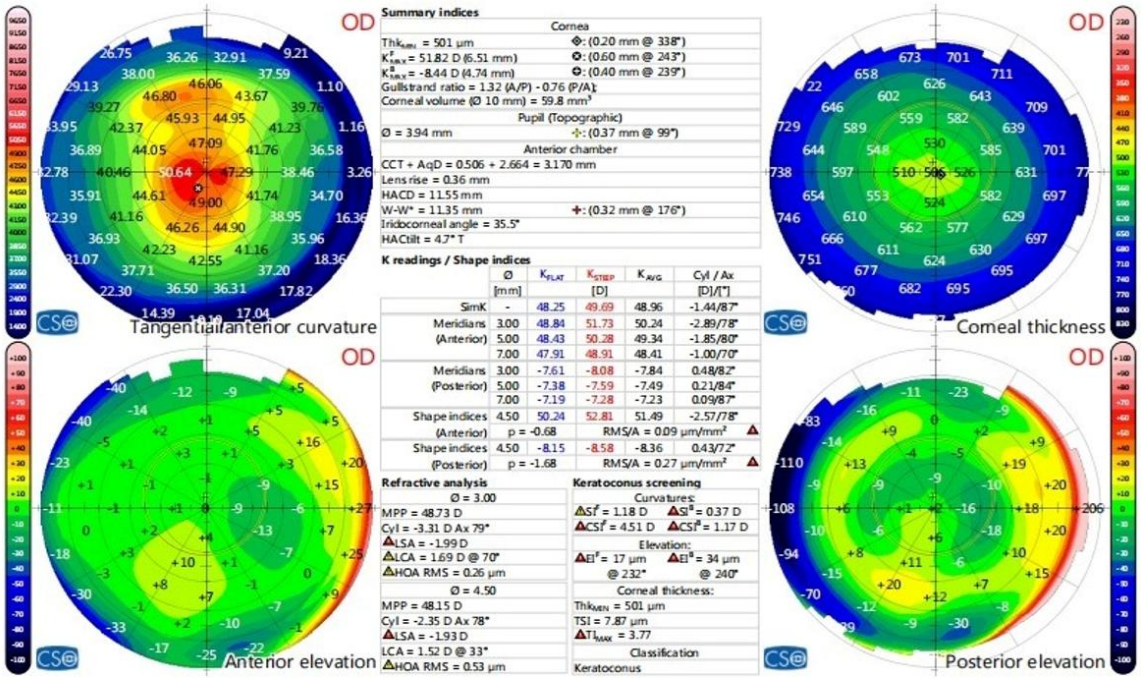

Figure 2. Post-corneal collagen cross-linking (CXL) corneal topography of the same eye at 1-month follow-up, imaged using the Sirius Scheimpflug camera–Placido disc topography system (CSO, Florence, Italy). The topographic map reveals mild central corneal flattening and stabilization of keratometric readings. No progression of ectasia is observed, suggesting early postoperative biomechanical stabilization following epithelium-off CXL [19-22].

Relevant data were extracted from eligible patient records and entered into a Microsoft Excel spreadsheet (Microsoft Corp., Redmond, WA, USA) for analysis. To ensure patient confidentiality, identifying information was recorded on a separate master sheet accessible only to the principal investigator. Each eye that had undergone CXL was individually coded and analyzed. Statistical analyses were performed using IBM SPSS Statistics software, version 20.0 (IBM Corp., Armonk, NY, USA). The Shapiro–Wilk test was used to assess the normality of continuous data distributions. Descriptive statistics are used to summarize the dataset: categorical variables are expressed as frequencies and percentages, whereas continuous variables are reported as means and standard deviations (SDs). Pre- and post-CXL values for UCDVA, BCDVA, and average keratometry were compared using paired *t*-tests. A *P*-value of < 0.05 was considered statistically significant.

RESULTS

A total of 195 eyes with keratoconus were included in the study, comprising 96 right eyes and 99 left eyes. Among the 106 patients, 89 (84.0%) underwent bilateral CXL, whereas 17 (16.0%) received unilateral treatment. The mean (SD) follow-up duration after CXL was 7.5 (2.6) months. Most patients (n = 43, 40.6%) were in the 16–20-year age group (Table 1). The overall mean (SD) age was 19.4 (4.9) years, with ages ranging from 11 to 36 years. The mean patient ages according to keratoconus stage are summarized in Table 2. Most participants were male (n = 76; 71.7%). Sex distribution according to keratoconus stage is detailed in Table 2.

Table 1. Distribution of patients by age group

Age Group	n (%)
10 to 15 y	26 (24.5)
16 to 20 y	43 (40.6)
21 to 25 y	26 (24.5)
26 to 30 y	8 (7.6)
> 30 y	3 (2.8)

Abbreviation: y, years; n, numbers of patients; %, percentage.

Table 2. Demographic characteristics of participants by stage of keratoconus and in all

Stage	Eyes, n (%)	Male / Female, n (%)	Age (y), Mean ± SD
Stage I	108 (55.5)	41 (38.7) / 17 (16.0)	20.3 ±5.3
Stage II	66 (33.8)	25 (23.6) / 10 (9.4)	18.6 ±4.4
Stage III	10 (5.1)	6 (5.7) / 1 (0.9)	16.1 ±3.0
Stage IV	11 (5.6)	4 (3.8) / 2 (1.9)	17.6 ±2.4
Total	195 (100.0)	76 (71.7) / 30 (28.3)	19.4 ± 4.9

Abbreviation: n, numbers; %, percentage; y, years; SD, standard deviation. Note: Keratoconus severity was classified using the Amsler–Krumeich classification system, which stratifies the disease into four clinical stages (I–IV) based on topographic, refractive, pachymetric, and slit-lamp findings [23].

Table 3. Changes in variables of the patients with varying severities of keratoconus who underwent CXL

Stage	Variables	Pre-CXL	1 month Post-CXL	Changes	*P*-value
Stage-I	UCDVA (logMAR), Mean ± SD	0.6 ± 0.4	0.6 ± 0.4	+ 0.1 ± 0.2	0.078
	BCDVA (logMAR), Mean ± SD	0.1 ± 0.1	0.1 ± 0.9	+ 0.02 ± 0.1	**0.002**
	Average K (D), Mean ± SD	46.0 ± 1.5	46.4 ± 2.0	- 0.4 ± 1.4	**0.024**
Stage -II	UCDVA (logMAR), Mean ± SD	0.9 ± 0.4	0.9 ± 0.4	+ 0.1 ± 0.3	**0.012**
	BCDVA (logMAR), Mean ± SD	0.1 ± 0.1	0.1 ± 0.1	+ 0.02 ± 0.1	0.055
	Average K (D), Mean ± SD	50.1 ± 1.3	50.2 ± 1.4	- 0.2 ± 0.6	**0.004**
Stage -III	UCDVA (logMAR), Mean ± SD	1.1 ± 0.4	1.0 ± 0.4	+ 0.1 ± 0.3	0.103
	BCDVA (logMAR), Mean ± SD	0.1 ± 0.1	0.1 ± 0.1	+ 0.02 ± 0.1	0.148
	Average K (D), Mean ± SD	53.8 ± 0.6	53.9 ± 0.9	- 0.1 ± 0.8	0.425
Stage-IV	UCDVA (logMAR), Mean ± SD	1.2 ± 0.4	1.2 ± 0.4	- 0.01 ± 0.2	0.583
	BCDVA (logMAR), Mean ± SD	0.3 ± 0.2	0.2 ± 0.2	+ 0.1 ± 0.1	**0.007**
	Average K (D), Mean ± SD	58.8 ± 3.2	58.1 ± 3.4	+ 0.8 ± 2.5	0.098

Abbreviation: CXL, corneal collagen cross-linking; UCDVA, uncorrected distance visual acuity; logMAR, logarithm of the minimum angle of resolution; SD, standard deviation; BCDVA, best-corrected distance visual acuity; K, keratometry; D, diopters. Note: *P*-values < 0.05 are shown in bold; Keratoconus severity was classified using the Amsler–Krumeich classification system, which stratifies the disease into four clinical stages (I–IV) based on topographic, refractive, pachymetric, and slit-lamp findings [23].

Table 3 summarizes the mean values and changes in visual acuity and average keratometry across different stages of keratoconus in the 195 treated eyes. Statistically significant improvement in BCDVA with contact lenses was observed in stage I and stage IV eyes (both $P < 0.05$) at 1 month post-CXL, whereas BCDVA remained stable in stages II and III (both $P > 0.05$). UCDVA improved significantly in stage II eyes ($P < 0.05$) and remained stable in stages I, III, and IV (all $P > 0.05$) (Table 3). Significant reductions in average keratometry were noted in stage I and II eyes (both $P < 0.05$) at 1 month post-CXL, with mean flattenings of –0.4 D and –0.2 D, respectively (Table 3). In contrast, mean keratometry values in stage III and IV eyes remained comparable to those at baseline (both $P > 0.05$), suggesting disease stabilization (Table 3). These findings indicate that CXL is most effective in inducing topographic and visual improvement in early-stage keratoconus and may help arrest progression in more advanced stages.

DISSCUSSION

This study evaluated the visual and keratometric outcomes of CXL in Nepali patients with keratoconus across all clinical stages. Our findings demonstrate that CXL is most effective in early-stage disease, with significant improvements in vision and keratometric flattening in early stages. In contrast, stage III and IV eyes exhibited keratometric stability without significant regression, suggesting that, although CXL may not reverse advanced disease, it can still halt progression. These results highlight the importance of early diagnosis and timely intervention in preserving visual function.

CXL is a promising intervention for biomechanically stabilizing the corneal stroma and preventing ectatic progression [24-27]. In our cohort of 195 eyes, most were in early stages (stage I: 108 eyes; stage II: 66 eyes), with a marked male predominance (n = 76, 71.7%), consistent with findings in prior studies [28, 29]. Preoperative and follow-up assessments included UCDVA, BCDVA, and topographic analysis. Statistically significant improvement in BCDVA was observed in stage I and IV eyes, whereas UCDVA improved significantly in stage II. Keratometric flattening was evident in stage I and II eyes (–0.4 D and –0.2 D, respectively), whereas advanced stages remained stable. These outcomes align with previous reports demonstrating the efficacy of CXL in improving or stabilizing visual and topographic parameters in keratoconus [30-32].

Our findings corroborate the conclusions of a Cochrane systematic review [33], which reported that CXL may reduce the risk of keratoconus progression, particularly in early disease, although the evidence quality was low because of variability in trial designs and outcomes. Compared to the randomized controlled trials reviewed [33], our study included a wider patient age range, applied a standardized epithelium-off CXL protocol, and demonstrated a low rate of adverse events. Notably, no serious complications were observed, supporting the safety and feasibility of CXL in resource-limited clinical settings. This real-world evidence further supports the early use of CXL and underscores the need for broader implementation, particularly in regions with high disease burden.

A key strength of this study lies in its relatively large sample size and inclusion of all stages of keratoconus, enabling a stage-specific analysis of outcomes. Standardized treatment protocols and consistent postoperative follow-up enhanced the internal validity of the results. However, the retrospective design and single-center setting limit the generalizability of our findings. The lack of long-term follow-up precludes inferences of sustained efficacy beyond 1 year. Additionally, detailed sociodemographic data and allergy history were not documented, which may have influenced disease presentation and progression. Selection bias and incomplete records are also potential limitations. Further multicenter, prospective studies with extended follow-up and incorporation of corneal biomechanical parameters are warranted to validate these findings and support the development of region-specific clinical guidelines.

CONCLUSIONS

This study provides important region-specific evidence of the efficacy of CXL in halting the progression of keratoconus among Nepali patients, particularly in early stages. Among 195 treated eyes, significant improvements in visual acuity and keratometric stability were observed, particularly in early-stage disease. Average keratometry readings flattened significantly in stage I and II eyes, reflecting a measurable biomechanical response to CXL in the earlier stages of keratoconus. Stage III and IV eyes maintained topographic stability without significant flattening, indicating that, although structural progression may be slowed, reversal of corneal steepening is less likely in advanced disease. These findings reinforce the value of timely intervention with CXL to preserve visual function and stabilize corneal architecture in keratoconus. Considering the younger age distribution and male predominance in our cohort, early screening and timely referral remain critical in these high-risk populations. Further prospective studies with longer follow-up periods and broader geographic Nepalese representation are warranted to expand on these findings, guide national protocols for keratoconus management, and optimize outcomes for patients with keratoconus in Nepal.

ETHICAL DECLARATIONS

Ethical approval: Ethical approval was obtained from the Institutional Review Committee of Biratnagar Eye Hospital (BEH-IRC-81/A). The study adhered to the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants prior to inclusion, and strict confidentiality was maintained throughout the study. No physical or psychological harm was inflicted on any participant.

Conflict of interests: None.

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