

Pregnancy-induced keractesia – A case series with a review of the literature

Mukesh Taneja, Pravin K Vadavalli¹, Vikas Veerwal², Ruchi Gour³, Jagadesh Reddy¹, Varsha M Rathi¹

We report a case series of patients who developed post-laser-assisted *in situ* keratomileusis (LASIK) ectasia or had a progression of keractesia during pregnancy. We reviewed the medical records of 12 patients (20 eyes) who had reported deterioration of vision during their pregnancy and were diagnosed with keractesia. All 12 patients had experienced symptoms of deterioration of vision between 2 months to 1 year of onset of their pregnancies. A total of 17 eyes of 10 patients had developed post-refractive surgery keractesia. Sixteen of these had undergone LASIK and one had undergone femtosecond lenticule extraction (FLEX). Three eyes of two patients had an exacerbation of keratoconus during pregnancy while one patient had associated hypothyroidism. The results indicate that the hormonal changes that take place in pregnant women can affect the biomechanical stability of the cornea and may trigger the onset of keractesia.

Key words: Keractesia, keratoconus progression, pregnancy, post-LASIK ectasia

There is a consensus among refractive surgeons worldwide that the refractive status of women during pregnancy is not stable, and therefore, refractive surgery is generally avoided during pregnancy or in the immediate postpartum period.^[1]

For more than two decades, refractive surgeons have dreaded the postoperative complication of keractesia seen in some subjects following refractive surgery mainly laser-assisted *in situ* keratomileusis (LASIK) but also seen after photorefractive keratectomy (PRK) and small incision lenticule extraction (SMILE) surgeries. The widely followed Ectasia Risk Score system validated by Randleman *et al.* mentions variables like topographic pattern, predicted residual stromal bed (RSB) thickness, age, preoperative corneal thickness (CT), and manifest refraction spherical equivalent (MRSE) as the possible risk factors for developing ectasia following laser refractive

surgery.^[2] Many reports have been published regarding cases of post-refractive surgery ectasia and many of these have tried to look into the possible risk factors for developing iatrogenic ectasia.^[3,4] Most of these reports did not note any variation in the numbers of ectasia cases among males and females.

However, in the past decade, reports have been published where an association has been noted in female patients developing post-LASIK ectasia when they were pregnant.^[5,6] Herein, we report a case series of 12 female patients presented at our hospital, where we noted a definite relationship between pregnancy and onset or exacerbation of corneal ectasia and also review the literature regarding similar cases reported earlier.

Case Reports

We retrospectively evaluated case records of 12 patients who developed corneal ectasia after LASIK related to their pregnancy or had onset or progression of keratoconus during pregnancy and presented to our tertiary eye care center for evaluation. Their visual acuity and refraction and pachymetry at presentation were noted and tomographs were obtained at presentation to the refractive clinic. This data was compared to the preoperative data wherever available and possible risk factors for ectasia were analyzed.

Twenty eyes of 12 patients had keractesia, the onset or progression of which was related to their pregnancy. All 12 patients had experienced symptoms of deterioration of vision between 2 months to 1 year of onset of their pregnancies. A total of 17 eyes of 10 patients had developed post-refractive surgery keractesia, 16 after LASIK surgery, and one after femtosecond lenticule extraction (FLEX) surgery. Three eyes of two patients had an exacerbation of keratoconus during pregnancy. Only two of the 10 patients had got their refractive surgery done at our center and their preoperative scan was available for review, which did not show any risk factors before getting operated, though the tomography features of patient number one can be considered as borderline. Preoperative scans of the other eight patients were not available for review, and therefore, one cannot comment with surety regarding the absence of any preoperative subclinical ectasia in their preoperative topographic maps. Of the 10 patients, nine had undergone LASIK surgery (eight – keratome-assisted LASIK and one – femtosecond-assisted LASIK), one patient had undergone FLEX surgery. Patient number 2 also gave a history of hypothyroidism. None of these patients had a history of any eye allergies or that of eye rubbing. All the details of the patients regarding their refractive and tomographic parameters and duration between surgery and onset or exacerbation of ectasia are summarized in Table 1. The three representative cases are mentioned below.

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Ophthalmic Eye Center, Janak Puri, New Delhi, ¹Cornea Institute, L V Prasad Eye Institute, KAR Campus, Hyderabad, Telangana, ²L V Prasad Eye Institute, GMRV Campus, Vishakhapatnam, Andhra Pradesh, ³Hajari Hospital, Jogeshwari East, Mumbai, Maharashtra, India

Correspondence to: Dr. Mukesh Taneja, Ophthalmic Eye Centre, C-2C/236A, Janakpuri, New Delhi – 110 058, India. E-mail: mukeshtaneja@yahoo.co.in

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Case 1

A 25-year-old woman presented to our refractive clinic complaining of decreased vision after 4 years of femtosecond laser-assisted LASIK done at our center. At the time of LASIK surgery, she had a stable refractive error of moderate myopia of -3.0 DS/-0.5 DC \times 90° in the right eye and -4.0 DS in the left eye. The patient had a thinnest CT of 589 μ and 594 μ in the right and left eye, respectively and tomography done on Orbscan did not show any suspicious parameters, though the best fit sphere and posterior elevation values could be considered as being borderline [Fig. 1]. The patient had an uneventful Femtosecond laser-assisted (Visumax – Carl Zeis Meditech, Germany) LASIK with Excimer Laser (Wavelight EX500- Alcon, USA). The flap thickness was 120 μ in both eyes with an optic zone of 6.5 mm in both eyes. The residual bed thickness was 386 μ and 370 μ in the right and left eye, respectively. She had an uncorrected visual acuity (UCVA) of 20/20 in both eyes and had a routine postoperative course over the next 3 months without any adverse events. She presented 4 years later after 6 months of delivering a baby, having noticed a slight decrease in her vision in the left eye in the latter part of her pregnancy. Her UCVA was 20/20 in the right eye and 20/60 in the left eye improving to 20/40p with -1.0 DS/-1.0 DC \times 140. In the right eye, the Kmax was 43.3 D and thinnest pachymetry was 483 μ and the left eye showed a Kmax of 46.5 D and thinnest pachymetry of 477 μ . The Oculyzer scan of the left eye showed a mild elevation in posterior float and the possibility of ectasia was considered. As she had a chalazion in her left upper lid, she was asked to

review after 1 month. However, she returned to the clinic after 5 months with her UCVA having dropped to 20/100 in the left eye even though her best-corrected visual acuity (BCVA) and refraction remained the same. The left eye tomography scans showed further increase in K readings with Kmax of 54.4 D and with thinnest pachymetry of 457 μ with elevation in both the anterior and posterior elevation maps with clear evidence of ectasia in the left eye [Fig. 2]. Collagen cross-linking was done for the left eye after which no progression was seen till 1 year of follow-up.

Case 2

A 32-year-old woman from Bangladesh presented to our refractive clinic with a complaint of gradually decreasing vision in both eyes for the past 4 years, having first noticed her symptoms in the latter half of her pregnancy. She was also detected to have hypothyroidism during her pregnancy. She had a history of having undergone keratome-assisted LASIK in both eyes 5 years before her pregnancy for stable refraction of -6.0 DS/-0.50 DC \times 25° and -6.0 DS/-0.50 DC \times 170° in the right and the left eye, respectively. The patient did not have records of her preoperative tomography scans, and therefore, one cannot comment with surety regarding the absence of any preoperative subclinical ectasia in the topography maps but according to her the surgery was uneventful and she had good visual recovery and she never had to wear any glasses till she got pregnant 5 years after the LASIK surgery. At a presentation to our hospital, her UCVA was 20/400 in the

Table 1: Summary of 20 eyes of 12 patients with keractesia

Patient No	Age at presentation (years)	Eye	Diagnosis	Time between surgery and presentation	Time between the onset of pregnancy and increased visual disturbance	BCVA at diagnosis	Refraction (SE) at diagnosis	Kmax at diagnosis	Thinnest pachy (in microns) at diagnosis/ progression	Surgical intervention
1	25	OS	Post-LASIK Ectasia	4 years	6 months	20/40p	-1.5	54.4	457	CXL
2	32	OD	Post-LASIK Ectasia	9 years	6 months	20/25p	-7.75	57.3	385	CXL
		OS	Ectasia			20/25p	-6	53.1	433	CXL
3	29	OS	Keratoconus	NA	2 months	20/50p	-5	58.3	441	CXL
4	25	OD	Post-LASIK Ectasia	4 years	6 months	20/20	-3	52.6	484	NIL
		OS	Ectasia			20/25	-3.25	54.7	412	CXL
5	28	OD	Keratoconus	NA	5 months	20/60p	-4	59.7	446	CXL
		OS				20/60p	-2.5	65.3	415	CXL
6	30	OD	Post-LASIK Ectasia	5 years	6 months	20/25p	-2.25	49.6	473	NIL
		OS	Ectasia			20/40	-2.75	51.3	471	NIL
7	31	OS	Post-LASIK Ectasia	5 years	4 months	20/30	-3.75	52.4	485	NIL
8	37	OD	Post-LASIK Ectasia	13 years	1 year	20/20p	-6.5	51.1	472	CXL
		OS	Ectasia			20/40	-7.25	56.7	412	CXL
9	26	OD	Post-LASIK Ectasia	4 years	1 year	20/100	-16	57.4	459	NIL
		OS	Ectasia			20/30	-13.5	57.1	422	NIL
10	34	OD	Post-LASIK Ectasia	4 years	6 months	20/50p	-5.25	64.2	439	CXL
		OS	Ectasia			20/60	-5	64.6	430	CXL
11	24	OD	Post-FLEX	3 years	6 months	20/30p	-3.5	66	388	CXL
12	37	OD	Post-LASIK Ectasia	13 years	6 months	20/20p	-3	54.2	466	CXL + PRK
		OS	Ectasia			20/20p	-2.75	57.8	461	CXL + PRK

BCVA=Best-Corrected Visual Acuity, SE=Spherical Equivalent, FLEX=Femtosecond Lenticule Extraction

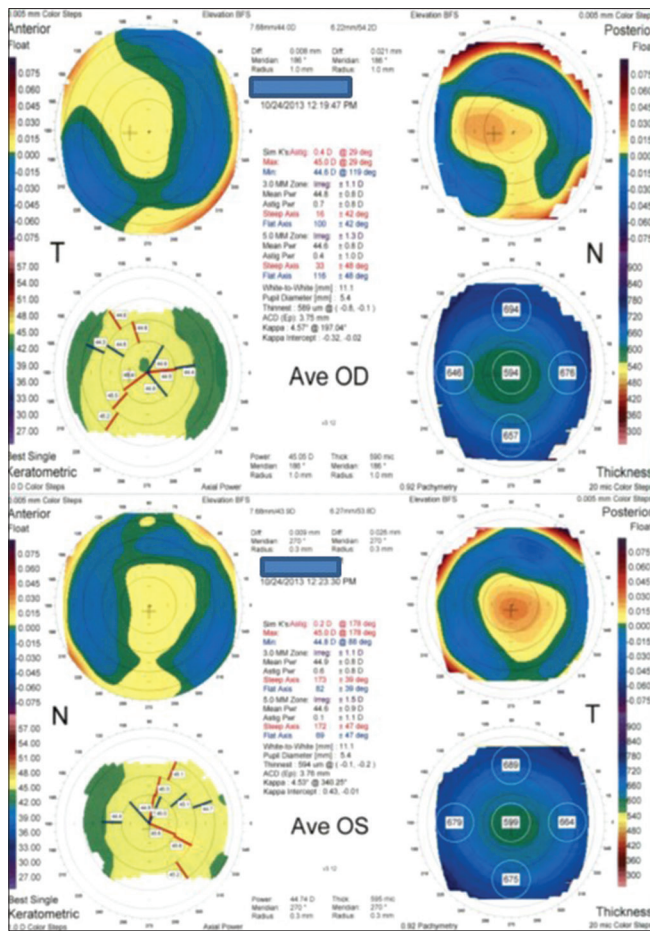


Figure 1: Pre-LASIK Orbscans of Patient No. 1

right eye and 20/320 in the left eye which was improving to 20/25p in both eyes with -6.0 DS/-3.50 DC × 35° in the right eye and -4.5 DS/-3.00 DC × 60° in the left eye. Her tomography scans on Oculyzer showed an obvious keractesia in both eyes with Kmax of 57.3 D in the right eye and 53.1 D in the left eye. Her minimum corneal pachymetry was 385 μm in the right eye and 433 μm in the left eye [Fig. 3]. According to the patient, her vision had been continuously deteriorating over the past 4 years, which pointed towards the progression of keractesia, and as her pachymetry was borderline for corneal collagen cross-linking (CXL). Since she belonged to another country, she was unable to come for regular follow-up, therefore, we decided not to wait to document progression and performed collagen cross-linking in her both eyes 4 days apart and a week later she left for her country.

Case 3

A 29-year-old well-educated woman presented to our clinic after 1 year of delivering a healthy baby with a complaint of gradually decreasing vision in her left eye since the 2nd month of her pregnancy. According to her she had normal vision in both eyes before pregnancy and had never worn glasses in her life before pregnancy. She had consulted a local ophthalmologist recently who prescribed glasses for her and referred her to our center for evaluation of keratoconus. The power of glasses in her right eye was -0.75DC × 85° with BCVA of 20/25. In the left eye, she was using a plano lens and her visual acuity in the left

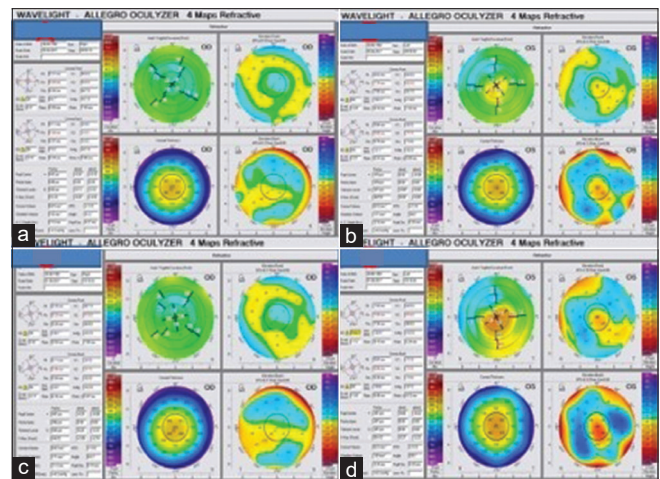


Figure 2: Oculyzer scans of Patient No. 1 after developing post LASIK ectasia in the left eye. (a) 4 maps scan of the right eye (No obvious ectasia) (b) 4 maps scans of the left eye with possible ectasia. (c) 4 maps scan of the right eye on follow-up with no ectasia. (d) 4 maps scan of the left eye on follow-up with progressed ectasia

eye was 20/400. On doing refraction she improved to 20/20p in the right eye with -1.50 DC × 90° and 20/50p in the left eye with -2.0 DS/-6.00 DC × 100° in the left eye. The tomography scan was suggestive of Forme fruste pattern in the right eye with Kmax of 45.8 D and minimum corneal pachymetry of 481 μm. The left eye scan showed obvious keratoconus with Kmax of 58.3 D and minimum corneal pachymetry of 441 μm [Fig. 4]. As the history of continuous deterioration of vision during the pregnancy was pointing towards the progression of keratoconus and she was keen to go for second pregnancy about a year later, we explained the situation to her and did collagen cross-linking for her left eye and advised regular follow-up for the right eye.

Discussion

Ever since the first three cases of post-LASIK ectasia were reported by Seiler *et al.* in 1998, the causes responsible for such adverse events, happening following refractive surgery, particularly LASIK, have remained an enigma for the refractive surgeons and remains a nightmare for both the surgeons and the affected patients.^[3] In an editorial very aptly titled “The riddle of iatrogenic keratectasia,” Koch in 1999 had wondered regarding the reasons and possible risk factors for post-LASIK ectasia and possible strategies to prevent such eventuality in refractive surgery patients.^[4] However, even after two decades of that editorial, the post-LASIK keratectasia remains just that “A Riddle.” The risk factors that were contemplated at that time as causal factors were mainly the quantum of preoperative refractive error, forme fruste keratoconus, and residual bed thickness of fewer than 250 μm. With time and as more cases were reported, more risk factors were added to the list, in a possible endeavor to prevent such cases after refractive surgery. Even after more than two decades, this puzzle of unexplained iatrogenic ectasia after elective refractive surgery remains unraveled. There have been many attempts by many researchers to look into the possible risk factors responsible for post-LASIK ectasia.

Randleman *et al.* proposed an Ectasia Risk Score system which comprised of preoperative topography, RSB thickness, age, preoperative CT, and degree of myopia.^[2] This system is

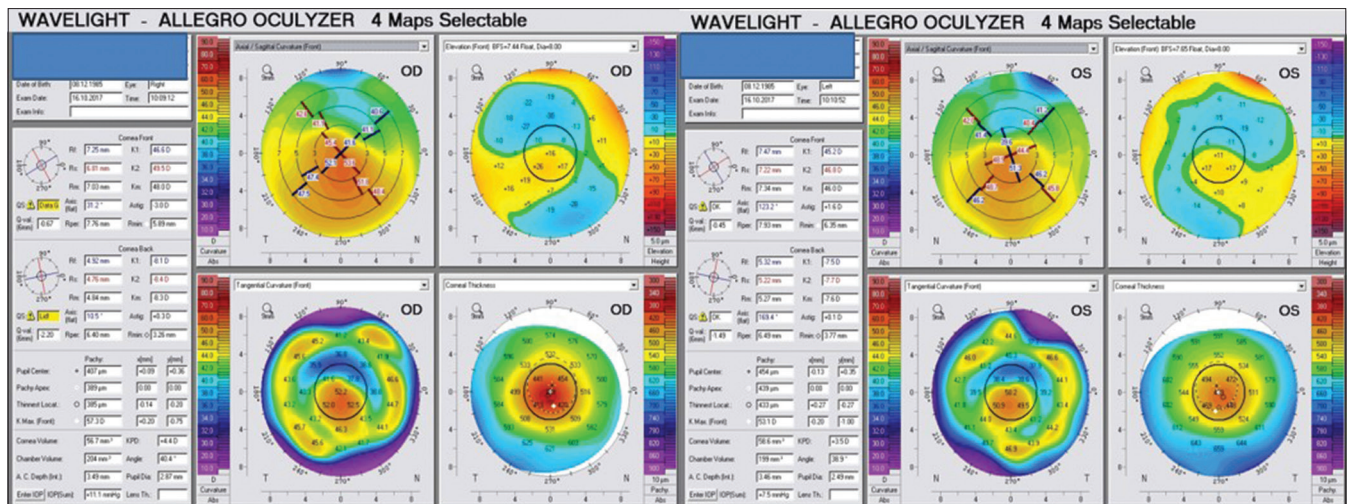


Figure 3: Oculyzer scans of Patient No. 2 with post-LASIK ectasia in both eyes

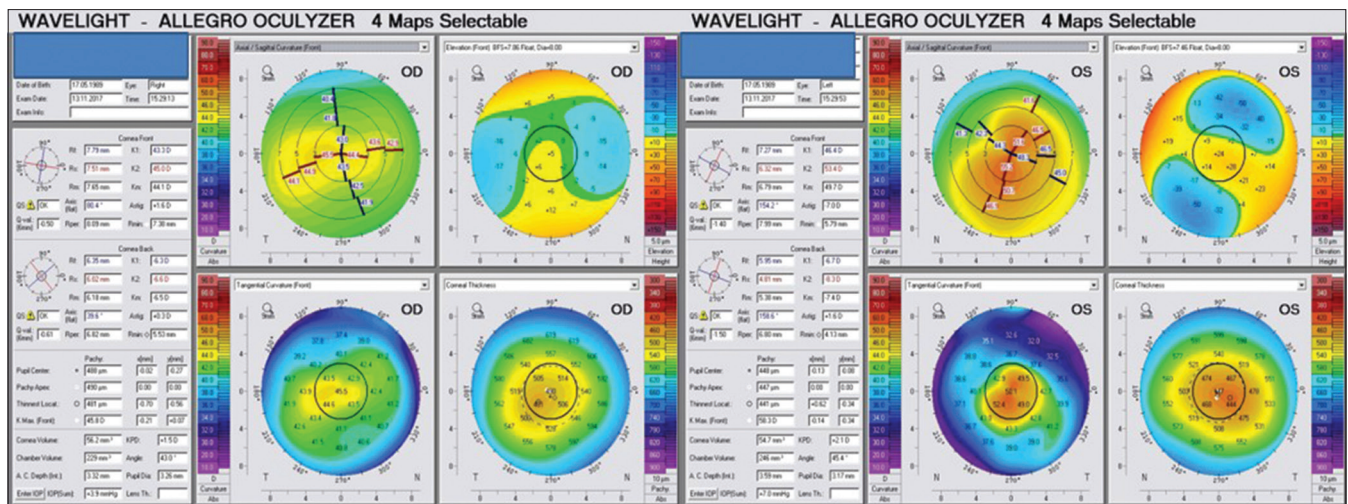


Figure 4: Oculyzer scans of Patient No. 3 with Forme Fruste Keratoconus in the right eye and Keratoconus in the left eye

widely accepted and followed by many refractive surgeons worldwide. Through careful screening of potential candidates for refractive surgery, the number of iatrogenic keractesia cases has decreased but has not been eliminated. And this has led to the belief that there are other unrecognized risk factors which could be causative factors that are involved in the pathogenesis of this complication in some cases of unexplainable ectasia.

It is an acknowledged fact that younger age is a risk for developing post-LASIK ectasia as has been mentioned in many reports. In the Randleman report, the median age of patients with ectasia was 34.4 years whereas the median age of the patients in the control group, without ectasia, was 40 years. Most of these reports did not note any variation in the numbers of ectasia cases between the male and female genders and did not put the female gender at any greater risk of ectasia compared to males. In fact, in the report by Randleman *et al.*, out of 171 patients with ectasia, 59.7% of patients with iatrogenic ectasia were males while the rest 40.3% were females.

However, in the past decade, there have been few sporadic case reports which have reported possible association of pregnancy with the onset of post-LASIK ectasia.

In 2008, Hafezi *et al.* reported a curious case of a woman who had bilateral keratome-assisted LASIK done in both eyes at the age of 33 years, and no apparent risk factors were noted before the surgery. Two years later, in the 7th month of pregnancy, she developed post-LASIK ectasia and underwent CXL in both eyes but during her second pregnancy, an exacerbation in keractesia was noted again in her right eye. This probably was the first time that pregnancy was considered as a possible triggering factor for post-LASIK ectasia in literature.^[5]

About a decade ago, Padmanabhan *et al.* in 2010 reported a case of a 21-year-old woman who developed post-LASIK ectasia in her first trimester of pregnancy after 18 months of an uneventful LASIK with no other preoperative risk factors.^[6] In 2012, Hafezi *et al.* reported five cases of post LASIK ectasia which were noted during the pregnancy of these patients, 4 to 9 years after their LASIK surgery.^[7] In our case series too, all the patients had the onset of post-LASIK ectasia 2 months to 1 year of the start of their pregnancies.

In case number 3, the onset of keratoconus was triggered by a patient's pregnancy who otherwise never had any vision problem before getting pregnant. In patient number 5, the

otherwise stable keratoconus progressed during pregnancy. Bilgihan *et al.* reported seven eyes of four patients in whom, keratoconus had progressed during their pregnancy.^[8] Soeters *et al.* also described two cases of keratoconus which presented for the first time during their pregnancies.^[9]

Park *et al.*, in their study on 24 pregnant women have reported an increase in corneal curvature in the second and third trimester of pregnancy.^[10] These reports give credence to the thought that hormonal changes may affect the corneal biomechanics. Furthermore, Suzuki *et al.* in 2001 reported the presence of estrogen, progesterone, and androgen receptors in human corneas.^[11] In an experimental setup, Spoerl *et al.* demonstrated that *ex vivo* porcine corneas show a distinct reduction in biomechanical stiffness when exposed to high doses of estradiol.^[12]

Some researchers have also noted a relationship between thyroid dysfunction and corneal ectasia. Gatzoufas *et al.* reported a case of a pregnant woman whose keratoconus worsened significantly as she developed hypothyroxinemia during her pregnancy.^[13] Tabibian *et al.* prospectively studied 48 eyes of 24 pregnant women during their entire pregnancy and the postpartum period and noted that significant differences in corneal biomechanical and topographic parameters were found during pregnancy with serum T3 and T4 levels. They proposed that pregnancy-induced changes in corneal biomechanics and topography maybe thyroid hormone-related.^[14] In our case series, only one patient— patient number 2, gave a history of hypothyroidism.

Till about a decade ago, patients of post-LASIK ectasia would be managed with spectacles, contact lenses, intracorneal ring segments, or keratoplasty, depending on the severity and progress of the ectasia.^[15] However, with the advent of collagen cross-linking in the past decade, CXL has become the standard of care in most cases of progressive keractesia.^[16] In our case series, 12 of the total 20 eyes with keractesia underwent CXL while in two eyes concurrent CXL and PRK procedure was done.

Conclusion

Summing up, we believe that there is increasing evidence linking corneal ectasia to hormonal changes happening during pregnancy and newer research is also suggesting that a combination of thyroid dysfunction coinciding with pregnancy may be responsible for triggering the biomechanical changes in the cornea which may lead to ectasia in some cases. Any suggestion to avoid LASIK in women in the reproductive age group would be too immature at this stage as that segment makes almost half of the potential subjects for LASIK surgery but future research to find some kind of hormonal markers for determining the future risk of ectasia might be prudent. In our practice, for the past few years, we have actively started taking history regarding any hormonal imbalance or thyroid dysfunction for all women in the reproductive age group and prefer doing surface ablation in place of LASIK in female patients of the reproductive age group who give a history of thyroid dysfunction or any hormonal imbalance. Nevertheless, we have become more aggressive in advising CXL for progressive keratoconus for women who intend to plan for pregnancy in near future.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

- Pizzarello LD. Refractive changes in pregnancy. *Graefes Arch Clin Exp Ophthalmol* 2003;241:484-8.
- Randleman JB, Woodward M, Lynn MJ, Stulting RD. Risk assessment for ectasia after corneal refractive surgery. *Ophthalmology* 2008;115:37-50.
- Seiler T, Koufala K, Richter G. Iatrogenic keratectasia after laser *in situ* keratomileusis. *J Refract Surg* 1998;14:312-7.
- Koch DD. The riddle of iatrogenic keratectasia. *J Cataract Refract Surg* 1999;25:453-4.
- Hafezi F, Iseli HP. Pregnancy-related exacerbation of iatrogenic keratectasia despite corneal collagen crosslinking. *J Cataract Refract Surg* 2008;34:1219-21.
- Padmanabhan P, Radhakrishnan A, Natarajan R. Pregnancy-triggered iatrogenic (post-laser *in situ* keratomileusis) corneal ectasia—a case report. *Cornea* 2010;29:569-72.
- Hafezi F, Koller T, Derhartunian V, Seiler T. Pregnancy may trigger late onset of keratectasia after LASIK. *J Refract Surg* 2012;28:242-3.
- Bilgihan K, Hondur A, Sul S, Ozturk S. Pregnancy-induced progression of keratoconus. *Cornea* 2011;30:991-4.
- Soeters N, Tahzib NG, Bakker L, Van der Lelij A. Two cases of keratoconus diagnosed after pregnancy. *Optom Vis Sci* 2012;89:112-6.
- Park SB, Lindahl KJ, Temnycky GO, Aquavella JV. The effect of pregnancy on corneal curvature. *CLAO J* 1992;18:256-9.
- Suzuki T, Kinoshita Y, Tachibana M, Matsushima Y, Kobayashi Y, Adachi W, *et al.* Expression of sex steroid hormone receptors in human cornea. *Curr Eye Res* 2001;22:28-33.
- Spoerl E, Zubaty V, Raiskup-Wolf F, Pillunat LE. Oestrogen-induced changes in biomechanics in the cornea as a possible reason for keratectasia. *Br J Ophthalmol* 2007;91:1547-50.
- Gatzoufas Z, Thanos S. Acute keratoconus induced by hypothyroxinemia during pregnancy. *J Endocrinol Invest* 2008;31:262-6.
- Tabibian D, de Tejada BM, Gatzoufas Z, Kling S, Meiss VS, Boldi MO, *et al.* Pregnancy-induced changes in corneal biomechanics and topography are thyroid hormone related. *Am J Ophthalmol* 2017;184:129-36.
- Randleman JB. Post-laser *in-situ* keratomileusis ectasia: Current understanding and future directions. *Curr Opin Ophthalmol* 2006;17:406-12.
- Richoz O, Mavrakanas N, Pajic B, Hafezi F. Corneal collagen cross-linking for ectasia after LASIK and photorefractive keratectomy: Long-term results. *Ophthalmology* 2013;120:1354-9.