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The Relationship between the Severity of Keratoconus and Clinical Characteristics of People with Visual Impairment

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ABSTRACT

Background and Objective: Keratoconus (KC) is a progressive ocular disorder affecting the cornea, which is the outer layer of the eye, causing gradual thinning and protrusion, leading to a conical shape and visual distortion. The aim of this study was to investigate the severity of KC with clinical characteristics of people with visual impairment.

Methods: In this cross-sectional study, 525 eyes in 276 patients with visual impairment in seven provinces in central and southern Iraq, including Al-Basrah, Mesan, Wasit, Babel, Al-Najaf, Kerbala, and Dhi-Qar, were studied from February 2022 to March 2023. Patients were classified into four groups based on disease severity and stage: non-keratoconus with astigmatism>1 diopter (D), mild KC, moderate KC, and severe KC. Keratoconus severity was assessed based on gender, age, total corneal thickness (TCT), keratometry (K), and astigmatism.

Findings: Out of 525 eyes, 363 normal eyes, 92 mild KC eyes, 32 moderate KC eyes, and 38 severe KC eyes were included. The mean age of the patients was 27.13±10.05. Only astigmatism showed a statistically significant association with age group achieving a p-value of 0.024 and total corneal thickness with gender group with a p-value of 0.031. Overall, the sample in this study had at least 1.0 D of corneal astigmatism. A linear regression model was utilized to assess the relationship between KC severity and astigmatism, keratometry, and central corneal thickness, which provide significant results, achieving a p-value of <0.001.

Conclusion: The results showed varied patterns of KC distribution among individuals aged 10 to 76 years, as well as significant differences in the severity of the KC. Furthermore, the findings indicated that total corneal thickness steadily declines as keratoconus becomes more severe. Astigmatism and keratometry readings are increasing.

Keywords: *Keratoconus Severity, Total Cornea Thickness, Keratometry, Astigmatism, Human Vision.*

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Introduction

Keratoconus is a progressive ocular disorder affecting the cornea, which is the outer layer of the eye, causing gradual thinning and protrusion, and leads to a conical shape and visual distortion. Initial symptoms include basal epithelial cell fragmentation, basement membrane fibrillation, Bowman's layer fragmentation, Descemet's membrane folding, and endothelium flattening, particularly in advanced stages (1). It is a condition often considered non-inflammatory and has been questioned by recent studies on tear film and serum cytokines, enzyme levels, and tear proteomics. A study by Jun et al. found no significant differences in serum cytokine levels between keratoconus patients and control subjects, indicating that keratoconus is not necessarily linked to significant systemic inflammation (Figure 1) (2).

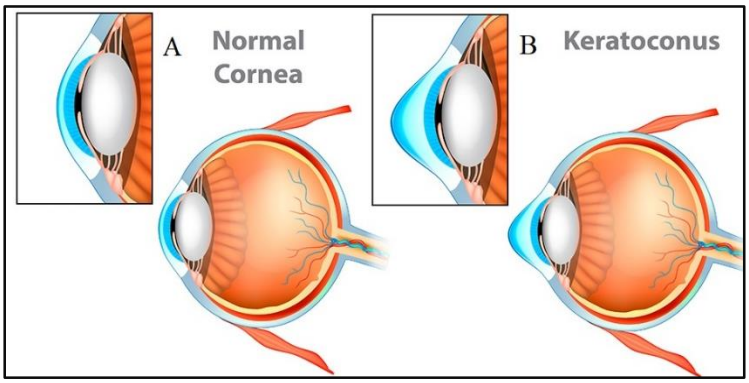


Figure 1. A: normal cornea, B: keratoconus cornea

The exact etiology of keratoconus is unknown; however, it is most likely to be a combination of environmental and genetic factors. Certain genetic abnormalities, according to some studies, may increase the risk of developing keratoconus, while environmental factors such as constant eye rubbing, allergies, and ultraviolet (UV) light exposure may also contribute. Constant inflammation induced by allergens or irritants can damage corneal tissue, potentially leading to keratoconus (3, 4). Keratoconus is suspected to have a genetic basis due to family clustering. Linkage and association studies have investigated possible genes coding for collagen and proteinase inhibitors, antioxidant genes, and homeobox family genes. Environmental factors like eye rubbing, UV radiation exposure, and chemical exposure can also contribute to keratoconus (5). It can affect both eyes; however, the severity and progression of the condition differ between eyes. It may take years after the initial diagnosis of keratoconus in one eye for the condition to become apparent in the other eye (6).

Keratoconus symptoms often occur in the teenage years or early adulthood and may include reduced or distorted vision, a high degree of astigmatism, increased light sensitivity, and frequent changes in eyeglass or contact lens prescriptions (7). Keratoconus can be diagnosed using keratometry and corneal topography examinations. Keratometry, a manual technique, can reveal signs like a steep cornea, high astigmatism, and distorted vision. Corneal topography, a non-invasive technique, allows for qualitative and quantitative analysis of the cornea's morphology. Healthcare professionals can use corneal topography to understand the structural characteristics of the cornea in cases of keratoconus (8). Diagnosis is uncommon after the age of 35, an exception to this is the diagnosis of older patients when presenting for other reasons, e.g., as candidates for cataract or keratorefractive surgery, where ectasia went undetected in earlier life due to either mild symptoms or less sophisticated imaging. A younger age of diagnosis may imply different etiological factors (9, 10). Keratoconus treatment options vary based on severity. Mild to moderate cases can be

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managed with eyeglasses or contact lenses. Corneal cross-linking is another therapeutic approach that can be employed to halt progression. In severe cases, corneal transplant surgery may be necessary to restore visual function (11). Corneal cross-linking (C-CXL) is a preventive approach to keratoconus progression. However, the initial Dresden protocol has setbacks due to its unique physicochemical characteristics (12). Challenges include rapid oxygen depletion, limited riboflavin penetration, a depth-dependent concentration gradient, prolonged treatment duration, and potential endothelial toxicity in thin corneas (13). Novel approaches and alternative (C-CXL) methods are being developed to overcome these challenges (14, 15). The main aim of the research is to demonstrate and assess the relationship between the severity of keratoconus and changes in TCT, K, and astigmatism.

Methods

The retrospective cases included 525 eyes from 276 patients, 140 cases of which were excluded because they were non-kc with astigmatism less than 1 D, and 385 were included since their astigmatism of more than 1 D. The study followed the tenets of the Declaration of Helsinki and was approved by the ophthalmologists. Patients were classified into four stages based on the severity according to Topographic Keratoconus Classification (TKC): non-KC with Astigmatism >1 D, mild KC, moderate KC, and severe KC as diagnosed by an ophthalmologist senior. Data were collected from February 2022 to March 2023 from seven governorates in the middle and south of Iraq; all cases were collected from private clinics that use different types of instruments for corneal topography, including the Ziemer Galilei G6, Allegro Oculyzer Wavelight, and Sirius Tomographer-CSO-Italy. The data were analyzed by SPSS "statistical package for Windows" (IBM SPSS Statistics, version 25). Descriptive statistics were presented with means, medians, and standard deviations. 95% confidence intervals were presented as an estimate of the prevalence of kc. The Kruskal-Wallis test and Chi-Squared test were used to analyze differences in relation to kc severity in age groups, gender, total corneal thickness (TCT), keratometry (K), and astigmatism. Univariate regression analysis was used on three dependent variables: total corneal thickness (TCT), keratometry (K), and astigmatism. In all analyses, a p-value$\leq$0.05 was considered statistically significant. The article's ethical code encourages honesty, integrity, and respect while maintaining accuracy and patient privacy. The authors commit to the private clinics' confidentiality, not displaying patient information, and using data exclusively for study and scientific research purposes.

Results

This study enrolled 525 eyes for patients 264 males and 261 females. Out of 525 eyes included in the study, 264 were males and 261 were females. The mean age of the patients was 27.13±10.05 (10 ranges to 76 years). Of the total 525 eyes, 363 were non-KC eyes (except Astigmatism>1): there were 223 non-KC eyes (2.0±0.91D), 23.9% were mild (92 eyes, Astigmatism 2.1±1.460D), 8.3% (32 eyes, Astigmatism 4.1±1.81D) were moderate, and the remaining 9.9% (38 severe) had Astigmatism 6.6±6.71D. Topographic characteristic data of Keratoconus including TCT, K, and astigmatism for oculus sinister (O.S) and oculus dextrus (O.D) is shown in Table 1. The left eye of the participants had an average total corneal thickness (TCT) of 502.70 ± 60.45 mm, K of 45.79±5.07 D, and Astigmatism 3.08±5.47 D, while the right eye had an average TCT of 503.49 ± 74.89 mm, K of 45.69±3.59 D, and Astigmatism of 3.05±8.53 D. The data demonstrate minor variation in clinical parameters between the left and right eyes, which are potentially significant but are actually minor. Figures 2, and 3 show that the majority of the cases affected by KC were in the age group of 20-29 years.

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Table 1. Clinical and topographic data

Parameter	TCT(mm) Mean±SD	K(D) Mean±SD	Astigmatism(D) Mean±SD
O.S	502.70±60.45	45.79±5.07	3.08±5.47
O.D	503.49±74.89	45.69±3.59	3.05±8.53

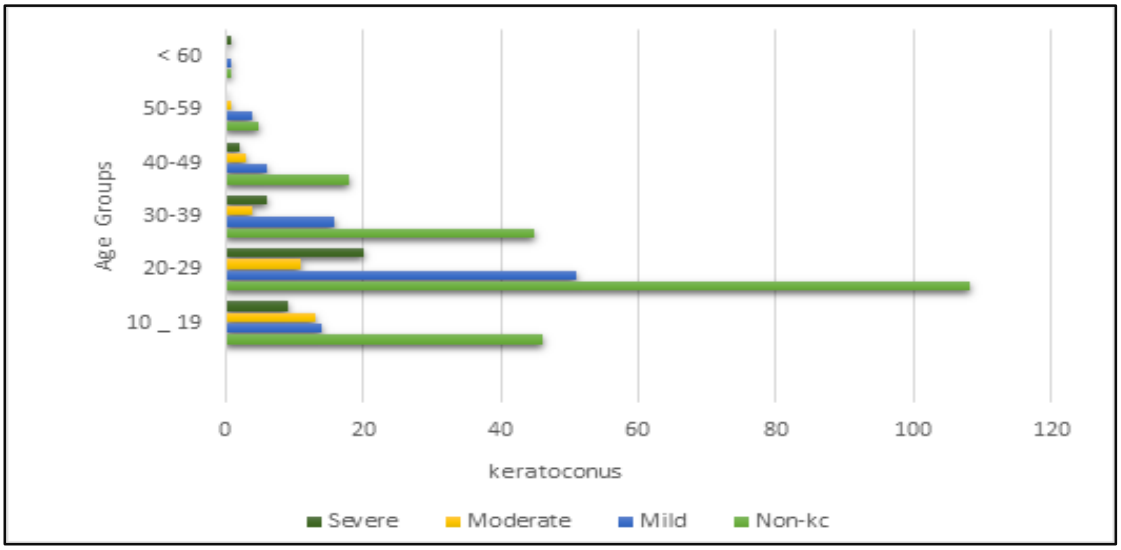


Figure 2. Frequency distribution of the patients' age groups with keratoconus severity

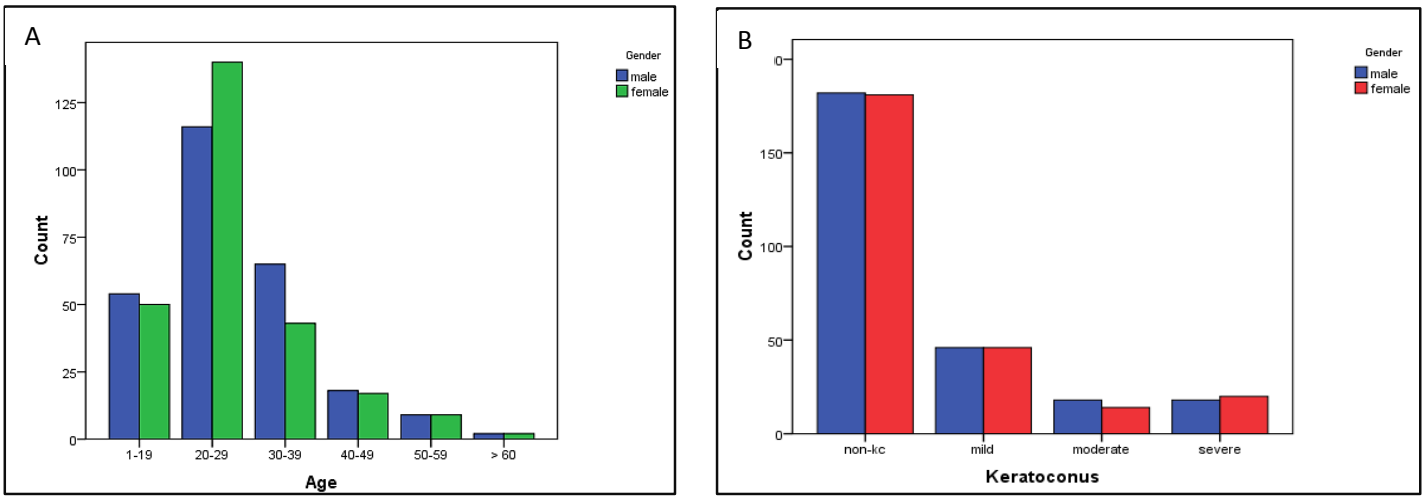


Figure 3. Relation between; A: Age and gender, B: Keratoconus and gender

The distribution of several parameters of the patients according to age groups is shown in Table 2. The mean magnitude of K (D) and TCT (mm) did not have a significant difference between genders in any age group. Moreover, KC severity stages did not change significantly among age groups, while the mean magnitude of astigmatism degree differs significantly with advancing age, achieving a P-value of 0.024, Figure 4.

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Table 2. Distribution of topographic parameters of the patient according to age groups

Parameter	10-19	20-29	30-39	40-49	50-59	>60	p-value
TCT (mm)	515(505.54)	515(502.91)	520(496.98)	531(509.03)	517.50(519)	497(482.67)	0.761**
K (D)	45.65(46.70)	45.00(45.73)	44.90(45.23)	45.30(44.76)	42.85(44.47)	46.20(46.46.13)	0.146**
Astigmatism (D)	2.50(2.81)	1.80(2.88)	1.80(4.32)	2.30(2.50)	1.40(1.46)	1.50(2.17)	0.024**
KC stages							
Non-kc	46	108	45	18	5	1	
Mild	14	51	16	6	4	1	0.383*
Moderate	13	11	4	3	1	0	
Severe	9	20	6	2	0	1	
Total	82	190	71	29	10	3	

TCT: Total Corneal Thickness, K: Keratometry Values. Values of TCT, K and Astigmatism presented as median (mean). Normal cases were astigmatism>1. *Analyzed by chi-square test, **Analyzed by Kruskal-Wallis test.

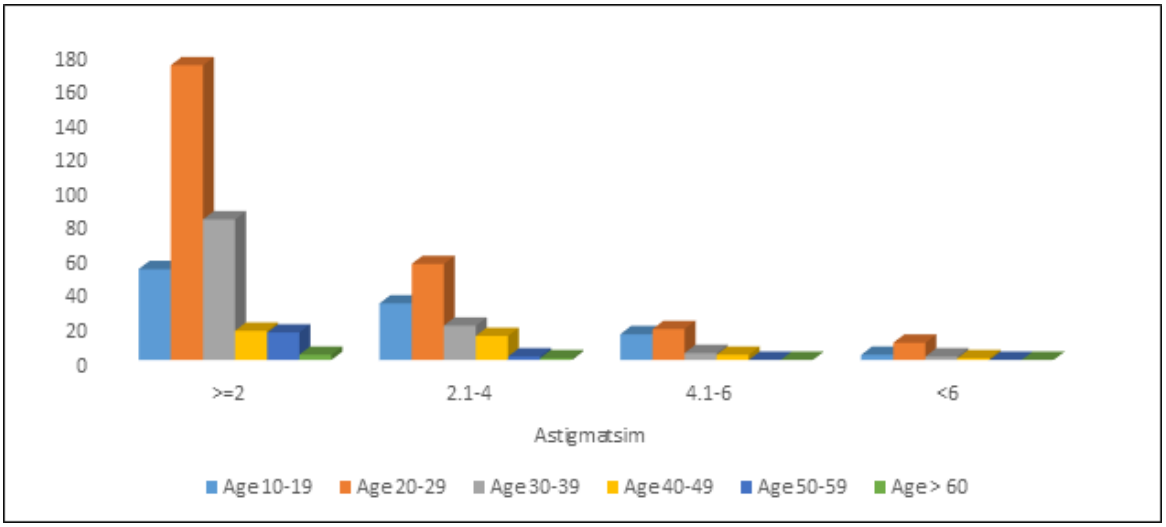


Figure 4. Distribution of astigmatism according to age

However, table 3 shows that the astigmatism magnitude, K(D), and the severity of kc among the participants according to gender were not statistically significant, achieving p-values of 0.626, 0.130, and 0.893, respectively. On the other hand, the TCT was significantly different with gender, achieving a p-value of 0.031, with females 518.5 (508.99±69.87) mm having a slightly higher average total corneal thickness (TCT) compared to males 511 (497.47±65.893) mm.

The distribution of KC stages according to clinical parameters is illustrated in Table 4 and Figure 5. As the severity of KC develops, the TCT decreases consistently, showing growing corneal thinning. Keratometry also shows a rising correlation with KC severity, indicating visual distortion. Furthermore, astigmatism readings increase gradually with severity. Indicating that the severity of the disease is directly linked to corneal abnormalities. There are significant differences between the KC severity and the clinical parameters, achieving a p-value of 0.001.

Table 5 shows a strong univariate regression analysis that demonstrates a strong association between keratometry, total corneal thickness, and astigmatism, all of which are statistically significant with p-values less than 0.001.

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Table 3. Distribution of keratoconus according to gender

Parameter	Male	Female	p-value
TCT(mm)	511(497.47,65.893)	518.5(508.99,69.87)	0.031**
K(D)	44.90(45.59,4.021)	45.45(45.89,4.74)	0.130**
Astigmatism(D)	1.9(2.441,1.56)	1.9(2.4,1.53)	0.626**
KC stages			
Non-kc	115	108	
Mild	46	46	0.893*
Moderate	18	14	
Severe	18	20	
Total	197	188	

TCT: total corneal thickness, K: keratometry values. Values of TCT, K and Astigmatism presented as median (mean, standard deviation) Normal cases were astigmatism>1. *Analyzed by chi-square test, **Analyzed by Kruskal-Wallis test.

Table 4. Distribution of keratoconus according to topographic parameters

Parameter	Non-kc	Mild	Moderate	Severe	p-value
TCT (mm)	531(529.78)	501.5(500.63)	428(429.17)	416.5(414.76)	0.001
K(D)	44.00(43.93)	46.15(45.93)	49.50(48.71)	51.85(53.43)	0.001
Astigmatism(D)	1.70(2.00)	1.75(2.08)	4.15(9.04)	4.80(6.62)	0.001

Analyzed by Kruskal-Wallis test. TCT: total corneal thickness, K: keratometry values. Values of TCT, K and Astigmatism presented as median (mean) non-kc cases were astigmatism>1

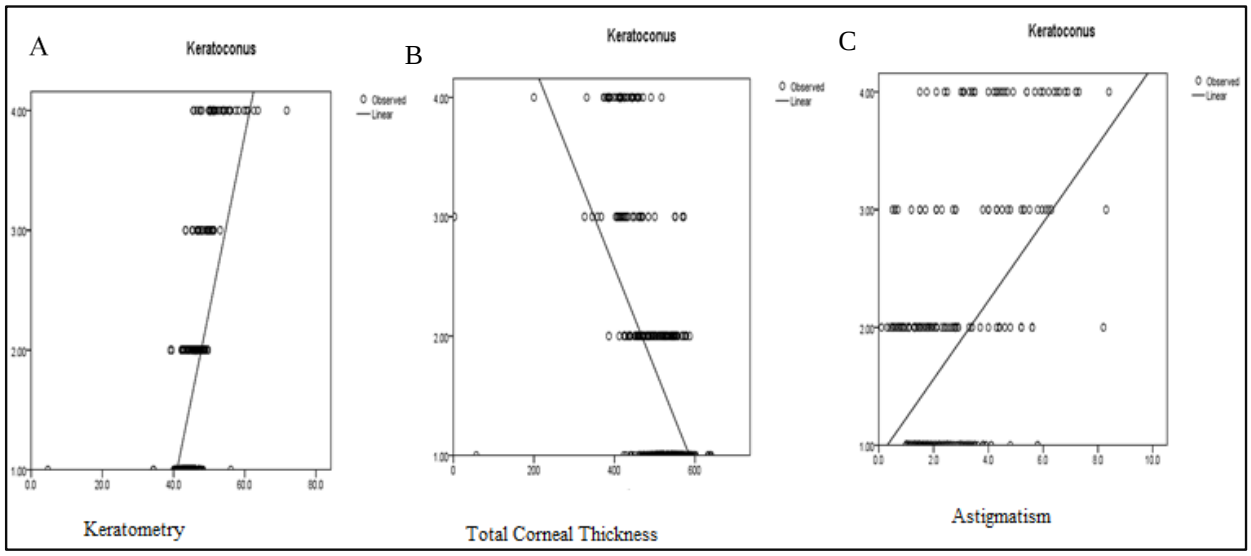


Figure 5. Curve estimation between keratoconus severity and: A-Keratomerty, B- TCT and C-Astigmatism

Table 5. Univariate Regression statistics

Dependent	R	R square R2	Adjusted R square	p-value
TCT(mm)	0.584	0.341	0.339	0.001
K(D)	0.653	0.427	0.425	0.001
Astigmatism(D)	0.257	0.066	0.064	0.001

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Discussion

The study's findings support earlier research, concluding that keratometry readings, astigmatism degrees, and total corneal thickness are all parameters in determining the severity of keratoconus. Total corneal thickness has been utilized as an indicator of keratoconus severity (16). The distribution of keratoconus patients based on topographic classification indicated significant differences in TCT values among severity levels. The non-kc group had the highest TCT value (531 mm), followed by the mild (501.5 mm), moderate (428 mm), and severe (416.5 mm) groups. This indicates that cornea thins gradually as the severity of keratoconus increases. On the other hand, numerous studies have found a gradual rise in keratometry readings as keratoconus severity increases. Higher keratometry levels are related to disease progression (17). Keratometry can give useful information on the shape of the cornea and aid in making informed clinical decisions. TCT, K, and astigmatism degree are used to classify KC, determine treatment choices, and evaluate the effects of therapies like corneal cross-linking or contact lens fitting (3). Keratometry measurements demonstrate a gradual rise in severity, starting with the non-kc group having the lowest K value (44.00 D), followed by the mild (46.15 D), moderate (49.50 D), and severe (51.85 D) groups. The astigmatism measurements also indicate a significant difference across severity levels, with the non-kc category having the lowest astigmatism value (1.70 D), followed by the mild (1.75 D), moderate (4.15 D), and severe (4.80 D) categories, indicating that astigmatism increases with keratoconus severity. The more advanced the cone, the greater the impact of high-order aberration on manifest refraction. As a result, the severity of KC correlates with an increase in astigmatism (18). Afterward, the study revealed that the values of TCT, K, and astigmatism vary significantly across keratoconus severity levels and demonstrate increased corneal thinning, steepening, and greater astigmatism readings in patients with more severe forms. It also contributes to a better understanding of the link between topographic classification and corneal parameters in keratoconus cases, which can assist in diagnosis and monitoring. The study also showed a clear and statistically significant relationship between all measures and the severity stages of keratoconus, highlighting the need for more research for better diagnosis, monitoring, and therapy.

This study investigates the relationship between keratoconus severity and three corneal characteristics: TCT, K, and astigmatism. It showed a substantial association between keratoconus severity and these characteristics. As keratoconus progresses, TCT decreases, indicating corneal thinning. Keratometry readings show a growing correlation, indicating maximum readings due to the increased curvature of corneal surfaces. The study also showed substantial variation in astigmatism measurements, indicating that keratoconus severity is directly related to corneal abnormalities. This might aid and support the previous study that relied on these characteristics in the diagnosis and monitoring of keratoconus severity, allowing for improved disease management and therapy choices. More studies are needed to investigate and analyze these parameters in various corneal abnormalities and diseases.

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