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Topographic Patterns and Demographic Profile of Keratoconus in the Qassim Province of Saudi Arabia: A Retrospective Analysis.

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Running Title: Patterns of Keratoconus in Qassim

Abstract

Background: While the Middle East is recognized as a high-prevalence region for keratoconus (KC), significant local variations exist, and there is a notable lack of epidemiological data from the Qassim province of Saudi Arabia. This study aimed to characterize the demographic and topographic patterns of KC in this previously unstudied population.

Methods: A retrospective, cross-sectional study was conducted on the records of 62 patients diagnosed with KC at different hospitals in the Qassim province between January 2020 and

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March 2023. Demographic data and corneal topographic parameters from Scheimpflug imaging were extracted. Non-parametric tests (Mann-Whitney U, Kruskal-Wallis H) and Spearman's correlation were used for statistical analysis.

Results: The cohort demonstrated a male predominance (62.9%, n=39), with the largest proportion of patients (48.4%, n=30) in the 26-35 year age group. The most prevalent morphological pattern was an inferiorly located cone, observed in 67.7% of right eyes and 80.6% of left eyes. A statistically significant difference in maximum keratometry (Max K) was found across age groups in the left eye ($p=0.043$), specifically between the 26-35 and 46-55 age groups ($p=0.047$). Cone location was also significantly associated with disease severity ($p<0.05$). A strong, statistically significant inverse correlation was confirmed between Max K and thinnest corneal pachymetry in both right ($rs = -0.754$, $p < 0.001$) and left eyes ($rs = -0.676$, $p < 0.001$).

Conclusion: This study provides the first clinical and topographic profile of keratoconus in the Qassim province, revealing a pattern of male predominance and a typical diagnosis in the third decade of life, which may suggest a delay in detection. The findings establish an essential evidence-based baseline for regional clinical management and underscore the need for public health initiatives aimed at earlier diagnosis.

Keywords: Keratoconus, Qassim, Saudi Arabia, Corneal Topography, Epidemiology, Ectasia, Keratometry, Pachymetry

Word Count: 5112

- **Introduction/Background**

Keratoconus (KC) is a progressive, non-inflammatory ectatic corneal disorder characterised by biomechanical instability that leads to conical protrusion, thinning, and irregular astigmatism of the cornea. This structural alteration significantly degrades visual function, often commencing during puberty and advancing through the third or fourth decade of life (Kreps et al., 2020). While the global prevalence of keratoconus was historically cited as approximately 1 in 2,000, recent advancements in diagnostic imaging have revealed that this figure is a considerable underestimation, with the actual burden of disease varying substantially across different geographic and ethnic populations (Papali'i-Curtin et al., 2019; Kreps et al., 2020).

The epidemiological landscape of keratoconus is notably heterogeneous. Studies have consistently demonstrated a higher prevalence and incidence in Asian and Middle Eastern populations compared to their Caucasian counterparts (Ziaei et al., 2012). For instance, research in the Asir province of Saudi Arabia reported a high incidence of 20 cases per 100,000, a rate significantly greater than that observed in most European and North American studies (Assiri et al., 2005). Similarly, investigations in neighbouring countries have corroborated the

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finding of a heightened prevalence in the region (Ziaei et al., 2012). This pronounced regional and ethnic variability suggests a complex interplay between genetic predispositions and environmental factors in the pathophysiology of the disease, underscoring the necessity for population-specific data to inform public health strategies and clinical management.

The advent of corneal topography and tomography has revolutionised the diagnosis and management of keratoconus. These technologies facilitate the detailed characterisation of corneal morphology, enabling clinicians to precisely map key parameters such as curvature (keratometry), thickness (pachymetry), and the specific location and severity of the ectatic cone (Belin and Khachikian, 2009). The analysis of these topographic patterns is crucial not only for accurate diagnosis and staging but also for monitoring disease progression and planning therapeutic interventions, such as corneal cross-linking or keratoplasty (Kreps et al., 2020). Despite the availability of these advanced diagnostic tools, a paucity of data exists regarding the specific clinical and topographic characteristics of keratoconus in many regions.

Within the context of Saudi Arabia, while the study by Assiri et al. (2005) provided invaluable insights into the disease profile in the Asir province, the nation's vast and diverse geography warrants further regional investigation. The Qassim province represents a distinct demographic and environmental setting, and to date, there has been no comprehensive study to delineate the patterns of keratoconus within its population. Consequently, a significant knowledge gap persists regarding the presentation of the disease in this area. Therefore, the primary objective of this study is to investigate and characterise the demographic, clinical, and topographic patterns of keratoconus in a cohort of patients from the Qassim province. The specific aims are to: 1) describe the distribution of the disease with respect to age and gender; 2) identify the predominant morphological patterns of the cone, including its location; 3) evaluate the relationships between demographic factors and key keratoconic indices; and 4) analyse the correlation between corneal steepness and thickness. By elucidating these patterns, this research aims to provide essential baseline data that can enhance diagnostic accuracy, guide clinical decision-making, and contribute to the broader understanding of keratoconus in the Middle East.

- **Method**
  - **Study Design and Setting**

This study employed a retrospective, cross-sectional design to analyze the records of patients diagnosed with keratoconus. Data were collected from Different hospitals in Qassim province. The study period encompassed all patient records from January 2020 to March 2023.

  - **Study Population and Data Collection**

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The study population included all patients who underwent corneal topography at the participating centers during the specified timeframe. A diagnosis of keratoconus was established based on clinical signs, such as Vogt's striae or a Fleischer's ring, and characteristic topographic findings, including evidence of corneal thinning, steepening, and irregular astigmatism. The medical records of eligible patients were systematically reviewed to extract the necessary data using a standardized data collection form. Inclusion criteria stipulated a confirmed diagnosis of keratoconus with complete and high-quality topographic scans, while exclusion criteria included any history of prior corneal surgery (e.g., cross-linking, keratoplasty), the presence of other confounding corneal pathologies, such as pellucid marginal degeneration, or incomplete medical records. After applying these criteria, a final sample of 62 patients with bilateral keratoconus was included, yielding a total of 124 eyes for statistical evaluation.

- **Variables and Measurements**

For each patient, demographic and clinical data were collected.

- **Demographic Data:** Age at the time of examination and gender were recorded. Patients were categorized into four age groups for analysis: 15-25, 26-35, 36-45, and 46-55 years.

- **Topographic Data:** All patients underwent a comprehensive corneal assessment using a standard Scheimpflug-based corneal topographer. The following quantitative parameters were extracted for both the right (OD) and left (OS) eyes:

  - **Keratometry:** Mean Keratometry (Mean K) and Maximum Keratometry (Max K) in diopters (D).

  - **Pachymetry:** Corneal thickness in micrometers (μm) at the pupillary center, the pachymetric apex, and the thinnest location.

  - **Cone Location:** The anatomical location of the cone's apex was qualitatively classified into one of five categories: inferior, temporal, nasal, superior, or central.

- **Ethical Considerations**

The study was conducted in strict accordance with the ethical principles outlined in the Declaration of Helsinki. Approval was obtained from the relevant institutional review board prior to the commencement of data collection. To ensure patient privacy and confidentiality, all collected data were fully de-identified, and personal identifiers were removed from the final dataset before analysis.

- **Statistical Analysis**

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All statistical analyses were performed using IBM SPSS Statistics for MacOS, Version 30.0 (IBM Corp., Armonk, N.Y., USA). The normality of the distribution for continuous variables was assessed using the Shapiro-Wilk test. As the data were found to be not normally distributed ($p < 0.05$ for most variables), non-parametric tests were utilized for inferential analysis.

- **Descriptive statistics** were used to summarize the data. Frequencies and percentages were calculated for categorical variables (gender, age group, cone location). For continuous variables (keratometry and pachymetry), means, standard deviations (SD), medians, and ranges were reported.
- The **Mann-Whitney U test** was used to compare the distributions of corneal parameters between male and female patients.
- The **Kruskal-Wallis H test** was employed to compare the distributions of corneal parameters across the different age groups and cone locations.
- The **Chi-Square test of independence** was used to evaluate the association between categorical demographic variables (gender, age group) and the location of the cone.
- **Spearman's rank-order correlation (**rs**)** was calculated to assess the strength and direction of the monotonic relationship between keratometry and pachymetry measurements.

For all statistical tests, a two-tailed p-value of less than 0.05 was considered to indicate statistical significance.

- **Results**

This study included a total of 62 patients diagnosed with bilateral keratoconus, resulting in 124 eyes for analysis. All data were analyzed using SPSS Statistics version 30.0. The analysis was conducted to describe the demographic and clinical characteristics of the cohort and to identify significant patterns and correlations among various parameters. The data did not follow a normal distribution, as confirmed by the Shapiro-Wilk test ($p < 0.05$ for most variables), necessitating the use of non-parametric statistical tests for analysis.

- **Demographic and Clinical Characteristics**

The study population consisted of 39 males (62.9%) and 23 females (37.1%). Patients were categorized into four age groups: 15-25 years (n=13, 21.0%), 26-35 years (n=30, 48.4%), 36-45 years (n=15, 24.2%), and 46-55 years (n=4, 6.5%). The largest proportion of patients was in the 26-35 age bracket. The distribution of patients across age and gender is shown in Figure 1.

- **Descriptive Analysis of Corneal Parameters**

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Descriptive statistics for key keratometric and pachymetric variables for both the right eye (OD) and left eye (OS) are summarized below.

For the right eye (OD), the mean value for Mean Keratometry (Mean K) was 47.43±6.13 D, and for Maximum Keratometry (Max K), it was 54.19±9.38 D. The mean corneal thickness at the thinnest location was 473.16±64.78μm (Table 2)

For the left eye (OS), the mean value for Mean K was 47.08±6.19 D, and for Max K, it was 53.59±10.41 D. The mean corneal thickness at the thinnest location was 476.27±57.07μm. (Table 2)

The most common location for the cone was inferior in both eyes, accounting for 67.7% of cases in the right eye and 80.6% of cases in the left eye (Figure 2).

- **Inferential Statistical Analysis**
  - **Comparison of Corneal Parameters by Gender**

A Mann-Whitney U test was conducted to compare corneal parameters between male and female patients. The results indicated no statistically significant differences in keratometry or pachymetry between genders for either eye. For Max K (OD), the test yielded $U = 400.0$, $Z = -0.707$, $p = 0.480$. For Max K (OS), the results were $U = 415.0$, $Z = -0.488$, $p = 0.625$. All other p-values for keratometric and pachymetric variables were also > 0.05, suggesting that gender was not a significant factor influencing these corneal characteristics in this cohort.

- **Comparison of Corneal Parameters by Age Group**

A Kruskal-Wallis H test was performed to evaluate differences in corneal parameters across the four age groups. A statistically significant difference was observed for Maximum Keratometry in the left eye (Max K OS) across age groups ($H=8.128$, $df=3$, $p=0.043$). Post-hoc analysis using Dunn's test with a Bonferroni correction for multiple comparisons indicated that this difference was specifically between the 26-35 year age group and the 46-55 year age group ($p = 0.047$). A borderline non-significant trend was noted for Mean Keratometry in the left eye (Mean K OS) ($H=6.746$, $df=3$, $p=0.080$). No other keratometric or pachymetric variables showed statistically significant differences across age groups ($p > 0.05$).

- **Influence of Cone Location on Corneal Parameters**

The Kruskal-Wallis H test was also used to assess whether the location of the cone had a significant effect on corneal steepness and thickness. The results revealed a statistically significant relationship between cone location and disease severity.

- **For the right eye (OD):** Cone location had a significant effect on Max K ($H=8.331$, $df=3$, $p=0.040$).

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- **For the left eye (OS):** Cone location significantly influenced both Max K (H=8.241, df=3, p=0.041) and the Thinnest Location thickness (H=8.915, df=3, p=0.030).

These findings indicate that the anatomical position of the cone is associated with variations in maximal corneal curvature and thinning.

- **Association Between Demographics and Cone Location**

A Chi-Square test for independence was performed to examine the association between demographic variables (gender, age) and the location of the cone. The analysis found no statistically significant association between gender and cone location in either the right eye ($\chi2(3)=4.452, p=0.217$) or the left eye ($\chi2(3)=2.947, p=0.400$). Similarly, there was no significant association between age group and cone location for the right eye ($\chi2(9)=12.963, p=0.164$) or the left eye ($\chi2(9)=4.645, p=0.864$).

- **Correlation Between Keratometry and Pachymetry**

Spearman's rank-order correlation was used to assess the relationship between corneal steepness (keratometry) and corneal thickness (pachymetry). The analysis revealed a strong, statistically significant inverse correlation between these variables in both eyes, consistent with the pathophysiology of keratoconus.

- **For the right eye (OD):** A strong negative correlation was found between Max K and the Thinnest Location thickness ($rs=-0.754$, $p<0.001$). Similarly, significant negative correlations were observed between Max K and thickness at the pupillary center ($rs=-0.687$, $p<0.001$) and the pachymetry apex ($rs=-0.735$, $p<0.001$).
- **For the left eye (OS):** A strong negative correlation was also found between Max K and the Thinnest Location thickness ($rs=-0.676$, $p<0.001$). Significant negative correlations were also present between Max K and thickness at the pupillary center ($rs=-0.439$, $p<0.001$) and the pachymetry apex ($rs=-0.544$, $p<0.001$).

These results confirm that as the cornea becomes steeper (higher Max K), it also becomes significantly thinner, a defining characteristic of keratoconic progression (Figure 3, Table 3).

- **Discussion**

This study provides the first detailed analysis of the demographic and topographic characteristics of keratoconus in the Qassim province of Saudi Arabia. By characterizing the disease patterns in this specific population, our findings contribute valuable regional data to the broader understanding of keratoconus epidemiology in the Middle East, a region known for its high prevalence of the disease. The key findings reveal a male predominance, a peak presentation in the third decade of life, a high frequency of inferiorly located cones, and a

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strong inverse relationship between corneal steepness and thickness, which aligns with the fundamental pathophysiology of the disorder.

- **Demographic Patterns and Comparison**

In our cohort, keratoconus was more prevalent in males (62.9%) than females (37.1%). This finding is consistent with a growing body of evidence from recent studies in Saudi Arabia and the wider region. For instance, a 2022 study of patients seeking refractive surgery in Qassim also reported a higher prevalence in males (Al-Saleh et al., 2022), as did studies in the Jazan (Alghamdi et al., 2024) and Najran (Alqahtani, 2021) provinces. However, our result contrasts with an earlier, seminal study from the Asir province by Assiri et al. (2005), which reported a female predominance (59.2%). This discrepancy is noteworthy and may reflect true regional variations in disease distribution influenced by unique genetic or environmental factors. Alternatively, it could be attributed to temporal shifts in healthcare-seeking behaviors over the past two decades, with potentially greater awareness and presentation among males in more recent years, possibly linked to occupational screening or different social dynamics.

Interestingly, our statistical analysis revealed no significant differences in the severity of keratometric or pachymetric parameters between genders. This suggests that while more males may present with the condition in our cohort, the intrinsic clinical severity at the time of diagnosis is comparable between sexes. This aligns with the findings of Ziaei et al. (2012) in a large Iranian population and suggests that gender may not be a primary determinant of disease severity in all Middle Eastern populations. This contrasts with other international studies that have reported more severe or aggressive disease in one gender, highlighting the heterogeneity of keratoconus presentation globally.

The age distribution in our study, with the largest proportion of patients (48.4%) in the 26-35 year age group, points towards a diagnosis typically occurring in the third decade of life. This is notably older than the mean age of 18.5 years reported by Assiri et al. (2005) in Asir, but is more consistent with the mean age of 27.1 years in Iran (Ziaei et al., 2012) and 24.7 years in a European cohort (Kreps et al., 2020). The later age of presentation in our cohort compared to the Asir study could suggest a later biological onset of the disease in the Qassim region. However, a more probable explanation is a significant delay between the initial onset of symptoms and the eventual diagnosis. Kreps et al. (2020) highlighted that even in developed countries with advanced diagnostic tools, keratoconus is often diagnosed at a relatively late stage, well after the initial changes have begun. This has significant public health implications, as earlier detection is crucial for effective intervention with treatments like corneal cross-linking, which can halt progression. The impact of this diagnostic delay on an individual's life cannot be overstated. Clinically, it can be the deciding factor that shifts the therapeutic pathway

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from a minimally invasive, vision-preserving procedure like corneal cross-linking to a major surgical intervention like keratoplasty. A patient diagnosed in their late twenties may already have corneal thinning beyond the safety threshold for cross-linking, thereby losing the opportunity to halt the disease. This forces them down the path of a full corneal transplant, which involves a prolonged recovery, the lifelong risk of graft rejection, and the long-term use of immunosuppressive medications. On a personal level, for individuals in their third decade—a pivotal period for career establishment, higher education, and starting a family—progressive, uncorrected visual deterioration can be devastating. It can impose substantial barriers to employment, particularly in roles requiring sharp vision or driving, thereby impacting socioeconomic status and independence. The daily struggle with poor vision that cannot be corrected with simple eyeglasses, combined with the anxiety of a progressive condition, creates a significant psychosocial and economic burden. Therefore, the age of diagnosis found in our study is not just a statistic; it is a critical indicator of a potential window of opportunity being missed for many patients. Our finding of a statistically significant difference in Max K (OS) across age groups further suggests that the disease process is active and evolving within the studied population, reinforcing the need for timely diagnosis and vigilant monitoring.

- **Topographic Characteristics**

A principal finding of this study was the overwhelming predominance of an inferiorly located cone, which was present in 67.7% of right eyes and 80.6% of left eyes. This pattern is the most classic presentation of keratoconus and is widely reported in the literature globally. The predilection for inferior corneal involvement is thought to be related to inherent biomechanical weaknesses in this region, which may be exacerbated by external factors such as eye rubbing, where pressure is often directed inferiorly. This high prevalence of inferior cones confirms that the morphological presentation in the Qassim population is consistent with established global patterns.

Furthermore, our analysis demonstrated that the anatomical location of the cone had a statistically significant impact on disease severity. Specifically, cone location was significantly associated with Max K in both eyes and with the thinnest pachymetry reading in the left eye. This implies that the morphological presentation is not just a qualitative feature but is directly linked to the quantitative measures of disease severity. Patients with certain cone locations, such as decentered cones, may exhibit steeper and thinner corneas, placing them at higher risk for progression and visual compromise. This finding underscores the importance of detailed topographic mapping in clinical assessment. It allows clinicians to move beyond a simple diagnosis of keratoconus to a more nuanced risk stratification, identifying patients who may require more aggressive monitoring or earlier intervention based on these high-risk topographic characteristics.

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- **Correlation of Steepness and Thinning: Clinical Implications**

The strong, statistically significant inverse correlation between maximum keratometry and corneal thickness (pachymetry) is a cornerstone finding of this study (rs up to -0.754, $p < 0.001$). This result robustly confirms the cardinal pathophysiological feature of keratoconus within our Qassim cohort: as the cornea protrudes and steepens, it concurrently thins. This validation is critical for two reasons. First, it confirms that the fundamental disease process in this population is consistent with that seen worldwide. Second, it attests to the quality and internal consistency of our dataset, lending credibility to the other findings.

From a clinical standpoint, this relationship is paramount. It is the very principle upon which many modern topographic screening indices, such as the Belin/Ambrósio Enhanced Ectasia Display, are built. Our findings validate the application of these advanced diagnostic tools for the Qassim population. The strong negative correlation reinforces the need for a simultaneous and integrated evaluation of both keratometry and pachymetry in monitoring patients. A change in one parameter is a strong indicator of a corresponding change in the other. Together, these metrics provide a comprehensive and dynamic picture of disease stability or progression, which is essential for determining patient eligibility and optimal timing for interventions like corneal cross-linking, a procedure whose efficacy is highly dependent on sufficient residual corneal thickness.

- **Strengths and Limitations**

The primary strength of this study is its novelty, providing the first characterization of keratoconus patterns specifically within the Qassim province. This adds a crucial and previously missing data point to the puzzle of keratoconus epidemiology in Saudi Arabia, facilitating more accurate meta-analyses and comparative studies across the Arabian Peninsula. The use of standardized topographic data from modern Scheimpflug imagers and the application of rigorous non-parametric statistical analysis further strengthen the validity of our findings.

However, several limitations must be acknowledged. First, the retrospective nature of the study design is inherently limited by the reliance on pre-existing medical records, which may be subject to inconsistencies or missing data. Second, the sample size of 62 patients is relatively small. This may limit the generalizability of our findings to the entire Qassim population and reduces the statistical power to detect more subtle associations or to perform more granular subgroup analyses (e.g., comparing different types of inferior cones). Furthermore, as the data were collected from Different hospitals in Qassim province, there is a potential for selection bias, as the cohort may over-represent more severe or symptomatic cases of keratoconus and may not be fully representative of the disease spectrum in the general community. Third, and significantly, this study did not include data on potential risk factors such as atopy, eye rubbing,

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or family history. Given that studies like Assiri et al. (2005) found high rates of atopy (56%) and eye rubbing in a neighboring Saudi population, the absence of this data is a key limitation as these factors could be important confounding variables. Finally, the cross-sectional design of this study captures only a single snapshot in time, preventing any definitive conclusions about the rate of disease progression.

- **Future Directions and Conclusion**

This study lays the groundwork for future research on keratoconus in the Qassim province. A larger, prospective, multi-center longitudinal study, ideally tracking patients over a minimum of a 3- to 5-year period, is warranted to corroborate these findings, track progression rates over time, and establish a more precise estimate of the prevalence and incidence of the disease in this region. Future investigations should also systematically incorporate data on genetic and environmental risk factors by administering validated questionnaires on atopy, allergy, and eye-rubbing habits, and by exploring potential genetic markers, particularly given the societal relevance of consanguinity in the region.

This study demonstrates that keratoconus in the Qassim province predominantly affects males in their third decade of life and most commonly presents with an inferiorly situated cone. The location of the cone is significantly associated with disease severity, and the fundamental relationship between corneal steepening and thinning is strongly evident. These findings provide a vital clinical and epidemiological baseline that can serve to guide local ophthalmology services, improve public health awareness campaigns aimed at early detection, and ultimately enhance the clinical management of patients afflicted with keratoconus in this particular region of Saudi Arabia.

- **Conclusion**

In conclusion, this study provides the first comprehensive characterization of the demographic and topographic patterns of keratoconus in the Qassim province of Saudi Arabia. The findings establish a distinct clinical profile for the disease in this region, which is predominantly observed in males, with a typical age of diagnosis occurring in the third decade of life. The classic morphological presentation of an inferiorly located cone was found to be the most prevalent pattern.

Crucially, this research confirms that specific topographic features, namely the anatomical location of the cone, are significantly associated with disease severity as measured by maximum keratometry and corneal thickness. Furthermore, the fundamental pathophysiological relationship of progressive corneal steepening corresponding with significant thinning was strongly validated within this cohort.

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These results have significant clinical implications, providing an essential epidemiological baseline for ophthalmologists in the region and reinforcing the necessity of detailed topographic mapping for accurate diagnosis, risk stratification, and the monitoring of disease progression. The data suggest a potential delay in diagnosis, highlighting the need for enhanced public health awareness and targeted screening initiatives to facilitate earlier detection and intervention. Ultimately, this study fills a critical knowledge gap and serves as a foundation for future longitudinal and etiological research aimed at improving the management and outcomes for keratoconus patients in Saudi Arabia.

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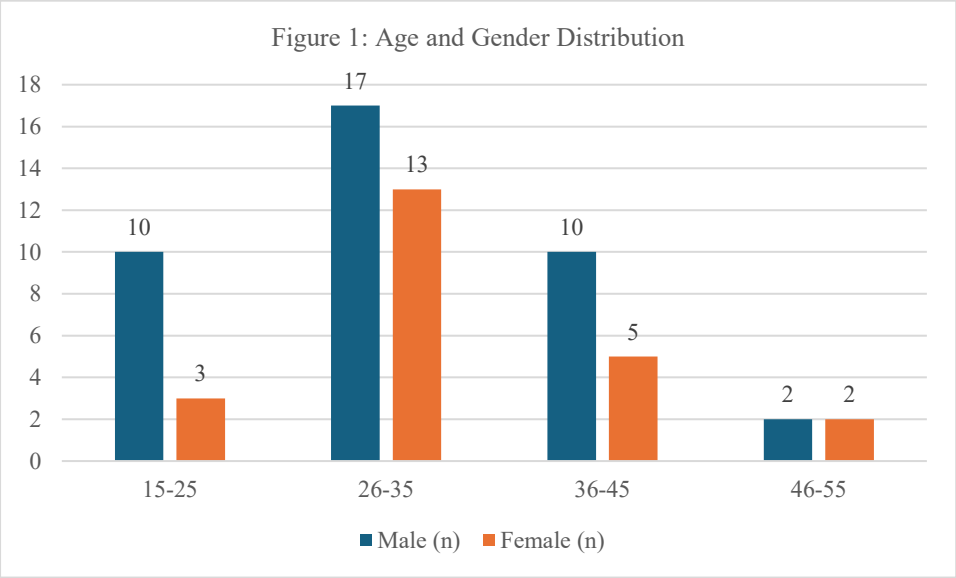
- **Tables and Figure**



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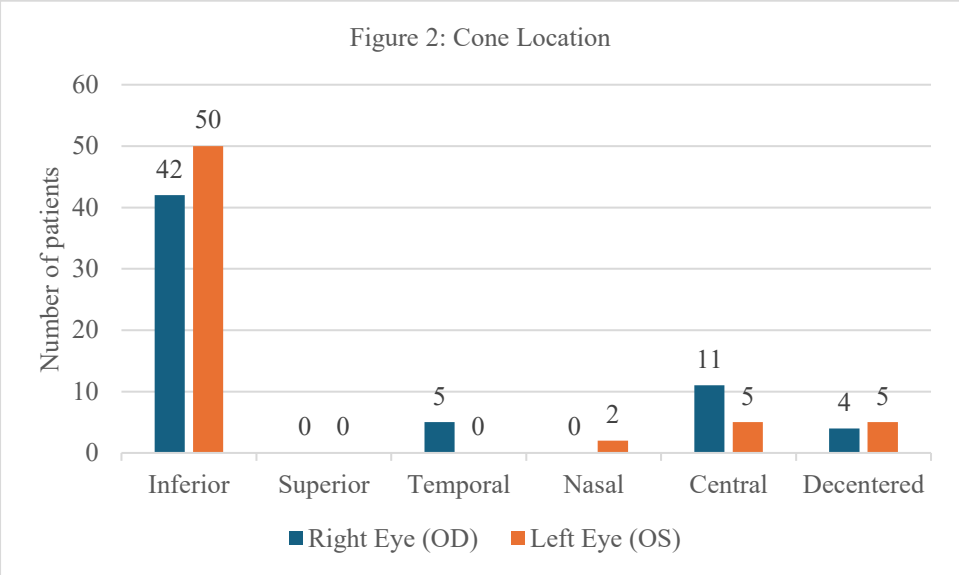

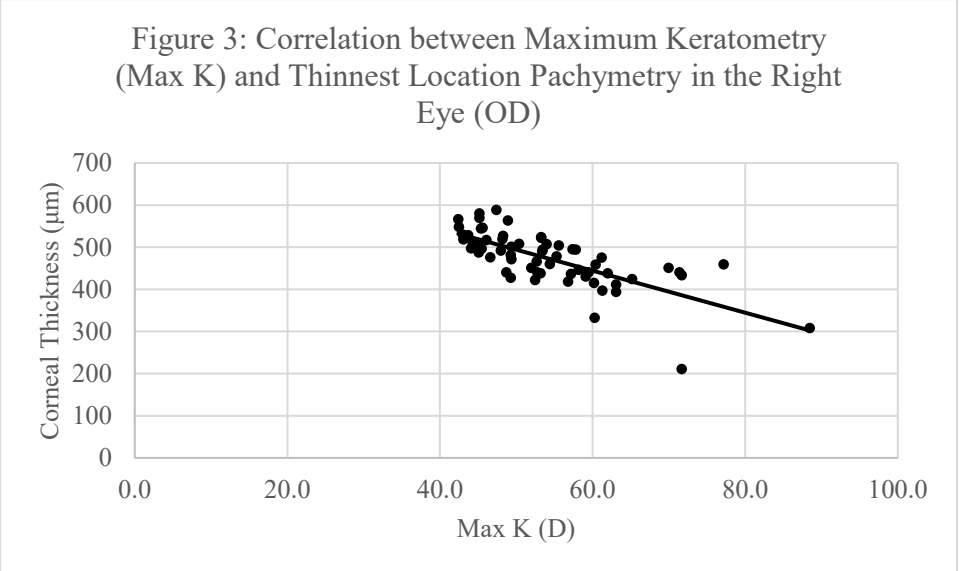

Table 2: Descriptive Statistics of Key Corneal Topographic Parameters

	Right eye		Left eye	
Parameter	Max K (D)	Thinnest Pachymetry (μm)	Max K (D)	Thinnest Pachymetry (μm)
Mean ± SD	54.19 ± 9.38	473.16 ± 64.78	53.59 ± 10.41	476.27 ± 57.07
Median	53.00	479.50	50.65	484.00

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Range (Min – Max)	42.4 – 88.5	211 – 588	41.7 – 107.5	255-576

Table 3: Spearman's Correlation Between Keratometry and Pachymetry

	Max K (OD)	Thinnest Pachymetry (OD)	Max K (OS)	Thinnest Pachymetry (OS)
Max K (OD)	1	-0.754*		
Thinnest Pachymetry (OD)	-0.754*	1		
Max K (OS)			1	-0.676*
Thinnest Pachymetry (OS)			-0.676*	1

Correlation is significant at the 0.01 level (2-tailed).