

Keratometric and Visual Outcome post Corneal Cross-Linking in Keratoconus Patients

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ABSTRACT

Background: Keratoconus is a bilateral, primary, progressive, non-inflammatory, and non-symmetric corneal ectasia induced declined visual acuity in young adults. It leads to continued myopia and irregular astigmatism, causing a reduction in best-corrected visual acuity (BCVA) and visual quality. Corneal Collagen Cross-linking (CXL) has progressively become a preferable cure tool and the frontline of therapy for keratoconus and other corneal ectatic illnesses. It creates a crossed bridge between the collagen fibrils (cross-linking), thus strengthening the Cornea.

Aim of the Work: This work purposes to assess the efficacy of CXL on eyes with keratoconus as regards uncorrected visual acuity (UCVA), best-corrected visual acuity (BCVA) keratometric readings.

Patients and Methods: This non-randomized, prospective, interventional study included twenty eyes of eighteen patients with mild and moderate degree keratoconus. All patients were subjected to complete ocular examination and Pentacam examination. CXL was done under surface anesthesia. Changes in UCVA, BCVA, and keratometric readings that follow CXL were evaluated.

Results: Mean \pm SD of UCVA, BCVA, SE, KI, K2. Preoperatively for the 20 eyes were 0.25 ± 0.18 , 0.51 ± 0.21 , 7.95 ± 4.66 , $46.93D \pm 2.35$, $51.90D \pm 3.55$ respectively. At the end of the follow-up period (Three months post-operatively), they were 0.28 ± 0.20 , 0.59 ± 0.21 , -7.73 ± 4.10 , 46.75 ± 2.23 , 51.75 ± 3.63 , respectively. No serious complications were reported in this study. Only two eyes (10%) showed mild corneal haze. They persisted until the study was finished. Two eyes (10%) showed delayed re-epithelization up to one week.

Conclusion: The CXL is an effective and safe technique for treating mild to moderate keratoconus, regarding stabilizing the condition and improving the visual outcome, regardless of the keratometric changes.

Keywords: Keratoconus, Corneal collagen cross-linking, Keratometric readings, Pentacam, Visual acuity.

INTRODUCTION

Keratoconus is a progressive, bilateral, asymmetric, and non-inflammatory ectasia. This disease is caused by continuing biomechanical instability of the Cornea, resulting in irregular astigmatism and progressive myopia, eventually induced a reduction in best-corrected visual acuity (BCVA) and visual quality⁽¹⁾. Keratoconus typically presents at puberty and progresses until the third and fourth decades of life. It progress more rapidly in young, although it can occur or progress at any age with various rates⁽²⁾.

The aetiology of Keratoconus is probably multifactorial (genetic and environmental)⁽³⁾. Most genetic researches approve of an autosomal dominant inheritance paradigm⁽²⁾. Most cases of keratoconus are sporadic, with family history demonstrated in about 6 to 10 %⁽⁴⁾.

The available options for managing keratoconus are glasses, corneal collagen cross-linking (CXL), contact lenses, epikeratoplasty, and intrastromal corneal ring segments corneal transplantation. Not until 1999 where CXL was introduced were corneal ectasia's underlying pathogenic mechanisms addressed. Using UVA light of 370 nm wavelength and the photosensitizer riboflavin, CXL has been defined as an innovative

new treatment efficacious in restricting the progression of keratoconus, leading to corneal strengthening⁽⁵⁾.

Patients of keratoconus may report that their eyes itch and have allergies, and they frequently rub their eyes with greater force than normal and a decrease in visual acuity. They every so often complain of visual discomfort similar to those with uncorrected astigmatism. Due to the distortion, they may report glare or halos around lights, particularly at night, ghost images, monocular diplopia, and multiple images. There are many areas of the Cornea having different refracting powers producing various confusing photos⁽⁶⁾. One of the first clues that something is wrong is the change in the patient's refraction⁽⁷⁾.

Keratoconus is divided into advanced, moderate, and mild⁽⁸⁾:

In mild keratoconus, there may be oblique astigmatism and moderate-to-high myopia. Diagnosis can be validated with computer-assisted videokeratography, which may disclosed low corneal steepening (almost 80% of keratoconus cases), central corneal astigmatic steepening (about 15% of keratoconus cases), or even bilateral temporal steepening (extremely rare)⁽⁹⁾.

In moderate keratoconus, usually one or more corneal signs are present including typically high keratometry values to 45.00-52.00 D, enhanced appearance of the corneal nerves, Vogt's striae in 40% of eyes, Fleischer's ring (Iron deposition in the basal epithelial cells at the cone base) in 50% of eyes, superficial corneal scarring in 20% of eyes, deep stromal scarring may occur, paraxial (usually inferior to the pupil) stromal thinning, distortion of the retinoscopy and direct ophthalmoscope red reflex, Munson's sign may be noted⁽⁹⁾.

In advanced keratoconus, keratometry values are 52.00 D or more, with enhancement of all corneal signs and symptoms. Vogt's striae are seen in about 60% of eyes, in addition to Fleischer's ring and/or scarring are noticed in about 70% of eyes. Besides, acute corneal hydrops may take place⁽⁹⁾.

Investigations of keratoconus include, Keratometry, Photokeratoscopy⁽⁶⁾, Computer-assisted Videokeratoscopy⁽¹⁶⁾, Placido-disc Topography systems⁽⁶⁾, The Orbiscan⁽¹⁰⁾ and Pentacam. The major criteria of diagnosis of keratoconus by Pentacam include, anterior elevation >15 μm above the best fit sphere, posterior elevation >20 μm , the difference between the thinnest location and pachymetry at the apex in pachymetry map is more than 10 μm , and the pachymetry progression is >1.5 μm ⁽¹¹⁾.

The main objective of the treatment of keratoconus is the prevention of the disease's progression. Treatment modalities include, glasses and contact lenses⁽¹²⁾, corneal Collagen Cross-linking (CXL)⁽¹³⁾. The mechanism of action of CXL is through the effect of UVA irradiation on the riboflavin molecules producing oxygen-free radicals that are linked to two collagen fibrils. It creates a crossed bridge between the collagen fibrils (cross-linking), thus strengthening the Cornea⁽¹³⁾. The main adverse effect of CXL is the corneal haze that may continue for months and usually resolves after 3-9 months⁽⁵⁾.

Other treatment modalities include, intracorneal Ring Segments⁽¹⁴⁾⁽¹⁵⁾, toric and Phakic Intraocular Lenses⁽¹⁶⁾ and keratoplasty⁽¹⁷⁾.

AIM OF THE STUDY

This study aims to assess the efficacy of CXL on eyes with keratoconus regarding best-corrected visual acuity (BCVA), uncorrected visual acuity (UCVA), and keratometric readings.

PATIENTS AND METHODS

This prospective, non-randomized, interventional study was held at Al-Zharaa University Hospital, in the period between April, 2012 and December, 2012. It included twenty eyes of eighteen patients, nine females (50%) and nine males (50%) with mild and moderate degree keratoconus.

Ethical approval:

The study was approved by the Ethics Board of Al-Azhar University and an informed written consent was taken from each participant in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria:

Patients were qualified for inclusion in this study if they fulfill the following criteria:

- Age older than 18 years and less than 40 years.
- The degree of keratoconus is mild to moderate.
- Clear Cornea.
- Maximum K-reading less than 60D (as measured by Pentacam).
- The least corneal thickness (as measured by Pentacam) is more significant than 400 μm .

Exclusion criteria:

Patients were disqualified from participating in this study if one or more of the following criteria were reported:

- Prior corneal surgery.
- Other corneal pathology (e.g., herpes simplex keratitis).
- Corneal scarring.
- Pregnancy.
- Systemic collagen diseases.
- Most negligible corneal thickness less than 400 μm .
- Concurrent infections.
- Poor epithelial wound healing history.
- Severe dry eye.

All patients were subjected to the following:

Complete ocular examination comprising uncorrected visual acuity (UCVA), manifest and cycloplegic refraction (using 1% cyclopentolate eye drops), best-corrected visual acuity (BCVA), indirect ophthalmoscopy, slit-lamp examination, and Pentacam examination. UCVA and BCVA were reported in the Decimal visual acuity scale, slit lamp examination for the anterior segment, applanation tonometry, indirect ophthalmoscopy and Pentacam examination. Contact lenses were removed at least two weeks before the Pentacam test.

Technique

Before treatment, the CXL system Opto XLink parameters are adjusted as follows: time: 30 min, irradiation: 3.0 mW/cm^2 (Power density: 0.5 mW/cm^2), spot size: 8mm, distance between eye and UVA source 4.5cm.

Surgical steps

- A topical anesthetic is applied (Benoxinate hydrochloride).
- Cleaning the eye with Povidone-iodine (betadine®) diluted 1:10.
- Insertion of a lid speculum.
- Removal of the corneal epithelium over 8 to 9 mm diameter mechanically by beaver blade.
- Installation of MEDIO CROSS® Riboflavin isotonic solution (Riboflavin 0.1% in Dextran 20%) was utilized to the Cornea (2-3 drops every 5 min for 30 min).
- After 30 minutes, the anterior segment is checked using a slit lamp with cobalt blue light to check the anterior chamber for the yellow coloration in its contents; if not, instillation of riboflavin solution is continued until the anterior chamber becomes yellow.
- UV-illumination therapy: the patient is positioned under an illumination device. CXL system is turned on and focused (distance between beam aperture and the eye is approximately 45 mm), and the beam diameter is adjusted to corneal diameter (only the de-epithelialized part of the Cornea should be irradiated; to protect limbal stem cells).
- Installation of 2-3 drops of riboflavin isotonic solution every 5 min is continued for 30 min.
- After 30 minutes of UV illumination, the corneal CXL system was switched off automatically.
- Cold BSS (Buffered saline solution) is used to irrigate the cornea.
- Antibiotic eye drops are applied to the Cornea then the Cornea is covered with a bandage contact lens.
- Postoperative topical antibiotics (Gatifloxacin 0.3%, five times daily for one week) topical steroid (fluoromethelone% five times daily for one week), oral NSAIDs (Sodium diclofenac) 50mg 2 times daily after meal if in the first day, Refresh plus eye drops four times daily after removal of contact lens, and oral Ascorbic acid (vitamin C tab 500 mg 2 times daily for one week).
- The patient is followed up closely until the Cornea is epithelialized.

Postoperatively, patients were instructed to wash hands thoroughly before administering any

eye drops, to sleep wearing acrylic ocular during the first week to avoid night traumas, to avoid splashing water in the eye in the first week, not to swim in the first month to prevent corneal infection, not to practice sports that might involve the contact with the ball or other players for three months, and to wear sunglasses when exposed to the solar light for three months.

Patients were examined after one, two, three, and five days and after one, two, and three months after CXL. Pentacam examination was requested again at 1,2 and 3 months after CXL

Table (1): Post-operative follow-up dates and recorded data

Test	DI	D2	D3	D5	M1	M2	M3
UCVA					*	*	*
BCVA					*	*	*
Slit lamp	*	*	*	*	*	*	*
Pentacam examination					*	*	*

Statistical analysis

The data collected were analyzed using SPSS for Windows version 25, using one-way Anova, followed by the LSD test. The results represented as mean ± SD. Level of significance (P-Value) was as follow: Non-significant (if P > 0.05), significant (P ≤ 0.05), and highly significant (P ≤ 0.01).



(Fig. 1) Opto Xlink System .



(Fig. 2) Only few surgical instruments are needed for CXL

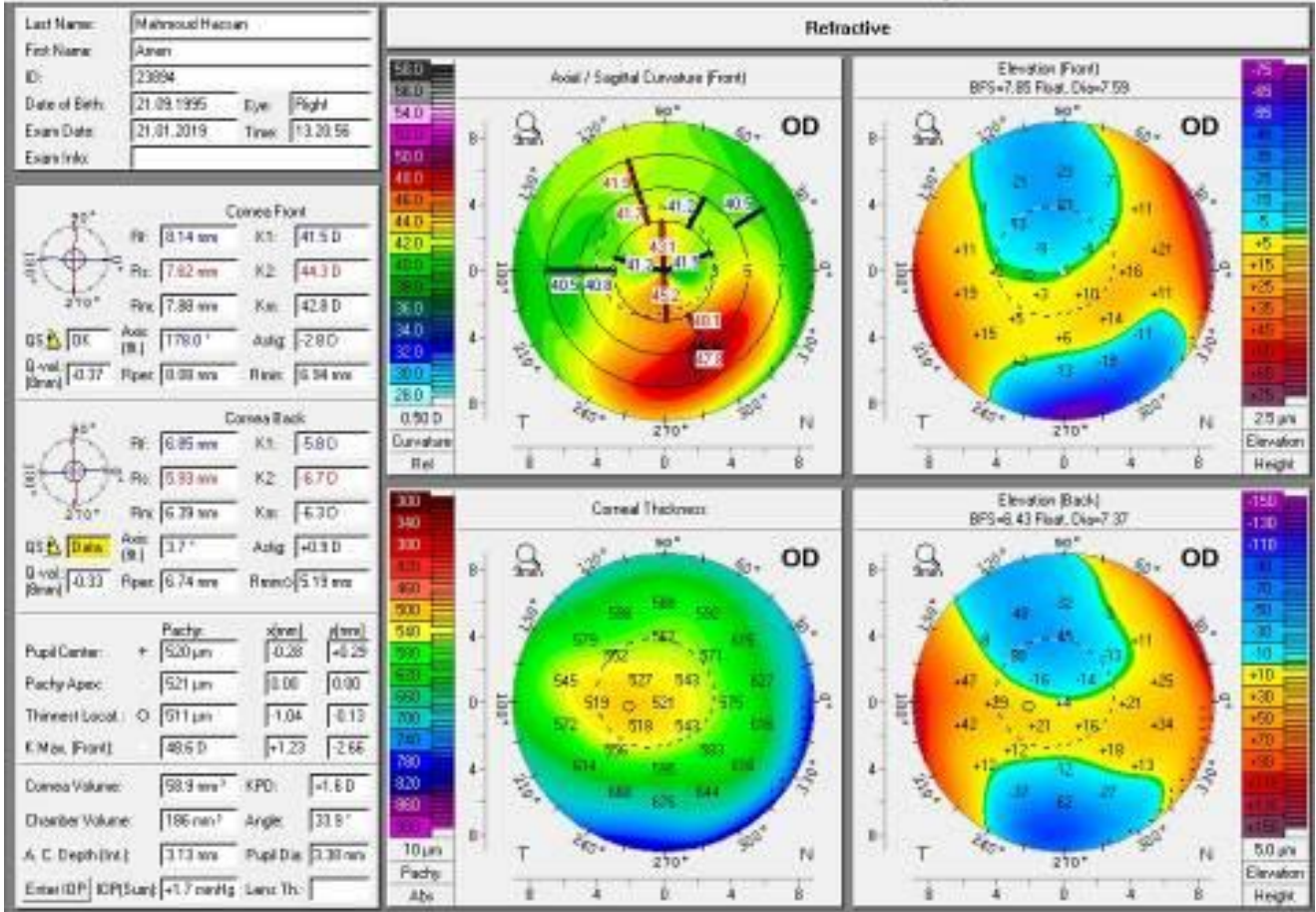


(Fig. 3) Riboflavin ampule



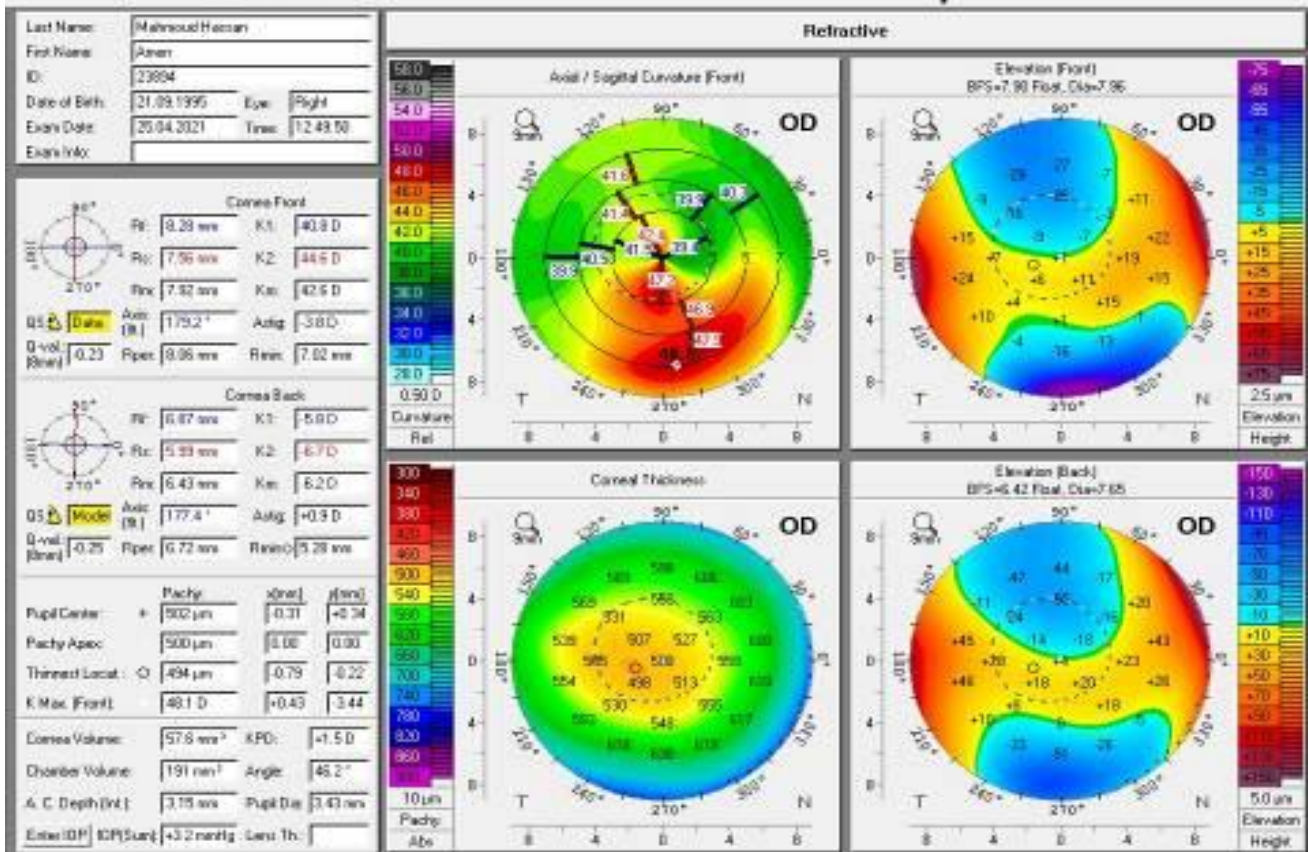
(Fig. 4) Fluorescence of the riboflavin-saturated cornea during illumination with UVA

WAVELIGHT - ALLEGRO OCULYZER 4 Maps Refractive



(Fig. 5) Pentacam (Four map display) preoperatively of eye No.9. K1=41.5, K2=44.3

WAVELIGHT - ALLEGRO OCULYZER 4 Maps Refractive



(Fig. 6) Pentacam (Four map display) 3 months preoperatively (the end of follow up period) of the same eye (Eye No.9). K1=41.5, K2=44.3

RESULTS

Twenty eyes of 18 patients had CXL. Nine eyes of nine males (45%) and eleven eyes of nine females (55%) were included in this study. Two female patients (10%) had bilateral CXL. Their mean age \pm SD was 24.15 ± 4.11 years (Range: 18- 32years).

Table (2) represent the mean \pm SD of UCVA, BCVA, SE, KI and K2 Preoperatively for the 20 eyes. Mean UCVA of all the 20 eyes was 0.25; SD was ± 0.18 , ranging from 0.03 to 0.60. Mean BCVA was 0.51; SD was ± 0.21 , range was from 0.3 to 1.00. Mean SE was -7.95; SD was ± 4.66 , range was from -1.00 D to -13.50 D. Mean KI was 46.93D, SD was ± 2.35 , range was from 44.00D to 51.50D. Mean K2 was 51.90D, SD was ± 3.55 , and range was 45.75D to 56.75D.

Table (2): Mean \pm SD, of UCVA, BCVA, SE, K1, K2 Preoperatively

	Mean	\pm SD	Range
UCVA	0.25	± 0.18	0.03-0.60
BCVA	0.51	± 0.21	0.3-1.0
SE	-7.95	± 4.66	- 1.00:-13.50
KI	46.93	± 2.35	44.00-51.50
K2	51.90	± 3.55	45.75-56.75

Table (3) represent the mean \pm SD of UCVA, BCVA, SE, KI, K2, one month postoperatively for 20 eyes, mean UCVA of all 20 eyes was 0.28; SD was ± 0.25 , range was from 0.03 to 1.00. Mean BCVA was 0.49; SD was ± 0.22 , range was from 0.3 to 1.00. Mean \pm SE was -7.80, SD was ± 3.86 , range was from -1.25 D to -13.50 D. Mean KI was 46.79D, SD was ± 2.3 , range was from 43.00D to 46.50D. Mean K2 was 51.87D, SD was ± 3.59 ; range was 45.50D to 56.50D.

Table (3): Mean + SD of UCVA, BCVA, SE, K1, K2 one month postoperative

	Mean	\pm SD	Range
UCVA	0.28	± 0.25	0.03 - 1.00
BCVA	0.49	± 0.22	0.3 - 1.0
SE	-7.80 D	± 3.86 D	-1.25 : -13.50 D
KI	46.79 D	± 2.31 D	43.00-46.00 D
K2	51.87 D	± 3.59 D	45.50 - 56.50 D

Table (4) represents mean \pm SD of UCVA, BCVA, SE, KI, and K2 two months postoperatively for 20 eyes. Mean UCVA of all 20 eyes was 0.28, SD was ± 0.20 , range was from 0.05 to 0.6. Mean BCVA was 0.54; SD was ± 0.21 , range was from 0.3 to 1.00. Mean SE was -7.74 D, \pm SD was ± 3.94 D,

range was from -2.00 D to -14.00 D. Mean KI was 46.77D, SD was ± 2.32 D, range was from 43.50D to 51.25D. Mean K2 was 51.78D, SD was ± 3.58 ; range was 46.00D to 57.00D.

Table (4): Mean \pm SD of UCVA, BCVA, SE, K1, K2 two months postoperatively

	Mean	\pm SD	Range
UCVA	0.28	± 0.20	0.05 - 0.60
BCVA	0.54	± 0.21	0.3 - 1.0
SE	-7.74	± 3.94	-2.00 : -14.00
KI	46.77	± 2.32	43.50-51.25
K2	51.78	± 3.58	46.00-57.00

Table (5) represent the mean \pm SD of UCVA, BCVA, SE, KI, K2, three months postoperatively for 20 eyes. Mean UCVA of all 20 eyes was 0.28, SD was ± 0.20 , range was from 0.05 to 0.60. Mean BCVA was 0.59; SD was ± 0.21 , ranging from 0.3 to 1.00. Mean SE was -7.76, SD was ± 4.07 , range was from -1.75 D to -14.00 D. Mean KI was 46.84D, SD was ± 2.23 D, the range was from 44.00D to 51.00D. Mean K2 was 51.75D, SD was ± 3.63 , ranging from 46.00D to 57.00D.

Table (5): Mean \pm SD of UCVA, BCVA, SE, K1, K2 three months postoperative

	Mean	SD	Range
UCVA	0.28	± 0.20	05 - 0.60
BCVA	0.59	± 0.21	0.3-1.0
SE	-7.76	± 4.07	5 : -14.00
KI	46.84	± 2.23	00-51.00
K2	51.75	± 3.63	00 - 57.00

Table (6) represents mean UCVA \pm SD pre & Postoperatively. Mean UCVA enhanced from 0.25 to 0.28 after the first month and remained stable over the study period. Mean UCVA improvement was one line measured by (automated projector chart) in 8 eyes out of 20 eyes (40%), ten eyes (50%) remain stable, and 2 eyes (10%) showed a decline in UCVA by one line.

Table (6): Mean UCVA \pm SD preoperatively one month, two months, and three months postoperatively.

UCVA	Mean	\pm SD	Range
Pre op	0.25	± 0.18	0.03-0.60
Impost Op.	0.28	± 0.25	0.03- 1.00
2m post-Op.	0.28	± 0.20	0.05-0.60
3m post-Op.	0.28	± 0.20	0.05 - 0.60

Figure (7) represents the graphic changes in UCVA over the study period.

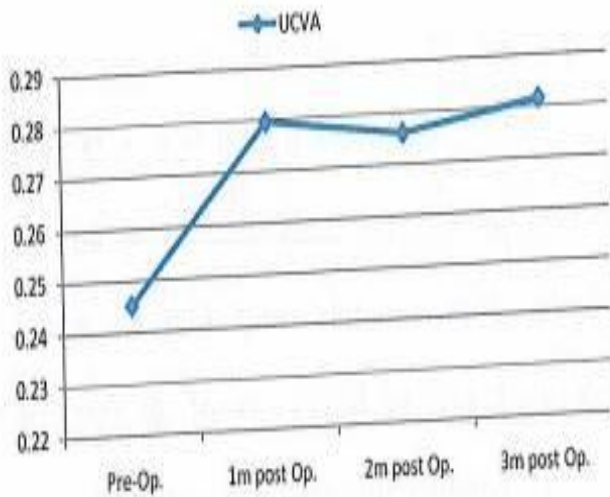


Figure (7): Mean UCVA pre and postoperatively.

Table (7) represent Mean BCVA \pm SD pre & postoperatively. There was a decline in mean BCVA at first-month postoperatively by 0.01, in the second month there was an improvement by 0.04, and in the third month the progress was 0.09. In 6 eyes out of 20 eyes (30%) mean BCVA improved one line, two eyes (10%) improved two lines. Ten eyes (50%) remained stable. Only two eyes (10%) lost one line of BCVA at 3 months follow up. The maximum change in BCVA occurred after the 3rd month.

Table (7): Mean BCVA \pm SD preoperatively one month, two months, and three months postoperatively.

BCVA	Mean	\pm SD	Range
Pre. Op	0.50	\pm 0.21	0.3-1.0
Impost Op.	0.49	\pm 0.22	0.3- 1.0
2m post-Op.	0.54	\pm 0.21	0.3- 1.0
3m post-Op.	0.59	\pm 0.21	0.3- 1.0

Figure (8) represents graphic changes in mean BCVA pre and postoperatively.

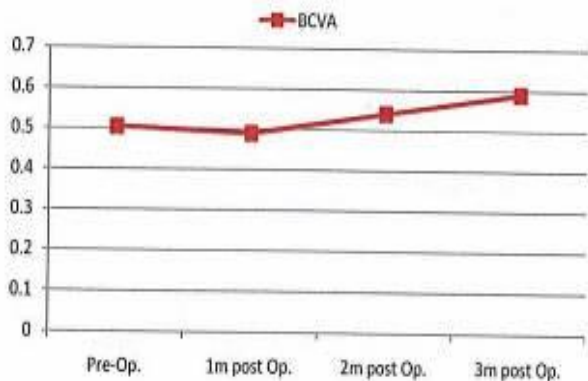


Figure (8): Mean BCVA pre and postoperatively.

Table (8) represent the mean SE \pm SD pre & postoperatively. It showed regression of mean SE by 0.15 D at the first month, 0.21 D at second month and 0.22 D at third month postoperatively. Eight eyes out of 20 eyes (40%) SE decreased by 0.20 D. In 3eyes (15%) SE remains stable, and in 9 eyes (45%) SE increased by 0.25D.

Table (8): Mean ES \pm SD pre and postoperatively

SE	Mean	\pm SD	Range
Pre. Op	-7.95	\pm 4.67	-1 : -14.00
Impost Op.	-7.80	\pm 3.86	-1.25 : -13.50
2m post-Op.	-7.74	\pm 3.94	-2 : -14.00
3m post-Op.	-7.73	\pm 4.10	-1.75 : -14.00

Figure (9) represents the mean SE changes pre and postoperatively.

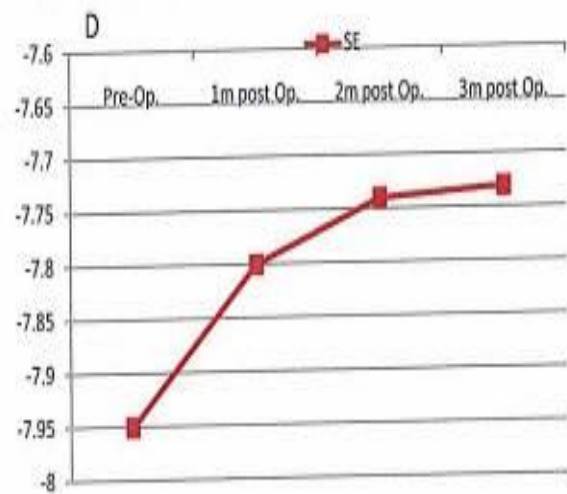


Figure (9): Mean SE pre and postoperatively.

Table (9) represent mean K1 \pm SD pre & postoperatively. Mean K1 decreased by 0.16 D in the first month, 0.17D in the second month and 0.19D in the third month; only six eyes out of 20 (30%) showed a reduction in mean K1 compared by preoperative mean K1 reading. In eight eyes (40%) mean K1 remained stable, and six eyes (30%) mean K1 increased by 0.20D compared with preoperative mean k1.

Table (9): Mean K1 \pm SD pre and post-operatively

Pre. Op	46.94	\pm 2.35	44.00-51.50
Impost Op.	46.78	\pm 2.33	44.00-51.75
2m post-Op.	46.77	\pm 2.32	43.50-51.25
3m post-Op.	46.75	\pm 2.23	44.00-51.00

Figure (10) represent the changes in K1 over the study period

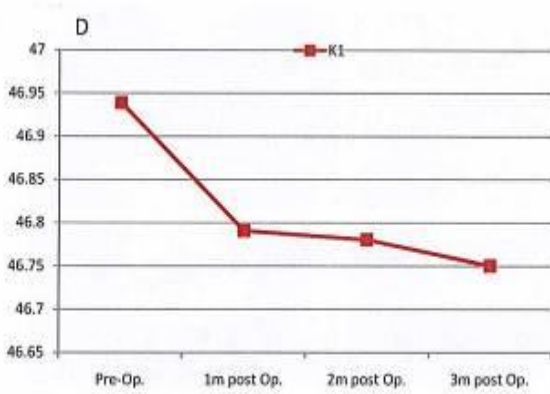


Figure (10): Mean K1 follow up over study period

Table (10) represent Mean K2 ± SD pre & postoperatively. Mean K2 decreased by 0.03 D in the first month, decreased in the second month by 0.12D, and decreased in the third month by 0.15D; mean K2 reduced in 11 eyes out of 20 (55%). The mean K2 remains stable in 7 eyes (35%) and only in two eyes (10%) the mean K2 reading increased compared to the mean preoperative K2 reading by 0.25 D.

Table (10): Mean K2 + SD pre and postoperatively

K2	Mean	±SD	Range
Pre. Op	51.90	±3.55	45.75-56.75
Impost Op.	51.87	±3.59	45.5-56.5
2m post-Op.	51.78	±3.58	46.00-57.00
3m post-Op.	51.75	±3.64	46.00-57.00

Figure (11) represent changes in K2 over the study period

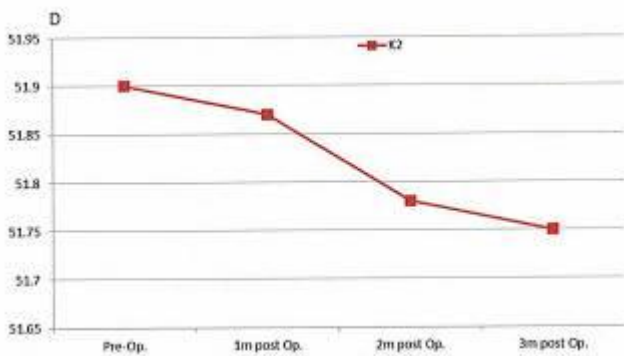


Figure (11): Mean K2 follow-up over the study period.

No severe complications were reported in this study; only two eyes out of 20 eyes (10%) showed mild corneal haze that appeared like a delicate sandy appearance in anterior stroma one month after CXL. They persisted until the study was finished. Despite this soft haze in these two cases, there was no visual

complaint, and the BCVA improved by one line compared to preoperative BCVA. Two eyes out of 20 (10%) showed delayed re-epithelization up to one week. However, no clear causes for this delayed re-epithelization were detected. Patients did not have diabetes, suffer from any chronic illness, are not smokers, or are under long systemic steroids or immune-suppressive treatment.

DISCUSSION

CXL is a promising innovative therapy for keratoconus. CXL is assumed to biomechanically stronger the corneal stroma and, subsequently delayed or even prohibit keratoconus and ectasia's progression. Moreover, in numerous cases CXL enhances the patient visual, topographic, and refractive outcome with a small number of reported complications⁽¹⁸⁾.

Our study included 20 eyes with mild-to-moderate keratoconus. Preoperatively visual acuity topography and refraction consequences were reported in all patients. CXL treatment was done, followed by a three-month follow-up for visual acuity, refractive and keratometric outcomes.

In our study, mean UCVA enhanced from 0.25 to 0.28 after the first month and remained stable over the study period measured by (the automated projector chart), mean UCVA improvement was approximately one line in 8 eyes out of 20 eyes (40%).while in 10 eyes (50%) remain stable and in 2 eyes (10%) UCVA decline by one line.

Vinciguerra et al.⁽¹⁸⁾ studied the effect of CXL on 28 eyes with a follow-up period of 12 months. They reported a significant enhancement in mean UCVA, from 0.77 logMAR preoperatively to 0.57 logMAR 12 months.

Caporossi et al.⁽¹⁹⁾ studied the effect of CXL on 44 eyes with 48 months follow-up period, results revealed a significant enhancement in mean UCVA by 2.41 Snellen lines.

Results of our study regarding UCVA were less than previously reported in *Vinciguerra et al.*⁽¹⁸⁾. Study and *Caporossi et al.*⁽¹⁹⁾ study, although there was an improvement in mean UCVA for many eyes over three months. And this most likely is due to the short study period as the two previous studies mentioned above, and the follow-up was for one year and three years, respectively.

Our study reported a decrease in mean BCVA at the first month postoperatively by 0.01, followed by improvement by 0.04 and 0.09 in the second and third months postoperative. BCVA improved in 6 eyes out of 20 (30%) by one line, in 2 eyes (10%), BCVA improved two lines and in 10 eyes (50%) remain stable. Only two eyes (10%) lost one line of BCVA at three months follow up. The maximum change in BCVA occurs after the third month.

In a study by *Vinciguerra et al.*⁽¹⁸⁾ the mean BCVA improved from 0.28 logMAR to 0.14 logMAR 12 months postoperatively. Similarly, *Caporossi et al.*⁽¹⁹⁾ and *Raiskup-Wolf et al.*⁽²⁰⁾ reported significant enhancements in BCVA (1.34 Snellen lines and 0.08 logMAR respectively), with continued enhancement after one year.

Raiskup-Wolf and colleagues⁽²⁰⁾ analyzed 480 eyes of 272 patients with progressive keratoconus with a maximum follow-up of six years. The BCVA significantly enhanced (> or = one line) in 53% of 142 eyes in the 1st year, 57% of 66 eyes in the 2nd year, and 58% of 33 eyes in the 3rd year or remained stable (no lines lost) in 20%, 24%, and 29%, respectively.

Wollensak⁽²¹⁾ reported with 3- 5 year results of the Dresden clinical study that, all 60 treated eyes had no progression of keratoconus, with 65% of cases having slight visual acuity improvement.

Wittig-Silva et al.⁽²²⁾ randomized controlled trial in Australia 66 eyes of 49 patients with reported progression of keratoconus showed a trend towards improved BCVA in the treated keratoconus eyes compared with that of the controls, which exhibited a continuous decrease.

Our study results regarding BCVA agreed with the previous studies considering that these studies were done with extended follow-up than our study.

Our study showed regression of mean SE by 0.15 D in the first month. 0.21 D at the second month and 0.22 D at the third month postoperatively. In 8 eyes out of 20 (40%), SE decreased by 0.20 D. In 3 eyes (15%), SE remained stable. And in 9 eyes (45%), SE increased by 0.25D.

Vinciguerra et al.⁽¹⁸⁾ with follow up 12 months, *Caporossi et al.*⁽¹⁹⁾ with follow up 48 months, and *Wollensak*⁽²⁰⁾ with follow up period of 48 months reported a decrease in the mean of SE of 0.4 D. 1.87 D. and 1.43 D respectively.

Our study results regarding SE changes in study period w agreed with the mode of the decline of mean SE. Still, our results are a bit pit less than the results of previous studies and this as we mentioned before because of the short follow-up period of our research.

In our study, the mean K1 decreased by 0.16 D in the first month, 0.17 D in the second month, and 0.19D in the third month. 6 eyes out of 20 eyes (30%) showed a reduction in K1 compared to preoperative K1 reading. Eight eyes (40%) K1 remained stable, and six eyes (30%) K1 increased by 0.20D compared with preoperative KI.

Mean K2 decreased by 0.03 D in the first month, 0.12D in the second month, and 0.15D in the third month. The mean k2 decrease in 11 eyes out of 20 (55%). In 7 eyes (35%), the mean K2 remained stable, and in Only two eyes (10%), the mean K2 reading increased compared to preoperative reading by 0.25 D.

This contradicts with the findings of *Caporossi et*

al.⁽¹⁹⁾ and *Raiskup-Wolf et al.*⁽²⁰⁾, who reported a progressive reduction in K values post the one-year follow-up. (The maximal K-readings significantly reduced by 2.68 D in the 1st year, 2.21 D in the 2nd year, and 4.84 D in the 3rd year). Further follow-up is essential to determine whether the maximum K value will remain reduction post 3 months in our study.

Vinciguerra et al.⁽¹⁸⁾, *Caporossi et al.*⁽¹⁹⁾, and *Wollensak*⁽²¹⁾ reported a reduction in the mean K value of 6.07 D, 1.96 D, and 1.46 D, respectively.

Wittig-Silva et al.⁽²²⁾ showed flattening of the steepest simulated K value (K_{max}) by an average of 0.74 D at three months, 0.92 D at six months, and 1.45 D at one year, while in the control eyes mean K_{max} steepened by 0.60 D in 3 months, 0.60 D in 6 months and by 1.28 D after one year.

Our results regarding keratometry reading change over the follow-up period agree with previous studies' results in the regression model. Still, our results reveal that the regression in keratometric readings is less than earlier results due to a short follow-up period.

Regarding topography changes pre and post-CXL, nine eyes (45%) showed mild improvement in topography picture compared with preoperative topography. This improvement became more apparent in the third-month postoperative. The remaining 11 eyes (55%) topography stay the same as preoperative. We noticed no correlation between improvement in UCVA and BCVA and changes in topography. Some patients showed improvement in UCVA and BCVA without changing topography shape. There were no changes in both UCVA, BCVA, and topography shapes.

Greenstein et al.⁽²³⁾ reported in their study that they included 71 eyes, 49 with keratoconus and 22 with post-LASIK ectasia. There were improvements in topographic pattern in all eyes one year after CXL, proposing an general improvement in corneal shape. Nevertheless, no significant correlation was established between topography pattern changes and visual acuity changes after CXL.

Our results agreed to some extent with *Greenstein et al.*⁽²³⁾, considering the short follow-up period of our study.

Regarding reported complications in our study. 2 eyes out of 20 eyes (10%) were complicated by a mild corneal haze that was seen one month after CXL and decreased gradually over the study period but continued till the end of the study, despite the presence of this mild haze in these two cases there was no visual complain and the BCVA was improved by one line in one case and two lines in the second case compared to preoperative BCVA. This haze was treated with topical steroid eye drops. Three times daily for three weeks *Greenstein et al.*⁽²⁴⁾ reported in their study that the corneal haze after CXL is maximal at one month postoperatively. With a continued decrease from 3 months. It is then found to significantly decrease

between 3 and 12 months, besides these changes in haze do not appear to correlate with postoperative clinical outcomes.

We reported that two out of 20 eyes (10%) showed delayed re-epithelialization for more than 4days. In these two eyes, re-epithelialization was completed one week post CXL. These cases were treated by removing bandge contact lenses and applying new ones, increasing the frequency of free preservative lubricant and low preservative antibiotics, and follow-up. After one week, the comeae were completely re-epithelialized. *Helwick* ⁽²⁵⁾ as reported in his study that included 206 eyes, four eyes were complicated by delayed epithelial healing up to 30 days.

CONCLUSION

Collagen cross-linking (CXL) is an effective and safe procedure for treating mild to moderate keratoconus, regarding stabilizing the condition and improving the visual outcome, regardless of the keratometric changes.

RECOMMENDATIONS

We recommend treating mild and moderate keratoconus cases by the collagen cross-linking before we resort to intra-corneal ring segments implantation or corneal transplantation. A large study with large sample size is recommended to obtain more accurate results. A more comprehensive study is recommended to assess the more predictable improvement in visual outcome.

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REFERENCES

1. **Bykhovskaya Y, Margines B, Rabinowitz Y (2005):** Genetics in Keratoconus: where are we? *Eye Vis (Lond)*, 3:16.
2. **Krachmer J (2005):** Non-inflammatory Ectatic Disorders. In Feder R. and Kshetry P (eds), *Cornea*, second ed. Mosby : pp. 1101-05.
3. **Edwards M, McGhee C, and Dean S (2001):** The genetics of keratoconus. *Clin and Experiment Ophthalmol J.*, 29(6): 345-51.
4. **Rabinowitz Y, Wang Y, Rotter J et al. (2000):** Genetic epidemiological study of keratoconus: evidence for major gene determination. *Am J Med Genet.*, 93(5): 403-9.
5. **Sarezyk D, Orlin S, Pan W et al. (2017):** Trends in Corneal Transplantation in Keratoconus. *Cornea*, 36 (2):131-137.
6. **Feder R (1997):** Non-inflammatory ectatic disorders. *Cornea*, 11: 1091-1106.
7. **Yanoff M and Duker J (1999):** Stromal Corneal Dystrophies and Ectasias. In Joel S (ed.), *Ophthalmology*, 2nd. ed. Mosby, Oxford : pp 1-10.
8. **Krachmer J, Feder R, Belin M (1984):** Keratoconus and related noninflammatory corneal thinning disorders. *Surv Ophthalmol.*, 28(4): 293-322.
9. **Zadnik K, Barr J, Gordon M et al. (1996):** Biomicroscopic signs and disease severity in keratoconus. Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study Group, *Cornea*, 15(2): 139-46.
10. **Assiri A, Yousuf B, Quantack A et al. (2005):** Incidence and severity of keratoconus in Asir province Saudi Arabia. *Br J Ophthalmol.*, 89(11): 1403-6.
11. **Belin M (2010):** Keratoconus, Ectasia Detection with the Oculus Pentacam: Belin/Ambrósio Enhanced Ectasia Display. [Http://www.oculus.de/us/downloads/dyn/oculus/presse/176/belin.pdf](http://www.oculus.de/us/downloads/dyn/oculus/presse/176/belin.pdf).
12. **Smiddy W, Hamburg T, Kracher G et al. (2006):** Keratoconus. Contact lens or Keratoplasty?. *Ophthalmol.*, 95(4): 487-92.
13. **Penilli R (2006):** Corneal cross-linking with riboflavin: entering a new era in ophthalmology. *Ophthalmology Times Europe*, 2(7): 211-20.
14. **Lovisolio C, Fleming J, and Pesando P (2002):** In Fabiano E (ed.) *Intrastromal Corneal Ring Segments*, 2nd ed., Canelli. Italy : pp. 133-140.
15. **Silvestrini T, Mathis M, and Loomas B (1994):** A geometric model to predict the change in corneal curvature from the intracorneal ring (ICR). *Invest Ophthalmol Vis Sci.*, 35 : 2023- 58.
16. **Kamiya K, Shimizu K, Ando W (2008):** Phakic toric implantable collamer lens implantation for the correction of high myopic astigmatism in eyes with keratoconus. *J Refract Surg.*, 24(8): 840-2.
17. **Jaycock P, Jones M, Males J et al. (2008):** (UK Transplant ocular tissue advisory group and contributing ophthalmologists), outcomes of same-sizing versus oversizing donor trephines in keratoconic patients undergoing first penetrating keratoplasty. *Ophthalmol.*, 115(2): 268- 75.
18. **Vinciguerra P, Albe E, Trazza S et al. (2009):** Refractive topographic, tomographic and aberrometric analysis of keratoconic eyes undergoing corneal cross-linking. *Ophthalmol.*, 116: 369-78.
19. **Caporossi A, Mazzotta C, Baiocchi S et al. (2010):** Long-term results of riboflavin ultraviolet A corneal collagen cross-linking for keratoconus in Italy: The siena eye cross study. *Am J Ophthalmol.*, 149: 585-93.
20. **Raiskup-Wolf F, Hoyer A, Spoerl E et al. (2008):** Collagen cross-linking with riboflavin and ultraviolet-A light in keratoconus: long-term results. *J Cataract Refract Surg.*, 34:796-801.
21. **Wollensak G (2006):** Crosslinking treatment of progressive keratoconus: new hope. *Curr Opin Ophthalmol.*, 17:356 - 60.
22. **Wittig-Silva C, Whiting M, Lamoureux E et al. (2008):** A randomized controlled trial of corneal collagen cross-linking in progressive keratoconus: preliminary results. *J. Refract. Surg.*, 24: S720-5.
23. **Greenstein S, Fry K, Hersh P (2011):** Corneal topography after corneal collagen cross-linking for keratoconus and corneal ectasia: one-year results. *J Cataract Refract Surg.*, 37:1282-90.
24. **Greenstein S, Fry K, Bhatt J et al. (2010):** Natural history of corneal haze after collagen crosslinking for keratoconus and corneal ectasia: Scheimpflug and biomicroscopic analysis. *J. Refract Cataract Surg.*, 36(12): 2105-14.

Helwick C (2012): Keratoconus cross-linking associated with early complications. [American Academy of Ophthalmology \(AAO\) Annual Meeting.](http://www.medscape.com/viewarticle/774447) <http://www.medscape.com/viewarticle/774447>.