ORIGINAL ARTICLE

Corneal Tomography and Biomechanical Characteristics in Siblings of Patients with Keratoconus: A Cross-Sectional Study

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ABSTRACT

Objective: To assess and compare corneal tomographic and biomechanical characteristics between siblings of patients with keratoconus and healthy siblings of individuals without ocular pathology, aiming to detect early subclinical changes indicative of increased KC risk.

Study Design: Prospective, observational, cross-sectional study.

Place and Duration of Study: This study was conducted at the Department of Opthalmology, Armed Forces Institute of Ophthalmology (AFIO), Pak Emirates Military Hospital (PEMH), Rawalpindi, Pakistan, from 21st August 2024 to 21st February 2025.

Methods: A total of 28 participants (14 in each group) were recruited. Group A included biologically related siblings of Keratoconus patients; Group B consisted of healthy siblings of individuals without ocular disease. Corneal tomography parameters (K1, K2, Kmax, Front Elevation Thinnest Pachymetry, Back Elevation Thinnest Pachymetry, and BAD-D) were measured using Pentacam. Biomechanical parameters, including CBI and TBI values, were assessed via Corvis® ST. Best Corrected Visual Acuity (BCVA) was recorded in logMAR. Data were analyzed using SPSS v25. t-tests and Mann-Whitney U tests were used based on normality, with $P < 0.05$ considered statistically significant. Effect sizes were calculated.

Results: K2 and Kmax were significantly higher in KC siblings ($P < 0.05$). D value, Front Elevation Thinnest Pachymetry, and Back Elevation Thinnest Pachymetry also showed significant differences ($P < 0.001$). CBI and TBI values were significantly higher in the KC sibling group compared to normal siblings ($P < 0.001$). No significant differences were observed for K1 or logMAR BCVA.

Conclusion: Siblings of KC patients demonstrate early tomographic and biomechanical corneal changes, despite being clinically asymptomatic. These findings support the value of advanced imaging for early detection and risk stratification in high-risk populations.

Keywords: *Corneal Diseases, Corneal Topography, Early Diagnosis, Keratoconus, Risk Factors, Tomography.*

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Introduction

Keratoconus (KC) is a progressive, non-inflammatory corneal ectasia which is described as thinning and distorting of the cornea, leading to a cone-shaped bulge.[1] This causes visual impairment and may eventually require surgery. As one of the most common reasons for corneal transplantation, KC becomes critical in its later stages.[1] The etiology of Keratoconus is uncertain, though both genetic and environmental factors have been seen to play significant roles in its development.[2] A key risk factor for the condition is a positive family history, with siblings of KC patients showing a heightened likelihood of developing the disease themselves.[2]

Clinically, Keratoconus is diagnosed using advanced corneal imaging techniques such as tomography and topography, which enable detailed mapping of

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corneal curvature and thickness.[2] Parameters like K1 (the first flat keratometry reading), K2 (the second steep keratometry reading), K max (the maximum curvature of the cornea), and pachymetry have been shown to offer valuable insights into the corneal characteristics of KC patients.[3] Additionally, advancements in corneal biomechanical assessments, such as deformation and stiffness measurements, help in understanding the mechanical properties of the cornea in Keratoconus, as well as in detecting mechanical abnormalities, even in asymptomatic individuals.[4,5] The Corvis Biomechanical Index (CBI) is a widely used parameter in this regard, with a clinical cutoff value of 0.55 for the diagnosis of keratoconus.[6]

Although systems like Pentacam and Corvis® ST are widely used for evaluating corneal tomography and biomechanical properties, limited studies have focused on their application in detecting early changes in siblings of Keratoconus patients.[7,8] These siblings are considered to be at increased risk of developing the condition due to their genetic predisposition.[9] Much research has been devoted to understanding the genetic factors associated with Keratoconus, with ongoing studies exploring the contribution of both genetic and environmental factors to its progression.[9,10] Additionally, systematic investigations of siblings of KC patients suggest that subtle corneal changes may occur even before clinical symptoms become apparent, highlighting the need for early screening.[9]

This study aims to examine the early, subtle corneal changes in siblings of Keratoconus patients, focusing on corneal tomographic and biomechanical parameters, and compare them with those of normal individuals. The goal is to determine whether these changes can be detected in siblings before the onset of the clinical disease, which could offer valuable insights into the pathogenesis and progression of Keratoconus and improve early detection strategies.

Methods

It is a prospective, observational, cross-sectional study that was developed in order to compare corneal tomography and biomechanical attributes in siblings of Keratoconus (KC) patients and healthy controls. This research was conducted at the Department of Ophthalmology, Armed Forces Institute of Ophthalmology (AFIO), Pak Emirates Military Hospital (PEMH), Rawalpindi, Pakistan, from 21st August 2024 to 21st February 2025. The study was in line with the principles of the Declaration of Helsinki, and approval was obtained from the Institutional Ethical Committee of the hospital, vide Letter No: 06/ERC/AFIO, dated 10th August 2024. All the participants gave written consent after being informed of the objectives of the study, procedures, and possible risks.

A total sample size of 28 (14 in each group) was calculated using the OpenEpi Software for cohort studies based on positive family history being a risk factor for Keratoconus.[11] The calculation assumed a two-sided significance level of 95% and 80% power. Non-probability convenience sampling was used, and participants were equally divided into two groups. Group A consisted of biologically related siblings of KC patients who did not have the disease, while Group B consisted of normal siblings of normal individuals (healthy controls). Strict inclusion and exclusion criteria were followed when recruiting the participants, as follows:

Inclusion Criteria: Age between 10 and 50 years. Biologically related siblings of individuals diagnosed with Keratoconus based on clinical findings and corneal tomography (Pentacam). Siblings with no history of systemic or ocular condition (other than refractive error). For Group B, healthy individuals with no history of systemic or ocular condition (other than refractive error).

The exclusion criteria: History of previous corneal surgery (e.g., LASIK, PRK) history of corneal trauma; other corneal pathologies (e.g., dystrophies, infections), ocular surface diseases, systemic connective tissue disorders. Pregnancy or lactation inability to comply with the study procedures; and inability to give informed consent. Once participants were selected, basic demographic details were collected, followed by a full ocular examination in all participants, including BCVA testing and slit-lamp biomicroscopy to exclude any ocular diseases or abnormalities. Prior to corneal imaging, the Schirmer I test (without anesthesia) was performed to assess tear secretion. Participants demonstrating evidence of clinically significant dry eye (Schirmer value <10 mm in 5 minutes) were excluded to minimize the potential effect of ocular surface abnormalities on Pentacam and Corvis® ST

measurements. Corneal tomography was performed using Pentacam (Oculus, Germany) to assess the corneal parameters, which included K1, K2, K max, axis of the corneal curvature, Front Elevation Thinnest Pachymetry, Back Elevation Thinnest Pachymetry, and BAD-D (Belin/Ambrósio Deviation index). Biomechanical parameters, including CBI (Corvis Biomechanical Index) and TBI (Tomographic and Biomechanical Index), were measured using Corvis® ST (Oculus). Each participant underwent corneal tomography for both eyes. All Pentacam and Corvis® ST scans were performed by a single experienced technician trained in corneal imaging, under the supervision of the ophthalmology department. Using a single operator minimized potential inter-observer variability in measurements. Measurements were repeated twice to ensure consistency and minimize error.

The entire data was entered in the IBM SPSS version 25 twice, and errors were checked. Frequencies, percentages, means and standard deviations were used in summarization of descriptive statistics such as demographic data age, and gender. The mean and standard deviation of each of the corneal tomographic parameters (K1, K2, K max, axis, Front Elevation Thinnest Pachymetry, Back Elevation Thinnest Pachymetry, and BAD-D) and biomechanical parameters (CBI, TBI), as well as BCVA, were calculated. Prior to the inferential statistical tests, the data were declared normally distributed or not by performing a Shapiro-Wilk test on each of the corneal topographic and biomechanical parameters. Parametric tests, including the independent sample t-test, were applied to the data that were normally distributed ($P > 0.05$). The Mann-Whitney U test was performed to compare the difference in the corneal tomographic and biomechanical parameters in both groups because they were not normally distributed ($P < 0.05$). Statistical significance between genders was compared using the Chi-Square test in both groups. All the given parameters were considered to have a statistically significant difference between the two groups with a *P*-value below 0.05. Effect size calculation was done to determine the magnitude of the differences between the groups. Cohen's d was used when the data was normally distributed, and the Mann-Whitney when the data was not normally distributed.

Results

In study 28 participants were included (both eyes of each participant were accounted for) which were divided across two groups. Group A (KC siblings) consisted of 14 participants (28 eyes) from biologically related siblings of Keratoconus patients while Group B (Normal siblings) also had 14 participants (28 eyes) but from healthy siblings of individuals with no prior ocular pathology. During the study, one sibling of a Keratoconus patient was incidentally diagnosed with Keratoconus and was referred to the cornea unit for further management, while one sibling was diagnosed as suspected Keratoconus and was advised to follow up for observation. These participants were retained in the analysis, as the study aimed to identify early or subclinical corneal changes in a high-risk population. No data were discarded from either Group A or Group B during the analysis.

The mean age of participants in the KC sibling group was 21.7 ± 3.7 years, while the mean age in the normal sibling group was 28.5 ± 4.4 years. An independent samples t-test showed a statistically significant difference in age between the two groups ($P < 0.001$), indicating that participants in the KC sibling group were meaningfully younger than those in the control group.

Gender distribution was equal in the KC group (50% male, 50% female), whereas the Normal group had a higher proportion of females (82.1% female, 17.9% male). A Chi-square test showed that this difference was statistically significant ($\chi^2 = 5.08$, $P = 0.024$), indicating a gender imbalance between groups.

Table 1 below shows the mean and standard deviation of the normally distributed corneal tomographic and biomechanical parameters.

For the normally distributed variables (K1, K2, Kmax, CBI, TBI and logMAR), independent samples t-tests were performed which revealed differences in K2 and Kmax among the two groups which were statistically significant. The mean K2 was significantly higher in the KC sibling group compared to the normal sibling group ($P < 0.05$), with a Cohen's d of 0.704, indicating a medium to large effect size. Similarly, Kmax was significantly elevated in the KC group ($P < 0.05$), with a Cohen's d of 0.667, also representing a medium to large effect. In contrast, K1

Table 1: Descriptive statistics of corneal tomographic and biomechanical parameters

Parameter	KC SIBLING Group (Mean ± SD)	Normal SIBLING Group (Mean ± SD)
K1 (D)	43.38 ± 2.11	43.26 ± 1.28
K2 (D)	46.03 ± 2.96	44.35 ± 1.64
Kmax (D)	46.83 ± 3.85	44.84 ± 1.72
Front Elevation Thinnest Pachymetry	11.3 ±1.39	3.618 ± 0.297
Back Elevation Thinnest Pachymetry	21.45 ± 3.18	5.314 ± 0.99
BAD D-Value	1.799 ± 0.24	0.902 ± 0.259
BCVA (logMAR)	0.011 ± 0.055	0.006 ± 0.028
CBI	0.429 ± 0.01	0.128 ± 0.010
TBI	0.459 ± 0.007	0.106 ± 0.011

Table 2 : Comparison of corneal tomographic and biomechanical parameters between groups

Tests applied	Parameter	Test value	*P*-value	Effect size (95% CI)
Independent sample t-test	K1	0.256	0.64	0.069 (−0.454 – 0.592)
	K2	2.635	0.03	0.704 (0.164 – 1.244)
	Kmax (D)	2.498	0.02	0.667 (0.129 – 1.205)
	CBI	20.517	<0.001	5.51 (4.36 – 6.66)
	TBI	26.958	<0.001	7.24 (5.80 – 8.68)
Mann-Whitney U test	LogMAR	0.354	0.6	0.096 (−0.428 – 0.620)
	BAD D-Value	190	0.001	0.442 (0.203 – 0.632)
	Front Elevation Thinnest Pachymetry	117	<0.001	0.608 (0.412 – 0.751)
	Back Elevation Thinnest Pachymetry	146.5	<0.001	0.539 (0.322 – 0.703)
	Axis	311	0.18	0.178 (−0.089 – 0.420)

and logMAR BCVA did not reveal any statistically significant differences between the groups ($P > 0.05$), with negligible effect sizes (Cohen's d = 0.068 and 0.096, respectively). The mean CBI was significantly higher in the KC sibling group compared to the normal sibling group ($P < 0.001$), with a Cohen's d of 5.51, indicating an extremely large effect size and near-complete separation between groups. Similarly, TBI values were markedly elevated in the KC sibling group ($P < 0.001$), with a Cohen's d of 7.24, also representing an extremely large effect size. These findings highlight the strong discriminative ability of both CBI and TBI in differentiating KC from normal sibling eyes. These can be seen in detail in Table 2.

Among the non-normally distributed variables, the Mann-Whitney U test demonstrated statistically significant differences in BAD D-value, Front Elevation Thinnest Pachymetry, and Back Elevation Thinnest Pachymetry. The BAD D-value was significantly lower in the KC sibling group (Z = -3.310, $P < 0.01$), with a medium effect size (r = 0.442).

Both Front Elevation Thinnest Pachymetry and Back Elevation Thinnest Pachymetry were significantly higher in the KC group (Z = -4.552 and -4.033, respectively; $P < 0.001$), with large effect sizes (r =

0.608 and 0.539, respectively). The axis of corneal curvature did not differ significantly between the groups (Z = -1.327, $P > 0.05$), and the effect size was small (r = 0.178).

Discussion

Keratoconus (KC) is more and more recognized now as a multifactorial disease that is predisposed by both genetic and environmental factors.[12] Our study contributes to the mounting evidence suggesting that siblings of patients with Keratoconus, although clinically asymptomatic, may exhibit early corneal changes that are detectable by advanced imaging and biomechanical analysis. These findings align with previous research indicating that family members of KC patients are at higher risk of developing subclinical or forme fruste Keratoconus.[13] Our study confirmed statistically significant differences in K2 and Kmax values between KC siblings and normal siblings, suggesting early tomographic changes in at-risk individuals. These results are consistent with a recent study by Ambrósio Jr R et al., who reported that higher keratometric values in family members of KC patients may reflect early ectatic changes that are not yet clinically evident.[14] Wang X et al. also emphasized the role of anterior segment imaging in detecting early signs of Keratoconus in genetically predisposed populations.[15]

The biomechanical and corneal topographic parameters, particularly the D Value, Front Elevation Thinnest Pachymetry, and Back Elevation Thinnest Pachymetry, showed highly significant differences between the groups in our study. Group with healthy siblings of Keratoconus patients exhibiting an elevated mean index. These parameters are increasingly recognized as valuable for early KC screening. Consistent with our findings, Kara N et al. found that siblings of KC patients showed significantly altered corneal biomechanics compared to age-matched controls.[16] Moreover, another study demonstrated that the BAD-D Value was a sensitive marker for distinguishing subclinical KC from normal eyes, supporting its diagnostic utility.[17]

Interestingly, our study found no significant differences in K1 or BCVA between the two groups. This reinforces the notion that BCVA may remain unaffected in the early or subclinical stages of Keratoconus, and this makes biomechanical assessment crucial for early detection.[18] This observation is also supported by a 2023 report by Bui AD et al., who noted that BCVA often remains preserved in the early stages of the disease, leading to delayed diagnosis.[19]

The significant difference in CBI and TBI values observed between groups underlines the importance of incorporating corneal biomechanics into routine screening protocols, especially for high-risk individuals. Previous literature has further reiterated that when you combine tomographic with biomechanical parameters, the diagnostic sensitivity in early KC detection is enhanced.[20] Similarly, elevated levels of Front Elevation Thinnest Pachymetry and Back Elevation Thinnest Pachymetry in the KC group are corroborated by findings from recent work by Duncan JK et al., who found that posterior elevation is often one of the earliest detectable changes in KC progression, especially in individuals with a positive family history.[21] This emphasizes the need for evaluating posterior corneal changes also in screening protocols.

Demographically, our study found a statistically significant age difference between the groups, with KC siblings being younger. While age-matching would reduce bias, this reflects the real-world challenge of recruiting unaffected older siblings who may have already developed the disease. The gender imbalance, with more females in the normal group, could influence corneal biomechanical properties, as recent studies suggest gender-related differences in corneal elasticity.[22] However, the observed trends remained statistically strong despite this limitation.

In a small group of healthy siblings of a Keratoconus patient, one participant was diagnosed with Keratoconus, and one participant was diagnosed with suspected Keratoconus; both were asymptomatic, indicating a non-negligible prevalence of undetected disease. This signifies that screening of siblings of Keratoconus patients is necessary. Our results reinforce the utility of combining Pentacam tomography with Corvis® ST biomechanical assessment for early KC risk stratification. This dual-approach strategy has been advocated in several recent studies, where researchers highlighted those early biomechanical deviations often preceded topographic changes in high-risk eyes.[23]

This study has some limitations that should be recognized. First, although the sample size was statistically calculated, it was relatively small, which may diminish the generalizability of the findings. Second, there was a significant age and gender imbalance between the KC sibling group and the control group. The KC group was significantly younger, and the control group had more females, both of which could introduce potential confounding effects, especially given that corneal biomechanics may vary with age and gender. Third, the study design was cross-sectional, which limits the ability to determine whether the observed changes in KC siblings will eventually lead to clinical Keratoconus. A longitudinal follow-up study would be necessary to confirm whether these subtle tomographic and biomechanical changes progress to Keratoconus over time. Lastly, while advanced imaging tools like Pentacam and Corvis® ST were used, genetic testing and epithelial thickness mapping were not included, both of which could provide deeper insight into subclinical disease states.

Conclusion

This study demonstrates that siblings of patients with keratoconus exhibit measurable corneal tomographic and biomechanical alterations despite being clinically asymptomatic. Significant differences in keratometric values, corneal elevation parameters, and biomechanical indices suggest the presence of early subclinical corneal changes in this high-risk population. These findings support the use of combined Pentacam tomography and Corvis® ST biomechanical assessment for early screening and risk stratification of keratoconus in first-degree relatives.

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Author Contributions

SIM: Conception, design of the work, and approval for final submission
AF: Revising, editing, supervising for intellectual content, and approving for final submission
AAS: Manuscript writing for methodology design, investigation, and approval for final submission
AS: Data acquisition, curation, statistical analysis, and approval for final submission
AS: Writing the original draft, proofreading, and approval for final submission
NM: Validation of data, interpretation, write-up of results, and approval for final submission
SIM is the nominated guarantor and takes full responsibility for the overall content and integrity of the work