Int Ophthalmol (2019) 39:1459–1465
https://doi.org/10.1007/s10792-018-0965-4

ORIGINAL PAPER

Prevalence and topographical characteristics of keratoconus in patients with refractive errors in the Egyptian delta

Hazem A. Elbedewy · Tamer E. Wasfy · Shaimaa S. Soliman · Moataz M. Sabry · Amr M. Awara · Sharif Y. El Emam · Heba M. Shafik · Mostafa R. Alam

Received: 12 January 2018 / Accepted: 16 June 2018 / Published online: 25 June 2018

Abstract
Purpose To study the prevalence of keratoconus (KC) and the topographical characteristics of the affected corneas in patients with refractive errors who were seeking refractive surgery in the Egyptian delta.
Methods A retrospective study covering four and half years (Jan 2012–June 2016) where the topographical data of 8124 participants were obtained from the records of a refractive center in the Nile delta region, Egypt. The diagnosis of KC was based on the Holladay criteria in one or both eyes, using the Pentacam scans, whereas grading of KC was based on the Amsler-Krumeich classification.
Results The prevalence of KC was 1.12% (91/8124 participants) with 95% confidence interval 0.91–1.3. Of all the affected cases, 5 cases (5.5%) had unilateral, and the other 86 cases (94.5%) had bilateral KC. The affected and unaffected subjects did not show any significant difference regarding gender. Sixty-eight (38.4%) eyes had stage 1 KC, 53 eyes (29.9%) had stage 2, 27 eyes (15.3%) had stage 3, and 29 eyes (16.4%) had stage 4 KC. It was most prevalent (1.2%) among cases with astigmatism ($P < 0.001$).
Conclusion Keratoconus was found in 1.12% of patients seeking refractive surgery, with no gender preference. Most cases had bilateral affection. Astigmatism was the most common refractive error to be associated with keratoconus.

Keywords Prevalence · Keratoconus · Pentacam · Refractive errors · Egyptian delta

H. A. Elbedewy (✉) · T. E. Wasfy · M. M. Sabry · A. M. Awara · S. Y. El Emam · H. M. Shafik · M. R. Alam
Ophthalmology Department, Faculty of Medicine, Tanta University, Tanta, Egypt
e-mail: hazemelbedewy@yahoo.com

S. S. Soliman
Public Health and Community Medicine Department, Faculty of Medicine, Menofia University, Menofia, Egypt

Introduction

Keratoconus (KC) is a degenerative, non-inflammatory disease, causing axial protrusion of the cornea and stromal thinning which eventually makes the corneal conical in shape [1]. It usually affects both eyes and is considered one of the most common corneal diseases [2]. Early detection of keratoconus is of utmost importance before proceeding with any refractive surgery to avoid unpredictable results [3].

KC can be diagnosed in late stages as an abnormal corneal shape detected on slit lamp examination associated with decreased visual acuity. However, in early stages, prior to the appearance of slit lamp findings or visual affection, corneal topographical analysis is crucial to detect signs of keratoconus [4, 5].

Nowadays, with the recent advances in corneal imaging techniques, the anterior and posterior corneal

surfaces can fully assess the thickness and elevation, providing valuable information [6, 7]. One of these techniques is the Pentacam system which uses the Scheimpflug imaging principal to provide the corneal topographical indices with good accuracy and repeatability [8].

Many criteria have been established to diagnose keratoconus based on the corneal topography. Holladay established 5 criteria in 2008 to detect keratoconus. These criteria are: (a) the apex of the cone is not centered at the 6 o'clock semi-meridian, (b) the cone should appear round on the tangential map, (c) K-readings should exceed 45.00 D, (d) at the apex of the cone, the corneal thickness is approximately 30 μm thinner than the corresponding distance above the center of the pupil, and (e) non-symmetrical topographical patterns [9].

From the many published population-based studies, it is clear that the prevalence of KC varies widely from 0.0003% in Russia to 2.3% in Maharashtra, India [10, 11]. Despite the well-known relation between KC and refractive errors, little is known about the prevalence of KC in patients with different types of refractive errors.

Patients and methods

A retrospective longitudinal study was conducted covering the period of four and half years from the beginning of January 2012 till the end of June 2016. The data were obtained from the records of a refractive Ophthalmic Center in the delta region in Egypt, with referrals from 5 neighboring governorates. This study reviewed the clinical and topographical records of 8124 patients, aged 18 years and more, who were seeking refractive corneal surgery. The patients were diagnosed as having keratoconus based on using the aforementioned Holladay criteria in one or both eyes, using the Pentacam scans (Oculus, Inc., Lynnwood, WA) with version 1.17r72 of the device software, and version 6.03r11 of the data management software. Ophthalmic biomicroscopic examination of all patients was performed with emphasis on the presence of clinical signs of KC which include the presence of corneal protuberance, stromal thinning, 'oil droplet' reflex, Munson sign, 'scissoring' reflex, Fleischer ring, and Vogt striae.

Patients were diagnosed topographically as having KC by the aforementioned Holladay 5 criteria (Fig. 1). Patients diagnosed with keratoconus were graded according to the Amsler-Krumeich classification for grading keratoconus, which is based on the mean K-reading on the anterior curvature sagittal map, corneal thickness at the thinnest location (CT), and the refractive error of the patient [12, 13].

Any participant with history of significant ocular trauma, corneal vascularization, degeneration, or corneal opacity was excluded from the study.

This study was agreed upon and performed in accordance with the ethical standards of the institutional and/or national research committee of the Faculty of Medicine, Tanta University, and with 1964 Declaration of Helsinki and its later amendment or comparable ethical standards. For this type of study, formal consent was not required.

Data were collected, tabulated, and statistically analyzed by Statistical Package for Social Sciences, version 23 (IBM Corp. Released 2015. IBM SPSS statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). Included participants were divided into 2 groups: affected and unaffected. Student's t test was used for comparison of quantitative variables between the two groups for normally distributed data, while Mann–Whitney's test was used for comparison of quantitative variables between the two groups when data were not normally distributed. Chi-square test (χ^2) was used to study the association between qualitative variables. Whenever any of the expected cells were less than five, Fischer's exact test with Yates' correction was used.

Results

This study included 8124 subjects, out of which 91 (1.12, 95% CI 0.91–1.37) subjects were diagnosed as having keratoconus in one or both eyes based on the recorded clinical and Holladay criteria for Pentacam topography. Unilateral KC was present in only 5 cases (5.5% of all the affected cases), while 86 cases (94.5%) had bilateral KC. A total number of 177 eyes (1.09%) suffered from KC out of the 16,248 studied eyes.

There was no significant difference between the affected cases and unaffected participants regarding

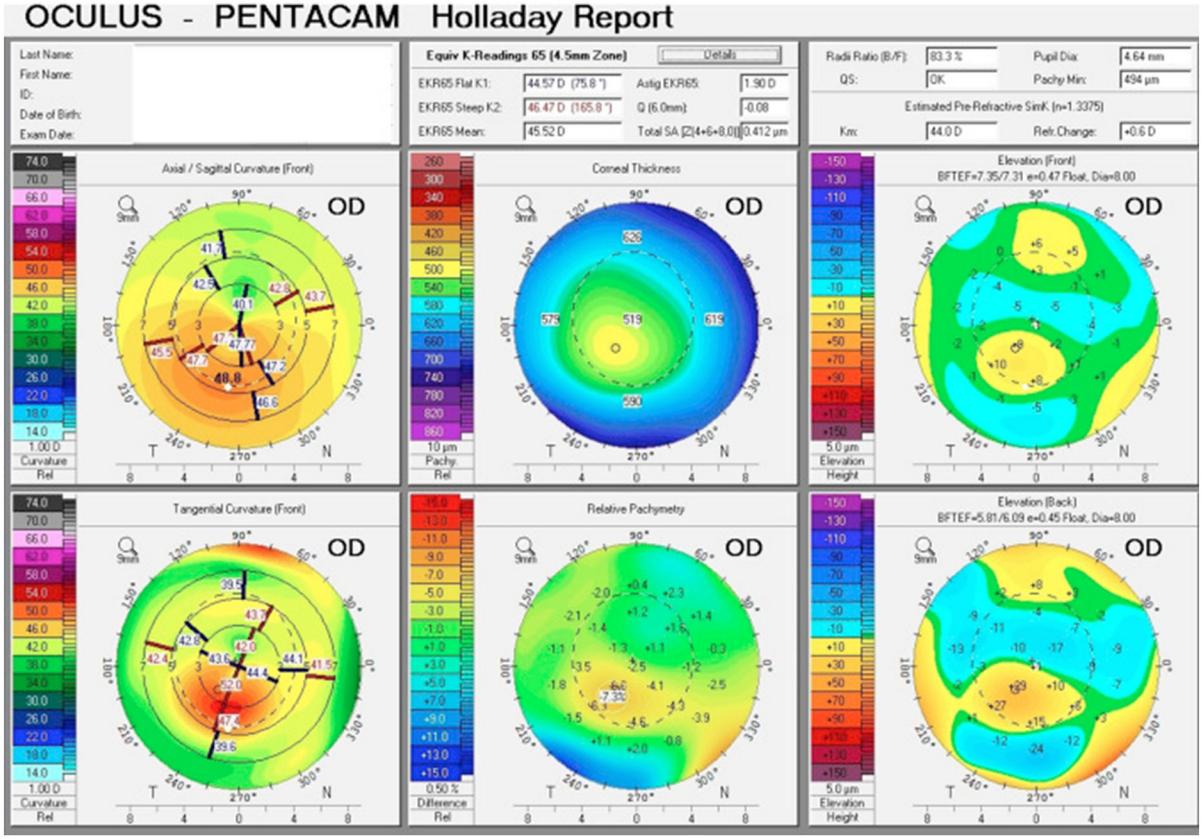

Fig. 1 Pentacam topography showing the Holladay topographical criteria of one eye with KC

Table 1 Personal characteristics of patients with and patients without KC

	Patients with KC Mean ± SD	Patients without KC Mean ± SD	*P* value
Age (y)	29.40 ± 9.79	28.20 ± 7.09	0.11
Gender	No. (%)	No. (%)	0.09
Male	41 (45.1)	2892 (36.0)	
Female	50 (54.9)	5145 (64.0)	

the mean age or gender distribution, as shown in Table 1.

Munson sign was recorded in 107 eyes (60.5%) and Vogt striae in 61 eyes (34.5%).

The topographical values of the anterior corneal surface (front K1, K2, and front astigmatism) were significantly higher in eyes with KC compared to normal eyes. Similarly, the values of the back surface (back K1, K2, and back astigmatism) in the affected eyes showed significantly higher negative values compared to normal eyes.

The mean thickness of the thinnest corneal location was significantly lower in the affected eyes. The location of the *Y* axis was significantly displaced than in normal corneas, while the location of the *X* axis did not differ between the affected and normal corneas. This is detailed in Table 2.

Out of the 177 eyes diagnosed with KC, 68 eyes (38.4%) had stage 1 KC [mean central K 46.34 ± 1.11 D, mean CT 465.14 ± 30.91 µm], 53 (29.9%) had stage 2 [mean central K 50.71 ± 2.12 D, mean CT 457.15 ± 39.63 µm], 27 (15.2%) had stage 3 [mean central K 54.03 ± 0.87 D, mean CT 345.28 ± 40.73 µm], and 29 (16.4%) had stage 4 [mean central K 58.47 ± 2.61 D, mean CT 344.17 ± 54.96 µm].

KC was most prevalent among cases with astigmatism (more than ± 1D of cylindrical power of the manifest refraction) ($P < 0.001$) as 1.2% of all corneas with astigmatism had KC. This percentage

Table 2 Topographical characteristics of eyes with and eyes without KC

	Eyes with KC Mean ± SD	Eyes without KC Mean ± SD	*P* value
Front K1(D)	45.73 ± 4.82	42.86 ± 1.26	< 0.001
Front K2(D)	49.08 ± 5.14	44.11 ± 1.38	< 0.001
Front astig	− 1.03 ± 3.50	− 0.82 ± 1.16	0.02
Back K1(D)	− 6.62 ± 0.94	− 6.10 ± 0.22	< 0.001
Back K2 (D)	− 7.44 ± 1.02	− 6.43 ± 0.25	< 0.001
Back astig.	0.44 ± 0.71	0.29 ± 0.19	< 0.001
Thinnest location (μm)	451.71 ± 32.42	537.94 ± 24.23	< 0.001
X	0.03 ± 0.52	0.01 ± 0.56	0.63
Y	− 0.63 ± 0.37	− 0.37 ± 0.26	< 0.001
Keratoconus index (KI)	1.20 ± 0.12	1.01 ± 0.01	< 0.001

was significantly higher in patients with astigmatism than both hypermetropia, with no eyes having KC, and myopia, in which 0.8% of eyes had KC (Table 3).

In those eyes with astigmatism and keratoconus (138 eyes), compound myopic astigmatism was the most prevalent (94 eyes, 68.1%), while 35 eyes (25.4%) had mixed astigmatism, and only 9 eyes (6.5%) had simple myopic astigmatism.

There was no statistically significant association between the stage of KC and the type of refractive error as shown in Fig. 2 (P value > 0.05).

Discussion

KC is a progressive disease causing rapid decrease in the visual acuity early in the adulthood life. The Pentacam topography is a reliable method to screen and diagnose cases with KC allowing early and effective management. In Egypt, population-based screening for KC is difficult due to the high cost of the topographical scan; however, topographical screening and refractive surgery are getting more and more popular among patients suffering from refractive errors who were the target group of this work.

In this study, the prevalence of patients with unilateral or bilateral KC was 1.12% (91/8124 patients), which represented 1.08% of all the studied eyes (177/16,248 eyes). The prevalence of KC in population-based studies greatly varied. Nielsen et al. [14] in Denmark estimated the prevalence of KC to be 86 patients per 100,000 residents. Ljubic in 2009 in Macedonia found KC in 68 out of 2254 patients [15]. In Iran, 35 patients out of 4592 (0.76%) were diagnosed with keratoconus in at least 1 eye [16]. On the contrary, a recent retrospective study performed in Saudi Arabia by Althomali et al. [17] reported an 8.69% prevalence rate of KC among patients seeking laser refractive surgery, which is relatively high compared to our study.

The high prevalence of keratoconus in the Middle East might be related to the high rate of chronic allergies and spring catarrh. Unpublished data in Egypt by Ahmed et al. [18] found the overall prevalence of eye allergies among children aged 12–15 years to be 20.05% with spring catarrh

Table 3 KC in different types of refractive errors

	Hypermetropia (n = 475) No. (%)	Myopia (n = 4637) No. (%)	Astigmatism (n = 11,136) No. (%)	*P* value	Pairwise comparison
Eyes with KC	0 (0.0)	39 (0.8)	138 (1.2)	< 0.01	P1 0.08
Eyes without KC	475 (100.0)	4598(99.2)	10,998 (98.8)		P2 0.02
					P3 0.03

P1: hypermetropia versus myopia, P2: hypermetropia versus astigmatism, P3: myopia versus astigmatism

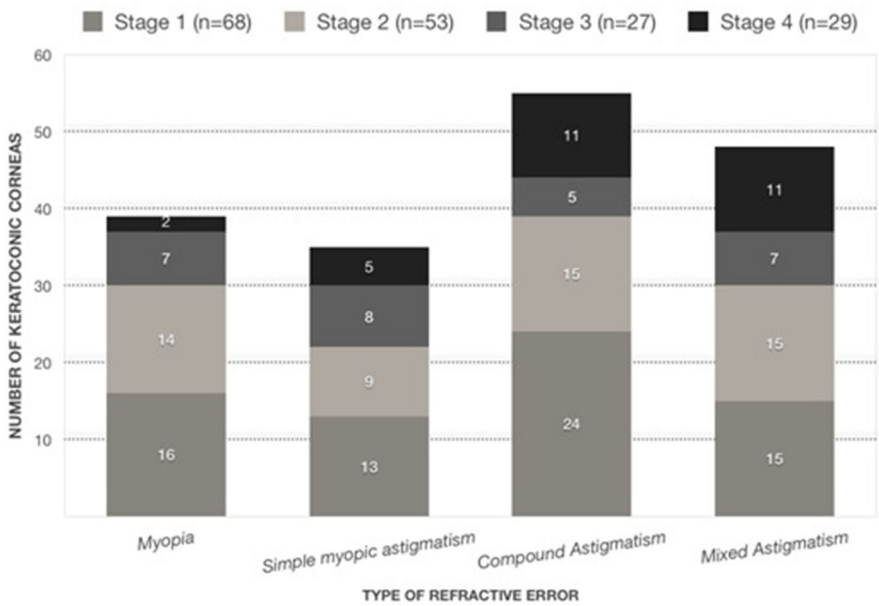

Fig. 2 Stages of KC in different types of refractive errors: (P value = 0.68)

representing 3.95%. In another study in Saudia Arabia, Sethi et al. [19] found that vernal keratoconjunctivitis was the most common eye disorder affecting 35.6% of the studied children. Many authors highly suggest that continuous eye rubbing exerts a mechanical influence on the corneal tissue that appears to be the only necessary inciting event resulting in permanent corneal warpage, which is known clinically as keratoconus [20].

In our study, KC was most prevalent among cases with astigmatism (1.2%), followed by myopia, in which 0.8% of eyes had KC. No cases of KC were found in patients with hypermetropia. Compound type was the most common form of astigmatism associated with KC, with 94 eyes (68.1%), followed by the mixed type with 35 eyes (25.4%), and finally the simple myopic type with 9 eyes (6.5%).

Very few authors have studied the association between KC and the type of refractive errors. The study published by Serdarogullan et al. [21] found that, out of 128 eye suffering astigmatism $\geq$ 2 D, 8 eyes (6.3%) were diagnosed with KC. A more recent study by Cruz-Becerril et al. assessed the prevalence of refractive errors in Mexican patients diagnosed with KC. They found that, out of 785 eyes with keratoconus, compound myopic astigmatism was the most frequent refractive error in eyes, being present in 87.5% of keratoconic corneas [22].

While the presence of KC was associated with certain types of refractive errors, its degree was not. We found no significant association between the degree of KC, either mild, moderate, or severe, and the type of refractive error, whether myopia, simple myopic, compound, or mixed astigmatism. Nevertheless, Cruz-Becerril et al. found that in all grades of KC, 3 refractive errors were most frequent: with-the-rule compound myopic astigmatism, oblique compound myopic astigmatism, and against-the-rule compound myopic astigmatism. Additionally, myopia was present in the advanced and severe stages, but no other refractive errors were observed at either stage [22].

KC usually starts to develop at the age of puberty. In this study, the mean age of patients with KC at time of diagnosis was 29.40 $\pm$ 9.79 years old, which is very close to Ljubic study in which the mean age of onset was 26.81 $\pm$ 1.25 years [15], the studies by Pobelle-Frasson et al. [23] with 33.4 years in males and 37.1 years in females, and Cruz-Becerril et al. [22] with an onset at 28.14 $\pm$ 10.30 years of age. This was much younger than Hashimi et al. [16] who reported a mean age of 47.6 years at the time of diagnosis. Asian patients showed a younger mean age at diagnosis of KC as reported by Assiri et al. [24] in Saudi Arabia with mean age 18.5 $\pm$ 3.9 years, and Saini et al. [25] (20.2 years).

Concerning gender distribution, there was a slight predominance of the female gender with 54.9% of the

KC cases and 45.1% for the male gender, with no significant difference between them. This was in agreement with Ljubic who found that 52.9% (36) of all KC patients were females [15]. Moreover, Jonas et al. [24] reported a significant prevalence of keratoconus in the female gender ($P < .001$) [11].

Affection of both eyes is a common feature of KC. This was evident in this work, as 94.5% of all cases (86 cases) showed bilateral affection and only 5 (5.5%) cases had unilateral affection. This is in agreement with the study by Ljubic where 58 cases (84.8%) were bilateral, and only 10 (15.2%) were unilateral [15]. Similarly, 88.5% of subjects in the study by Weed et al. [26] exhibited bilateral keratoconus.

From our topographical maps, more than half (54.2%) of the affected eyes had a mild degree of KC (mean steepest K 45.48 ± 1.67 D), 27.1% had a moderate degree (mean steepest K 50.29 ± 2.52 D), while 18.7% suffered from the severe form (mean steepest K 59.44 ± 8.28). Assiri et al. [24] reported comparable findings, as 39% of the affected eyes in their study had mild KC, 42.5% had moderate KC, and 18.3% had the severe form. In a similar study, Xu et al. [27] studied the data of 3166 subjects in China and detected abnormally steep cornea (K ≥ 48 D) in 27 subjects (0.9 ± 0.2%), 6 subjects with a corneal refractive power of ≥ 49 D(0.2 ± 0.1%), and only two subjects with a corneal refractive power of ≥ 50 D (0.06 ± 0.05%).

This study shows that keratoconus prevalence in Lower Egypt is comparable to those worldwide, with compound astigmatism being the most common associated refractive error. It adds to the literature about the topographical findings in eyes with keratoconus, contributing to a better understanding.

Acknowledgements Professor Dr. Mohamed Ghoraba, Professor of Ophthalmology, Tanta University, and Dr. Shaimaa Azzam M.Sc., Assistant Lecturer of Ophthalmology, Helwan University, and their team for their help in the process of data collection and management.

Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliation with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equality interest, and expert testimony, or patent-licensing agreements) or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

References

1. Mas Tur V, MacGregor C, Jayaswal R, O'Brart D, Maycock N (2017) A review of keratoconus: diagnosis, pathophysiology, and genetics. Surv Ophthalmol 62(6):770–783. https://doi.org/10.1016/j.survophthal.2017.06.009
2. Krachmer JH, Feder RS, Belin MW (1984) Keratoconus and related noninflammatory corneal thinning disorders. Surv Ophthalmol 28(4):293–322
3. Maeda N, Klyce SD, Smolek MK, Thompson HW (1994) Automated keratoconus screening with corneal topography analysis. Invest Ophthalmol Vis Sci 35(6):2749–2757
4. Randleman JB, Trattler WB, Stulting RD (2008) Validation of the Ectasia Risk Score System for preoperative laser in situ keratomileusis screening. Am J Ophthalmol 145(5):813–818. https://doi.org/10.1016/j.ajo.2007.12.033
5. Binder PS (2007) Analysis of ectasia after laser in situ keratomileusis: risk factors. J Cataract Refract Surg 33(9):1530–1538. https://doi.org/10.1016/j.jcrs.2007.04.043
6. Belin MW, Khachikian SS (2009) An introduction to understanding elevation-based topography: how elevation data are displayed - a review. Clin Exp Ophthalmol 37(1):14–29. https://doi.org/10.1111/j.1442-9071.2008.01821.x
7. Ambrosio R Jr, Belin MW (2010) Imaging of the cornea: topography vs tomography. J Refract Surg 26(11):847–849. https://doi.org/10.3928/1081597X-20101006-01
8. Chen D, Lam AK (2009) Reliability and repeatability of the Pentacam on corneal curvatures. Clin Exp Optom 92(2):110–118. https://doi.org/10.1111/j.1444-0938.2008.00336.x
9. Holladay JT (2009) Keratoconus detection using corneal topography. J Refract Surg 25(10 Suppl):S958–962. https://doi.org/10.3928/1081597X-20090915-11
10. Gorskova EN, Sevost'ianov EN (1998) Epidemiology of keratoconus in the Urals. Vestn oftalmol 114(4):38–40
11. Jonas JB, Nangia V, Matin A, Kulkarni M, Bhojwani K (2009) Prevalence and associations of keratoconus in rural maharashtra in central India: the central India eye and medical study. Am J Ophthalmol 148(5):760–765. https://doi.org/10.1016/j.ajo.2009.06.024
12. Amsler M (1946) Kératocône classique et kératocône fruste; arguments unitaires. Ophthalmologica 111(2–3):96–101
13. Krumeich JH, Daniel J, Knulle A (1998) Live-epikeratophakia for keratoconus. J Cataract Refract Surg 24(4):456–463
14. Nielsen K, Hjortdal J, Aagaard Nohr E, Ehlers N (2007) Incidence and prevalence of keratoconus in Denmark. Acta Ophthalmol Scand 85(8):890–892. https://doi.org/10.1111/j.1600-0420.2007.00981.x
15. Ljubic A (2009) Keratoconus and its prevalence in Macedonia. Maced J Med Sci 2(1):58–62. https://doi.org/10.3889/MJMS.1857-5773.2009.0034
16. Hashemi H, Beiranvand A, Khabazkhoob M, Asgari S, Emamian MH, Shariati M, Fotouhi A (2013) Prevalence of

keratoconus in a population-based study in Shahroud. Cornea 32(11):1441–1445. https://doi.org/10.1097/ICO.0b013e3182a0d014
17. Althomali TA, Al-Qurashi IM, Al-Thagafi SM, Mohammed A, Almalki M (2017) Prevalence of keratoconus among patients seeking laser vision correction in Taif area of Saudi Arabia. Saudi J Ophthalmol 32(2):114–118
18. Ahmed S, Said-Ahmed K, Elmorsy O, Soliman S (2017) Epidemiology of vernal keratoconjunctivitis among children aged (12–15) years—Menoufia Governorate
19. Sethi S, Sethi MJ, Saeed N, Kundi NK (2008) Pattern of common eye diseases in children attending outpatient eye department khyber teaching hospital. Pak J Ophthalmol 24(4):166–170
20. Carlson AN (2010) Expanding our understanding of eye rubbing and keratoconus. Cornea 29(2):245. https://doi.org/10.1097/ICO.0b013e3181bdefbc
21. Serdarogullari H, Tetikoglu M, Karahan H, Altin F, Elcioglu M (2013) Prevalence of keratoconus and subclinical keratoconus in subjects with astigmatism using pentacam derived parameters. J Ophthalmic Vis Res 8(3):213–219
22. Cruz-Becerril A, Valdivia A, Peralta R, Domínguez-Fernández R, Castro-Reyes M (2015) Prevalence of refractive errors in Mexican patients with keratoconus. Clin Optom 7:39–44
23. Pobelle-Frasson C, Velou S, Huslin V, Massicault B, Colin J (2004) Keratoconus: what happens with older patients? J Fr Ophthalmol 27(7):779–782
24. Assiri AA, Yousuf BI, Quantock AJ, Murphy PJ (2005) Incidence and severity of keratoconus in Asir province, Saudi Arabia. Br J Ophthalmol 89(11):1403–1406. https://doi.org/10.1136/bjo.2005.074955
25. Saini JS, Saroha V, Singh P, Sukhija JS, Jain AK (2004) Keratoconus in Asian eyes at a tertiary eye care facility. Clin Exp Optom 87(2):97–101
26. Weed KH, MacEwen CJ, Giles T, Low J, McGhee CN (2008) The Dundee University Scottish Keratoconus study: demographics, corneal signs, associated diseases, and eye rubbing. Eye (Lond) 22(4):534–541. https://doi.org/10.1038/sj.eye.6702692
27. Xu L, Wang YX, Guo Y, You QS, Jonas JB, Beijing Eye Study G (2012) Prevalence and associations of steep cornea/keratoconus in Greater Beijing. The Beijing Eye Study. PLoS ONE 7(7):e39313. https://doi.org/10.1371/journal.pone.0039313