

# Keratoconus Indices and their Determinants in Healthy Eyes of a Rural Population

Hassan Hashemi<sup>1</sup>, Reza Pakzad<sup>2</sup>, Samira Heydarian<sup>3</sup>, AbbasAli Yekta<sup>4</sup>, Hadi Ostadimoghaddam<sup>5</sup>, Mahdi Mortazavi<sup>1</sup>, Shahroukh Ramin<sup>6</sup>, Mehdi Khabazkhoob<sup>7</sup>

<sup>1</sup>Noor Research Center for Ophthalmic Epidemiology, Noor Eye Hospital, Tehran, Iran, <sup>2</sup>Noor Ophthalmology Research Center, Noor Eye Hospital, Tehran, Iran, <sup>3</sup>Department of Rehabilitation Sciences, School of Allied Medical Sciences, Mazandaran University of Medical Sciences, Sari, Iran, <sup>4</sup>Department of Optometry, School of Paramedical Sciences, Mashhad University of Medical Sciences, Mashhad, Iran, <sup>5</sup>Refractive Errors Research Center, Mashhad University of Medical Sciences, Mashhad, Iran, <sup>6</sup>Department of Optometry, Shahid Beheshti University of Medical Sciences, Tehran, Iran, <sup>7</sup>Department of Psychiatric Nursing and Management, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

## Abstract

**Purpose:** To determine the distribution of keratoconus indices in a 5-93-year-old healthy eyes of a rural population in Iran.

**Methods:** In this cross-sectional study, multi-stage cluster sampling was applied to select subjects from two villages in the north and southwest of Iran. After obtaining informed consent, all subjects underwent ophthalmologic and optometric examinations. Corneal imaging by the Pentacam was done in subjects above 5 years between 9 a.m. and 2 p.m., at least 3 h after wake-up. All subjects who had abnormal keratoconus indices were excluded. Our main outcome was keratometry-flat ( $K_f$ ), keratometry-steep ( $K_s$ ), keratoconus index (KI), and central keratoconus index (CKI).

**Results:** The mean  $\pm$  standard deviation of  $K_f$ ,  $K_s$ , KI, and CKI was  $43.12 \pm 1.74$ ,  $44.25 \pm 1.65$ ,  $1.02 \pm 0.02$ , and  $1.01 \pm 0.01$ , respectively. According to multiple linear regression analysis, the mean index surface variance (ISV) (b: -1.367,  $P < 0.001$ ), index vertical asymmetry (IVA) (b: -0.012,  $P < 0.001$ ), KI (b: -0.011,  $P < 0.001$ ), CKI (b: -0.001,  $P < 0.001$ ), index height asymmetry (IHA) (b: -0.491,  $P < 0.005$ ), and index height decentration (IHD) (b: -0.001,  $P < 0.001$ ) were lower in men compared to women. Moreover, age had an indirect association with ISV (b: -0.030,  $P < 0.001$ ) and average pachymetric progression index (RPI\_avg) (b: -0.001,  $P < 0.001$ ), and a direct association with KI, CKI, and IHA. Spherical equivalence had an indirect association with KI (b: -0.001,  $P < 0.001$ ) and RPI\_avg (b: -0.004,  $P < 0.001$ ) and a direct association with CKI (b: 0.001,  $P < 0.001$ ). Among all variables, sex had the greatest impact on ISV, IVA, KI, IHA, IHD, and minimum sagittal curvature.

**Conclusions:** The Keratoconus indices of our study were similar to other studies. Although age, living place, and type of refractive error were associated with some indices, sex was the strongest determinant of Keratoconus indices in a population of healthy eyes.

**Keywords:** Anterior-surface indices, Corneal tomography, Iran, Keratoconus indices, Pentacam

**Address for correspondence:** Mehdi Khabazkhoob, Department of Psychiatric Nursing and Management, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran.  
E-mail: khabazkhoob@yahoo.com

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## INTRODUCTION

Keratoconus is one of the most important corneal degenerative disorders<sup>1</sup> and an important reason for corneal transplantation.<sup>2</sup> Since progression and decreased vision can and often occur prior to the third and fourth decade of life, this disease can severely affect the vision-related quality of life of the patients.<sup>3,4</sup> Its prevalence varies in different populations. For

example, its prevalence is reported to be 2-5 in 10,000 general population<sup>3,5,6</sup> and 24% in refractive surgery candidates.<sup>7</sup> The etiology of keratoconus is still unknown, but it seems that different factors, including genetic, environmental, biochemical, and behavioral factors like eye rubbing have an important role in its development.<sup>3,8</sup>

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Although there are different curvature- and elevation-based method for diagnosis of keratoconus,<sup>3</sup> it is usually difficult to detect subclinical, suspicious, and forme fruste cases.<sup>9</sup> Therefore, to differentiate healthy eyes subjects from abnormal cases, knowledge of the distribution and range of keratoconus indices in the healthy eyes population is not only useful<sup>10</sup> but it can also help detect keratoconus corneas and manage that.<sup>1</sup> Hence, different studies have investigated the distribution and range of keratoconus indices<sup>1,11-19</sup> and reported different results. These discrepancies in results can be due to differences in the ethnicity and measurement tool. The Pentacam is one of the most advanced instruments for measurement of keratoconus indices.<sup>12,15</sup> Despite the importance of the knowledge of the distribution of keratoconus indices, few Iranian studies have been performed in this regard. Moreover, these studies often used instruments other than the Pentacam, which are less valid, or only studied some certain age groups. Therefore, we designed a study to investigate the distribution of keratoconus indices in healthy eyes of a rural population in Iran.

## METHODS

This cross-sectional, population-based study was conducted in Iran in 2015. The target population was the rural population of Iran. The methodological details of this study have already been published, and a summary is presented in the following.<sup>20,21</sup> The Ethics Committee of Shahid Beheshti University of Medical Sciences approved the study protocol which was conducted in accord with the tenets of the Declaration of Helsinki. All participants signed a written informed consent. Using multi-stage cluster sampling, from all underserved areas of Iran, two underserved districts were selected randomly from the north and southwest, including Shahyun (a district of Dezful County, Khuzestan Province, west of Iran) and Kojur (a district of Nowshahr County, Mazandaran Province, north of Iran). Then a list of all villages in each district was prepared, and 15 villages from Shahyun and 5 villages from Kojur were selected randomly. After clearance with local authorities, all residents above 1 year of age were invited to the study upon consent. Informed consent was obtained from the household head for individuals below 18 years. After obtaining informed consent from all participants, a day was scheduled and announced for examinations.

In each village, examinations were done in place with standard illumination. Demographic data such as age and sex were collected in predesigned forms via interviews with the participants, and complete ophthalmological examinations, including visual acuity and refraction measurement, slit-lamp biomicroscopy, and Scheimpflug imaging, were done in all individuals above 5 years by two optometrists and one ophthalmologist. First, visual acuity was measured without correction using a logMAR chart at six meters. Then the refractive state of the eye was measured in all subjects using Topcon AR, and the best corrected visual acuity was recorded accordingly. Retinoscopy was done to assess the presence

or absence of scissoring or the oil drop sign. In the next stage, slit-lamp biomicroscopy was done to investigate the presence of Fleischer rings, Vogt's striae, corneal thinning, and breaks in the Bowman's membrane. Finally, Pentacam imaging (Pentacam HR, Oculus, Inc., Lynnwood, WA) was done in all subjects above 5 years. The subjects were instructed to sit in front of the device, rest their chin on the chin rest and press their forehead on the forehead strap, and stare at a fixation target with both eyes open. Then the examiner moved the camera joystick to focus on the corneal apex. After completing the imaging setting, the images were taken automatically, and the results were recorded. If there were any errors in the Pentacam results, artificial tears were instilled, and imaging was repeated after 10 min. All imaging studies were performed between 9 a.m. and 2 p.m., at least 3 h after wake-up, to minimize the effect of diurnal variations.

To determine the distribution of keratoconus indices including keratometry-flat ( $K_f$ ), keratometry-steep ( $K_s$ ), index surface variance (ISV), index vertical asymmetry (IVA), central keratoconus index (CKI), keratoconus index (KI), index height asymmetry (IHA), index height decentration (IHD), analyzed area (AA), minimum sagittal curvature (RSagMin), and average pachymetric progression index (RPI\_avg) in the healthy population, it was tried to detect keratoconus patients using highly sensitive and specific criteria to exclude them from analysis.

Clinical findings (scissoring on retinoscopy, Vogt's striae, Fleischer ring, corneal thinning, and scarring on slit-lamp examination), abnormalities in axial, tangential, and anterior and posterior elevation maps, and the following Pentacam indices as proposed by Correia *et al.*<sup>12</sup> were used to diagnose keratoconus:

1. Belin/Ambrosio enhanced ectasia total deviation value (BAD-D) >1.34
2. Maximum Ambrosio relational thickness (ARTMax) ≤474
3. Average pachymetric progression index (PPI Ave) >1.05
4. Back surface elevation at the thinnest point using the 8 mm best-fit sphere (BFS) >12
5.  $K_s > 47.4$
6. ISV > 35
7. IHD > 0.021.

All patients who had difficulty in any of the above findings (clinical examinations, Pentacam maps, and indices) were first separated. Then, to reduce false positive, an anterior segment specialist who was an expert in the field of keratoconus took into account all criteria and excluded those who were keratoconus and subclinical keratoconus. Moreover, the data of the subjects with a history of corneal dystrophy, corneal surgery, cataract surgery, and ocular trauma as well as the data of the participants who used contact lenses within one week before examinations were not included in the analysis. The data of the subjects with low quality Pentacam images were also excluded.

**Statistical analysis**

Due to the high correlation of keratometric indices, the data of the right eyes were analyzed (correlation coefficients of all indices were above 0.8). The mean and 95% CI were used to assess the distribution of indices. T-test and analysis of variance (ANOVA) were applied to compare the mean values of the indices according to sex, age group, place of living, and type of refractive error. A multiple regression model was used to study the association of sex, place of residence, spherical equivalence (SE), and age with keratoconus indices. The level of significance was set at 0.05 for all tests.

**RESULTS**

Of the selected people, 3314 people participated in the study. Of these, 2681 met the inclusion criteria, and 9 of them had missing keratometry data. Finally, analyses were done using data from 2672 healthy eyes subjects whose mean age was 36.30 ± 18.51 years (range, 6-90 years), and 1553 (58.1%) of them were female. Mean spherical equivalent refraction in the total sample was 0.44 D ± 2.5 D.

The mean ± standard deviation of K<sub>f</sub>, K<sub>s</sub>, ISV, IVA, KI, and CKI was 43.12 ± 1.74, 44.25 ± 1.65, 17.39 ± 5.95, 0.13 ± 0.06, 1.02 ± 0.02, and 1.01 ± 0.01, respectively. The mean K<sub>f</sub> was 43.38 ± 1.91 in women, which was significantly higher than the mean K<sub>f</sub> in men (P < 0.001). The mean K<sub>f</sub> was 43.34 ± 1.47, 43.15 ± 1.99, and 42.73 ± 1.79, and the mean K<sub>s</sub> was 44.17 ± 1.51,

44.69 ± 1.67, and 43.87 ± 1.83 in emmetropic, myopic, and hyperopic subjects, respectively. There was a significant difference in all indices according to the type of refractive error (P value < 0.001 for all). For example, the mean K<sub>f</sub> was 43.34 ± 1.47 in the emmetropia group and 42.73 ± 1.79 in the hyperopia group, indicating a significant difference. Moreover, the mean K<sub>f</sub> was 44.69 ± 1.68 in the myopia group and 43.87 ± 1.83 in the hyperopia group, denoting a significant difference, too.

The mean ISV was 16.62 ± 5.69 in men, which was significantly lower than the mean ISV in women (P = 0.002). Moreover, the mean ISV was 16.24 ± 5.25 in southwest and 17.48 ± 6.00 in north villages, indicating a significant difference (P = 0.002). Table 1 presents other variables.

Table 2 shows the results of multiple linear regression analysis between keratoconus indices and the variables of sex, living place, SE, and age. According to the results of multiple linear regression analysis, the mean ISV (b: -1.367, P < 0.001), IVA (b: -0.012, P < 0.001), KI (b: -0.011, P < 0.001), CKI (b: -0.001, P < 0.001), IHA (b: -0.491, P: 0.005), IHD (b: -0.001, P < 0.001), AA (b: -0.350, P < 0.001), and RPI\_avg (b: -0.020, P < 0.001) were lower in men compared to women.

Age had a significant indirect association with ISV, AA, RSagMin, and RPI\_avg and a significant direct association with KI, CKI, and IHA. Each one-unit increase in SE was associated with a 0.001, 0.031, and 0.004 decrease in the mean KI, AA, and RPI\_avg while a one-unit increase in SE increased the mean CKI

**Table 1: Mean ± standard deviation of keratoconus indices in total and in terms of sex, age, place, and refractive errors in healthy eyes of the population**

	K <sub>f</sub>	K <sub>s</sub>	ISV	IVA	KI	CKI	IHA	IHD	AA	RSagMin	RPI_avg
Total	43.12±1.74	44.25±1.65	17.39±5.95	0.13±0.06	1.02±0.02	1.01±0.01	5.28±4.28	0.01±0.01	-	7.55±0.25	0.96±0.15
Gender											
Male	42.81±1.44	43.75±1.51	16.62±5.69	0.13±0.06	1.01±0.02	1.01±0.01	4.95±4.11	0.01±0.01	99.50±1.60	7.62±0.22	0.95±0.13
Female	43.38±1.91	44.64±1.67	18.01±6.09	0.14±0.07	1.02±0.03	1.01±0.01	5.54±4.40	0.01±0.01	99.77±0.91	7.49±0.26	0.97±0.16
Age											
6-20	42.78±1.11	43.91±1.78	17.87±5.37	0.13±0.05	1.02±0.02	1.01±0.01	4.65±3.15	0.01±0.00	99.79±1.17	7.63±0.20	0.96±0.14
21-30	43.19±1.12	44.10±1.13	18.36±5.46	0.14±0.06	1.02±0.02	1.01±0.00	6.93±5.50	0.01±0.01	99.86±0.69	7.57±0.21	0.99±0.13
31-40	43.36±1.81	44.61±1.57	17.76±6.83	0.13±0.08	1.02±0.03	1.01±0.01	4.24±4.16	0.01±0.01	99.56±1.53	7.49±0.24	0.98±0.15
41-50	42.99±2.22	44.70±1.86	16.91±5.88	0.12±0.06	1.02±0.02	1.01±0.01	5.40±3.88	0.01±0.01	99.54±1.26	7.51±0.23	0.98±0.12
51-60	43.16±1.92	43.93±1.70	15.89±5.86	0.12±0.05	1.01±0.02	1.00±0.01	4.70±3.80	0.01±0.01	99.68±1.23	7.58±0.31	0.94±0.18
61-70	44.19±1.04	44.86±1.22	18.27±6.83	0.16±0.07	1.00±0.02	1.00±0.01	5.72±4.82	0.01±0.01	99.19±1.71	7.37±0.21	0.89±0.09
>70	42.74±2.82	44.08±1.38	19.05±4.92	0.17±0.05	1.01±0.03	1.00±0.01	8.74±4.86	0.01±0.00	99.26±1.78	7.51±0.18	0.86±0.14
Place											
South-west	41.71±2.78	44.11±2.31	16.24±5.25	0.13±0.06	1.02±0.02	1.01±0.01	4.81±3.73	0.01±0.01	99.53±1.71	7.66±0.22	0.93±0.13
North	43.27±1.53	44.26±1.58	17.48±6.00	0.13±0.06	1.02±0.02	1.01±0.01	5.32±4.32	0.01±0.01	99.66±1.23	7.54±0.25	0.96±0.15
RE											
Emmetropia	43.34±1.47	44.17±1.51	16.44±5.59	0.13±0.07	1.02±0.03	1.01±0.01	4.85±3.78	0.01±0.01	99.77±1.01	7.55±0.24	0.96±0.16
Myopia	43.15±1.99	44.69±1.67	18.27±5.62	0.13±0.05	1.02±0.02	1.01±0.01	5.62±4.51	0.01±0.01	99.61±1.38	7.49±0.22	1.00±0.15
Hyperopia	42.73±1.79	43.87±1.83	18.46±6.74	0.15±0.06	1.01±0.02	1.00±0.01	5.75±4.92	0.01±0.01	99.50±1.51	7.60±0.28	0.91±0.12
P value of gender	<0.001	0.341	0.002	0.058	0.288	0.210	0.076	<0.001	0.331	<0.001	0.009
P value of place	<0.001	0.340	0.002	0.059	0.209	0.169	0.077	<0.001	0.332	<0.001	0.003
P value of RE	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

RE: Refractive errors, K<sub>f</sub>: Keratometry flat, K<sub>s</sub>: Keratometry steep, ISV: Index surface variance, IVA: Index vertical asymmetry, KI: Keratoconus index, CKI: Central keratoconus index, IHA: Index height asymmetry, IHD: Index height decentration, AA: Analyzed area, RSagMin: Minimum sagittal curvature, RPI\_avg: Average pachymetric progression index

**Table 2: Result of multiple linear regression between keratoconus indices with sex, place, spherical equivalence, and age**

Dependent variables	Independent variables	Coefficient	P	Standardized coefficient
IHD	Sex	-0.001	<0.001	-0.100
	Place	0.002	<0.001	0.075
	SE	0.001	0.554	0.012
	Age	-0.001	0.256	-0.023
AA	Sex	-0.350	<0.001	-0.138
	Place	0.222	0.018	0.047
	SE	-0.031	<0.001	-0.087
RSagMin	Age	-0.010	<0.001	-0.142
	Sex	0.133	<0.001	0.264
	Place	-0.102	<0.001	-0.109
RPI_avg	SE	0.008	<0.001	0.116
	Age	-0.001	<0.001	-0.098
	Sex	-0.020	0.001	0.006
	Place	0.044	<0.001	0.011
ISV	SE	-0.004	<0.001	0.001
	Age	-0.001	<0.001	0.001
	Sex	-1.367	<0.001	-0.114
	Place	1.577	<0.001	0.071
IVA	SE	0.008	0.821	0.005
	Age	-0.030	<0.001	-0.086
	Sex	-0.012	<0.001	-0.092
	Place	0.008	0.079	0.035
KI	SE	0.001	0.796	0.005
	Age	0.001	0.418	0.017
	Sex	-0.011	<0.001	-0.228
	Place	0.001	0.629	0.009
CKI	SE	-0.001	<0.001	-0.086
	Age	0.001	<0.001	-0.225
	Sex	-0.001	<0.001	-0.083
	Place	0.002	<0.001	0.101
IHA	SE	0.001	<0.001	0.068
	Age	0.001	<0.001	-0.435
	Sex	-0.491	0.005	-0.057
	Place	0.385	0.238	0.024
	SE	-0.015	0.551	-0.012
	Age	0.011	0.030	0.045

IHD: Index height decentration, AA: Analyzed area, RSagMin: Minimum sagittal curvature, RPI\_avg: Average pachymetric progression index, ISV: Index surface variance, IVA: Index vertical asymmetry, KI: Keratoconus index, CKI: Central keratoconus index, IHA: Index height asymmetry, SE: Spherical equivalence

and RSagMin by 0.001 and 0.008, respectively. Table 2 presents the status of other variables. Among all variables, sex had the greatest impact on ISV, IVA, KI, IHA, IHD, and RSagMin.

## DISCUSSION

Optical imaging, including Pentacam topometry, in addition to providing comprehensive information about irregularities of the anterior and posterior surface, can help diagnose keratoconus.<sup>16</sup> Different studies have underlined the importance of distribution of keratoconus indices and their

ability to diagnose keratoconus.<sup>13,15</sup> What is important is that these indices are influenced by genetics and ethnicity, and their distribution is not similar in different populations.<sup>22,23</sup> Therefore, studies defining their distribution at a local level can help to understand the natural course of keratoconus and the role of environmental and genetic factors.<sup>24</sup>

An advantage of the present study was that in order to present the keratoconus indices in the healthy eyes of the population, keratoconus patients were first identified using highly sensitive and specific criteria and removed from analysis. According to the ophthalmology literature, a keratometry reading above 47 D<sup>25</sup> or KI above 1.07<sup>16</sup> is considered keratoconus. This definition is false positive results, and therefore, a combination of indices should be used.<sup>15</sup> In this study, criteria with a high sensitivity and specificity were applied to avoid underestimation or overestimation in the diagnosis of keratoconus, and besides Pentacam maps, topometric and tomographic maps and clinical findings were used, as well.

Another advantage of the present study was that it presented a tolerance interval for the indices. Many researchers believe that absolute values cannot help determine the distribution of the indices; therefore, indices such as the tolerance interval may be helpful.

According to Table 1, most of the anterior-surface indices like ISV, IVA, IHA, and IHD were within the normal limits defined for adults in the Pentacam database.<sup>12,19</sup> Table 3 shows the distribution of keratoconus indices in different age groups of different populations in similar studies.<sup>1,12-15,17,19</sup> According to Table 3, although there are small differences in the distribution of these indices, they are mostly within the normal range. For example, the mean KI was 1.02 in the present study as well as studies conducted by Shetty *et al.*<sup>19</sup> and Hashemi *et al.*<sup>14</sup> while it was 1.06 in a study performed by Uçakhan *et al.*,<sup>1</sup> which are very close. Moreover, the  $K_s$  and  $K_f$  values were similar between our study and studies conducted by Correia *et al.*<sup>12</sup> and Fam and Lim.<sup>13</sup> Furthermore, the mean IVA was 0.13 in our study, which was higher than Hashemi *et al.*<sup>14</sup> (0.10) and Hashemi *et al.*<sup>15</sup> (0.10) and lower than Uçakhan *et al.*<sup>1</sup> (0.31) and Correia *et al.*<sup>12</sup> (0.18). As mentioned earlier, although it seems that the distribution of keratoconus indices is different in different populations, which could be due to ethnic differences, most indices are within the normal range. For example, studies have suggested a cut-off value of 37, 0.28, 1.07, 1.03, 19, and 0.014 for ISV, IVA, KI, CKI, IHA, and IHD, respectively, and have considered greater values as abnormal findings.<sup>11,16</sup>

The RPI\_avg is an important index in keratoconus that shows the course of corneal thickness changes in different meridians. Since many researchers believe that the corneal thickness value alone does not have a high diagnostic power and corneal thickness change may start from different parts of the cornea at different speeds, this index can have a high diagnostic value as

**Table 3: Results of similar studies about mean of tomographic and keratometry indices**

Author	Years	Place	Participants	Mean age (range)	K <sub>f</sub>	K <sub>s</sub>	ISV	IVA	KI	CKI	IHA	IHD	RSagMin	RPI_avg
Uçakhan <i>et al.</i> <sup>1</sup>	2010	Turkey	Normal cases	29.10	-	-	29.92	0.31	1.06	1.01	9.47	0.02	-	-
Fam and Lim <sup>13</sup>	2006	Island	Normal cases	34.44	43.00	44.38	-	-	-	-	-	-	-	-
Correia <i>et al.</i> <sup>12</sup>	2102	Brazil	Normal cases	30.95 (8-67)	-	44.57	20.61	0.18	-	-	4.25	0.01	-	0.85
Ruiseñor <i>et al.</i> <sup>18</sup>	2014	Argentina	Normal cases	32.30 (14-71)	-	-	-	-	-	-	-	-	-	0.97
Kanellopoulos and Asimellis <sup>16</sup>	2013	Greece	Keratoconus patient	31.90 (19-57)	46.78	51.05	98.99	1.05	1.28	1.06	30.60	0.09	-	-
Matheus <i>et al.</i> <sup>17</sup>	2017	Brazil	Normal cases	7-11	-	-	-	-	-	-	-	-	-	1.00
Ambrósio <i>et al.</i> <sup>11</sup>	2011	Brazil	Normal cases	11-78	-	-	-	-	-	-	-	-	-	0.87
Shetty <i>et al.</i> <sup>19</sup>	2017	India	Normal cases	-	-	-	16.00	0.13	1.02	1.01	4.30	0.01	-	0.98
Hashemi <i>et al.</i> <sup>14</sup>	2016	Iran	Normal cases	29.64	-	-	19.00	0.10	1.02	1.00	3.39	0.01	7.49	0.99
Hashemi <i>et al.</i> <sup>15</sup>	2018	Iran	Normal cases	-	-	44.45	18.03	0.10	1.01	1.01	3.60	0.01	-	-
Current study	2016	Iran	PPCS	6-90	43.12	44.25	17.39	0.13	1.02	1.01	5.28	0.01	7.55	0.96

K<sub>f</sub>: Keratometry flat, K<sub>s</sub>: Keratometry steep, ISV: Index surface variance, IVA: Index vertical asymmetry, KI: Keratoconus index, CKI: Central keratoconus index, IHA: Index height asymmetry, IHD: Index height decentration, RSagMin: Minimum sagittal curvature, RPI\_avg: Average pachymetric progression index, PPCS: Population-base cross-sectional study

some studies have reported a sensitivity of 90% for RPI\_avg.<sup>18</sup> A high RPI\_avg indicates the high speed of corneal changes and a high risk of ectasia.<sup>11,12</sup> Some studies have reported a RPI\_avg ≤1.2 as a cut-point in healthy corneas.<sup>11,12</sup> In the present study, RPI\_avg was less than 1 in the whole population and in all subgroups, which was similar to studies conducted by Hashemi *et al.*<sup>14</sup> in Iran (0.99), Matheus *et al.*<sup>17</sup> in Brazil, and Correia *et al.*<sup>12</sup> in Brazil (0.85).

Statistical analysis showed higher mean values of important keratoconus indices such as CKI, ISV, and IHD in subjects living in the north. It is difficult to explain this finding, and caution should be exercised when distinguishing the role of genetics and environment. However, it seems genetic and environmental factors play an important role in this regard because individuals living in the north of Iran are more exposed to allergens and sunlight (many locals are farmers), which increases the chance of eye rubbing.<sup>5,26</sup> On the other hand, these people have genetic differences that could affect topographic indices. Studies have shown the role of genetics in the above indices.<sup>26</sup>

The results of this study showed an indirect association between age and some important indices including KI, CKI, and IHD. Previous studies have shown changes of corneal parameters and keratoconus indices with aging. Hashemi *et al.*<sup>27</sup> showed a decrease in CKI and KI but an increase in IHD with age. Although there are controversies about the association of age and keratoconus indices,<sup>27-29</sup> the reason for this difference could be the occurrence of natural crosslinking in the corneal structure with age, resulting in corneal biomechanical changes and a shift towards keratoconus after the age of 30 years.

No study has investigated the inter-gender difference of the topographic and tomographic indices that were measured in our study, and some studies have compared a number of corneal indices between males and females. Ip *et al.*<sup>30</sup> reported greater mean corneal radius values in men while Twelker *et al.*<sup>31</sup> showed a greater corneal curvature in the vertical meridian in

girls. Some studies have shown no difference in the occurrence of keratoconus between men and women.<sup>3</sup> Therefore, while it seems that there is no difference in the keratoconus indices, our results showed the opposite. According to the results, the mean ISV, KI, CKI, IHA, IHD, AA, and RPI\_avg were significantly higher in men. The reason is believed to be hormonal and structural differences<sup>32</sup> more exposure of men to environmental factors and effective risk factors,<sup>3,26</sup> and corneal curvature and thickness differences between men and women that could result in differences in topographic and tomographic indices. The fact that sex had the strongest effect on ISV, IVA, KI, IHA, IHD, and RSagMin among the study variables (i.e., sex, age, living place, and refractive error) underlines the importance of sex.

According to simple and multiple regression analysis, although the mean values of the indices were within the normal range in all refractive types, they had a significant difference between different types of refractive errors. There are few similar studies in this regard. As for the corneal curvature radius, Hashemi *et al.*<sup>33</sup> reported a higher mean K<sub>s</sub> value in myopic individuals while the K<sub>s</sub> value was lower in hyperopic subjects compared to myopic and emmetropic individuals, which was similar to our results.

In general, previous studies have indicated the effect of refractive errors on the corneal tomographic and pachymetric indices; however, it is possible to compare the results due to differences in the evaluated indices and other methodological aspects.<sup>29,34</sup>

The strengths of our study were its large sample size, high participation rate, and inclusion of a wide age range (2-93 years). However, the history of vernal keratoconjunctivitis, allergic diseases, and eye rubbing was not evaluated although they could result in changes in the evaluated indices. Nonetheless, highly sensitive criteria were applied to diagnose subjects with keratoconus-like changes to exclude them from the study.

In conclusion, according to the results, topographic indices in the study population were similar to some Iranian and foreign studies, which could provide clinicians with valuable

information. Moreover, some associations were found between variables such as age, sex, place of living, and SE and tomographic indices. Sex had the greatest effect on some tomographic indices, which warrants further research to explain this relationship.

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### Conflicts of interest

There are no conflicts of interest.

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