Prevalence of Keratoconus Based on Scheimpflug Corneal Tomography Metrics in a Pediatric Population From a Chicago-Based School Age Vision Clinic

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Purpose: Determine the pediatric prevalence of keratoconus (KC) using Scheimpflug corneal tomography.

Methods: A prospective observational study was done on subjects aged 3 to 18 years at the Princeton Vision Clinic, Chicago, IL. Scheimpflug tomography (Pentacam HR, OCULUS Optikgerate GmbH) scans (Belin/Ambrósio Enhanced Ectasia BAD3) yielded BAD Final D (Final D) and Back Elevation at the Thinnest Point (BETP) measurements. Criteria differentiating non-KC from KC suspects & KC were, *Non-KC*—Final D <2.00 in both eyes; *KC suspect*—Final D ≥2.00 and <3.00 in combination with BETP ≥18 μm for myopia and ≥28 μm for hyperopia/mixed astigmatism in at least one eye; and *KC*—Final D of ≥3.00 with BETP ≥18 μm for myopia or ≥28 μm for hyperopia/mixed astigmatism in at least one eye. Two thousand two hundred and six subjects were recorded, removing duplicate and poor-quality scans leaving 2007 subjects.

Results: Of 2007 subjects, six were classified as *KC*—prevalence of 1:334, three subjects were *KC suspects*—prevalence of 1:669, and total prevalence of *KC suspects and KC* was 1:223.

Conclusion: The prevalence of KC in children is higher than previously reported, emphasizing the importance of sensitive screening for KC at its earliest manifestation as standard in pediatric comprehensive eye examinations.

Key Words: Keratoconus—Pediatric—Prevalence—Scheimpflug tomography.

Keratoconus (KC) is a progressive corneal ectasia, characterized by focal corneal thinning, steepening, and loss of biomechanical strength leading to irregular corneal astigmatism and decreased vision. The condition is bilateral, asymmetric, and progressive. Progression and worsening of the disease are more likely if disease manifestations occur at a younger age.[1] Genetic conditions, allergy, and environmental factors (e.g., eye rubbing, allergy, asthma, and eczema) have been suggested to be evident in more severe cases of KC.[2]

Before the advancement of corneal diagnostic technology, the literature has reported KC to manifest clinical signs and symptoms during the second to third decade of life.[3] The advent of corneal tomography allows for earlier diagnosis of KC with the ability to visualize and analyze global pachymetric and anterior and posterior elevation metrics of the cornea. Because of these advancements in technology, the commonly accepted prevalence of keratoconus, 1:2000 in the adult population, is considered an underestimate of the true prevalence. KC affects male and female subjects equally, and previous published reports have shown a higher prevalence in certain ethnicities.[4] The literature reporting on the prevalence of the disease in the adult population ranges between 1:50 and 1:750.[5] However, the prevalence of keratoconus in the pediatric population is not well established.

Globally, the current clinical interventional treatment designed to halt the progression of keratoconus is corneal collagen cross-linking (CXL).[6] When combined with a posttreatment device (spectacles, soft contact lenses, rigid corneal gas permeable contact lenses, hybrid lenses, or scleral lenses), the progressive decline in vision resulting from the KC is stabilized by CXL and best-corrected vision is optimized by device to lead to the highest quality of life for the affected individual.[7] CXL may be most beneficial to individuals when KC is identified as early as possible (before measurable vision loss), and progression of the disease has been demonstrated.[8,9]

Corneal tomography is currently not considered in the standard of care in pediatric comprehensive eye care. Thus, cases of keratoconus, specifically early keratoconus and keratoconus suspects, may be missed if no clinical signs are present. Identifying the disease earlier and implementing effective corneal stabilization treatment when appropriate will prevent decline in visual outcomes and, subsequently, prevent decline in long-term quality of life.

To establish the prevalence of keratoconus in a pediatric population, the Illinois College of Optometry (ICO) and International Keratoconus Academy of Eye Care Professionals (IKA) designed and developed a large-scale study that screened for the presence of KC based on objective metrics derived from Scheimpflug corneal tomography.

METHODS

Study design and materials were reviewed and approved by the Institutional Review Board as being in adherence to the tenets of the Declaration of Helsinki. Scheimpflug tomography (Pentacam HR, OCULUS Optikgerate GmbH, Germany) was included as a part of the comprehensive eye examination, and informed consent was signed by the parent or guardian allowing permission to provide a comprehensive eye examination by the eye care providers at the Princeton Vision Clinic, a community-based program, run by the Illinois College of Optometry. The clinic primarily served the pediatric population within the Chicago Public School system.

This study was a prospective, observational, single-center study. Subjects were recruited from the population of an urban school-based vision clinic who presented for a comprehensive eye examination. The demographics of the subjects reflected an income level primarily at or below the federal poverty level. The population included in the study was predominantly low income and primarily two minority racial/ethnicity groups (Black and Hispanic). Services were provided regardless of ability to pay or insurance coverage.

All patients aged 3 to 18 years who presented for comprehensive eye examinations between 2017 and 2019 at the Princeton Vision Clinic were eligible to participate. The examination included an assessment of visual acuity (presenting and best corrected), dry and wet refraction (dilating and cycloplegic agents used only with consent from legal guardian), autorefraction, color vision testing, ocular motor assessment, accommodative and binocular vision testing, and anterior and posterior eye health assessment. In addition to vision and ocular health assessment, image capture from the Pentacam (OCULUS Optikgerate GmbH, Germany) tomographer was obtained on each eye.

Automated multimetric analysis (Belin/Ambrósio Enhanced Ectasia BAD3, OCULUS Optikgerate GmbH, Germany) was run on each scan, and the Final D was derived.[10,11] The Belin/Ambrósio enhanced ectasia display (BAD3) uses nine variables in an enhanced regression analysis. Five of the variables are shown on the BAD3 display as Sub-D values. The Sub-D values (shown) denote the SD from the mean of the normative adult database including anterior elevation, posterior elevation, corneal thickness at the thinnest point, thinnest point displacement, and pachymetric progression. The results of the scan show five visible Sub-D values which are color coded based on their SD from the mean: white when values <1.6 SD, yellow when ≥1.6 SD, and red when ≥2.6 SD. Final D is calculated by considering all nine (five shown and four not shown) of these parameters and performing a linear regression analysis against the standard database of normal and abnormal corneas in an adult population.

Previous literature has reported the prevalence of KC in several populations using only the BAD3 Final D. The Generation 2 Raine Study cohort reported a prevalence of KC of 1.2% or 1 in 84 using a BAD3 Final D score of 2.6 or more.[12] However, the BAD3 was not designed to specifically diagnose KC, the index flags when a cornea is abnormal.[13] To improve specificity of KC detection using the BAD3 Final D, back elevation at the thinnest point (BETP) was added. Poor scan quality was automatically documented by the device, which included categorical errors of blinking, lid, align, data gap, fixation, and model deviation and removed.

As true unilateral KC does not exist,[2] either eye having abnormal metrics qualified the subject as having KC or being a KC suspect. The criteria listed in Table 1 were used to differentiate non-KC corneas from KC.

STATISTICAL ANALYSIS

Statistical analysis was performed with Microsoft Excel (Microsoft Corporation, 2018, Microsoft Excel). Variables included in the analysis were demographic variables (race, age, and sex) and tomography metrics (Final D and BETP). Descriptive statistical analysis was conducted on all variables.

RESULTS

The tomography data from 2098 subjects were recorded. Once duplicate scans and poor-quality scans were removed, data from 2007 subjects, 3,816 eyes, were analyzed. Poor-quality scans were due to poor fixation and/or poor cooperation. There were also children that either refused or were not able to sit long enough for any measurement. Over half of the subjects 56.1% (1,125/2007) were female, and 43.9% (882/2007) were male. Many subjects, 60.7% (1,218/2007), had their ethnicity recorded as Black, followed by Hispanic (692, 34.5%), Asian (40, 1.9%), Mixed (28, 1.4%), White (25, 1.2%), and Middle Eastern (4, 0.2%). The average age of the subjects was 11.4±3.2 years, ranging from 4 to 17 years.

Six of 2007 subjects were classified as KC resulting in a prevalence of 1:334 (Table 2). There were three male and three female subjects who were classified as KC. Their recorded ethnicity was Black (4) and Middle Eastern (2). The average age of subjects classified as KC was 14.8±2.9 years, ranging from 10 to 17 years.

Three of 2007 subjects were classified as KC suspects resulting in a prevalence of 1:669 (Table 2). All three who were classified as KC suspects were female subjects. Their recorded ethnicity was Black (1) and Hispanic (2). The average age of the KC suspects was 11.3±1.5 years, ranging from 10 to 13 years.

There were 9 of 2007 subjects classified as KC or KC suspect resulting in a prevalence of 1:223 (Table 2). Three male and six female subjects were classified as KC or KC suspect. Their recorded ethnicity was Black (5), Hispanic (2), and Middle Eastern (2). The average age of these subjects was 13.7±3.0 years.

TABLE 1. *Tomographic Criteria to Diagnose Keratoconus[a]*

Normal (no evidence of keratoconus)
Final D <2.00 in both eyes
Keratoconus suspect
Final D ≥2.00 and <3.00 in combination with back elevation at the thinnest point (BETP) ≥18 μm for myopia and ≥28 μm for hyperopia/mixed astigmatism in at least one eye
Keratoconus
Final D of ≥3.00 with a back elevation at thinnest point (BETP) ≥18 μm for myopia or ≥28 μm for hyperopia/mixed astigmatism in at least one eye

[a]Using the OCULUS Pentacam and software version 1.20r87.

TABLE 2. *Prevalence of Keratoconus and Keratoconus Suspects Based on Scheimpflug Tomography*

	KC	KC Suspect	Total KC and KC Suspect
Subjects (N)	6/2007	3/2007	9/2007
Prevalence	1:334	1:669	1:223

DISCUSSION

When KC is diagnosed in children or adolescents, the disease tends to become more advanced and individuals more likely to need corneal transplantation compared with individuals diagnosed later in life.[14] Keratoconus can significantly affect quality of life, social, and educational development in children.[15] Patients can maintain good binocular vision but are more likely to become symptomatic when their dominant eye deteriorates which will reduce binocularity.[16] The ocular aberrations in the cornea can also be partially compensated by the high accommodative power seen in younger patients.[17] These factors may contribute to parents seeking care later when the disease has been more significantly affected and why KC in the pediatric population may be more advanced at the time of diagnosis.

Rigid corneal gas permeable contact lenses were considered the primary mode of vision correction for patients with KC, and a penetrating keratoplasty was often the only alternative for severe cases of KC, those experiencing contact lens intolerance, or those who could not achieve an adequate visual outcome.[18] Currently, practitioners have multiple options for improving vision and reducing optical aberrations caused by KC, including custom soft contact lenses, rigid corneal gas permeable lenses, hybrid lenses, and scleral lenses. Treatment with corneal collagen cross-linking, approved by the US Food and Drug Administration (FDA) in 2016 (KXL Avedro, now iLink, Glaukos), has been found to be successful in slowing or halting the progression of the disease.[19] Early intervention may maintain best-corrected vision, particularly

in the pediatric population.[20] In a 2021 prospective study of CXL in adolescent patients with progressive KC, 230 eyes of patients between ages of 10 to 19 years (mean age of 15.8 ± 2.3 years) were evaluated. Early CXL not only halted disease progression but also significantly improved uncorrected and best-corrected visual acuity, reduced steepest measured corneal curvature (Kmax), and stabilized thinnest pachymetry over a 3-year period.[21]

Early diagnosis with utilization of corneal tomography, recognition of progression, and timely intervention with corneal collagen cross-linking is imperative to prevent progression of the disease, avoid vision loss from KC, and resulting impact on quality of life. Practitioners may have concerns about the ability to capture corneal tomography data in the pediatric population; however, this study demonstrated that reliable tomography scans could be acquired on pediatric patients.

Reports on the prevalence of KC vary based on the population studied and on how KC was defined. One of the most cited prevalence studies is from a US-based population, specifically from Olmsted County, Minnesota in 1986, which was before the utilization of any type of corneal topography or corneal tomography. The prevalence of KC from this study was reported to be 1 in 1835. Patients from this study were diagnosed with KC based only on the presence of irregular reflexes or mires during retinoscopy or keratometry, respectively.[22] With the development and utilization of more advanced corneal diagnostics, such as Scheimpflug tomography, the prevalence of KC has been reported to be higher.

One of the challenges in determining the prevalence of KC is the varying reported criteria used to diagnose the disease. Over the years, the literature has reported various metrics and multimetric analyses for the diagnosis of KC including anterior corneal power, anterior corneal curvature at the cone apex, and superior/inferior corneal curvature difference among others.[23] A thorough review of the literature investigating imaging modalities for detecting early KC yielded no universally agreed on metrics for differentiating normal corneas from early KC. Each of the previously published

TABLE 3. *Keratoconus Prevalence by Study and Diagnostic Criterion*

Author(s)	Year	Geographic Location of Study	Prevalence	Diagnostic Criterion for Keratoconus
Kennedy et al.[22]	1986	the United States	1:1835	Irregular reflexes or mires during retinoscopy or keratometry
Jonas et al.[27]	2009	India	1:2,737	Keratometry >48D
Millodot et al.[28]	2011	Israel	1:2,340	Cone apex ≥50D, inferior–superior dioptric difference ≥3.5 diopters, positive results from the software indices KISA, KCI, and KSI
Xu et al.[29]	2012	China	1:900	Anterior corneal refractive power >48 diopters measured by optical low-coherence reflectometry
Hashemi et al.[5]	2014	Iran	1:760–1:2,500	Topography+thinnest corneal point
Godefrooij et al.[30]	2017	the Netherlands	1:265	Database review, diagnosis by ophthalmologist
Torres-netto et al.[26]	2018	Saudi Arabia	1:4,790	Focal corneal steepening >3D with coincident focal paracentral corneal thinning and BAD-D scores >2.0
Papali'i-curtin et al.[25]	2019	New Zealand	1:520	BAD-D of 1.88
Hashemi et al.[24] (global meta-analysis)	2020	Global meta-analysis	1.38 per 1,000 1:725	Different methods used Topography Tomography Autorefractokeratometry Clinical examination Placido disk >90% of articles included used topography methods
Chan et al.[12]	2021	Australia	1:84	Belin/Ambrósio enhanced ectasia display score of >2.6 in either eye

prevalence studies has used slightly different criteria to diagnose KC. In more recent studies reporting on the prevalence of KC, Scheimpflug data, specifically the Pentacam BAD3 Final D score, were used to diagnose the disease.[12,24–26] A limitation of the previous data based on Pentacam findings is the utilization of BAD Final D exclusively as an indicator of KC. The Belin-Ambrósio Ectasia software was not developed to diagnose KC; its purpose is to aid in determining the presence of an abnormal cornea and differentiating it from a normal cornea for corneal refractive surgery decision-making.[8,9] Thus, a high Final D value alone lacks the specificity to confirm a diagnosis of KC. Table 3 presents a list of published studies including a description of subjects by location, reported prevalence, and criteria used to diagnose KC. Though imperfect, the utilization of objective multimeric analysis eliminates subjective interpretation bias. To eliminate subjective practitioner interpretation bias, previously established objective tomographic metrics were used for this study. The choice to use a combination of BAD3 Final D and Back Elevation at the Thinnest Point (BETP) was made since the Belin/Ambrósio Enhanced Ectasia Display (BAD3) was designed to only differentiate normal corneas from abnormal corneas and uses only an adult population in its normative database. The use of the BAD3 for KC diagnosis will result in high sensitivity but lower specificity. Combining the BAD3 Final D with BETP metrics significantly improves diagnostic specificity and thus was used in this study.[13]

Many of the studies on the prevalence of KC report on populations of only adult subjects. One of the limitations with current tomography indices used for the early diagnosis and monitoring of KC is that normative data with the Pentacam tomographer have not been well-established for the pediatric population. As such, there is limited evidence in the literature on the prevalence of KC in a pediatric population.

The results of this study found a prevalence of tomographically determined KC to be 1 in 334 in an underserved, minority pediatric population (predominantly Black and Hispanic) using the criteria of a Final D ≥3.00 in at least one eye with a posterior elevation at thinnest point of greater than 18 μm for myopia and 28 μm for hyperopia and mixed astigmatism. Combining the total number of pediatric patients who had scans which demonstrated the results of KC suspect or KC, the prevalence was even higher, 1 in 223.

The outcomes of this study indicate that the prevalence of KC in the pediatric population is significant. In this US-based pediatric population, the prevalence is higher than previously reported US-based data on KC, highlighting the importance of earlier screening for KC. The frequency of abnormal corneal findings in this population warrants consideration to expand universal screening for KC with tomography that can detect KC before vision loss as part of a comprehensive ocular examination. Identification of both KC and KC suspects is important, so these patients can be diagnosed early, monitored closely and early intervention can be initiated to prevent disease progression. Increasing awareness by eye care practitioners and the overall health care community about KC prevalence is imperative. Early diagnosis, hopefully before significant vision loss, and implementation of treatment can result in prevention of advanced disease states, preservation of vision, and the ability to maintain long-term quality of life. As such, screening for KC and KC suspects should be part of a routine pediatric eye examination, particularly for those patients showing risks factors such as high astigmatism, reduced best-corrected visual acuity,

family history of KC, or aberrant corneal presentation. Patients with subclinical disease (KC suspects) will demonstrate posterior corneal changes and/or pachymetric abnormalities, but they will not have anterior corneal surface changes. Anterior corneal surface changes and visual acuity loss are a later finding of clinical ectatic disease.[13] Technologies that can detect the presence of KC suspects and KC before significant vision loss such as corneal tomography are required to achieve this goal. Investment in these technologies by eye care professionals (ECPs) who provide pediatric eye care should be considered. In addition, pursuit of a CPT code for Pediatric Keratoconus Screening may influence adoption and widespread use and carry a reduced burden on the health care system. Furthermore, instrument manufacturers are encouraged to develop affordable instruments capable of early KC diagnosis so that more ECPs can incorporate them into their practices.

Limitations of this study include the lack of diversity of the population demographics, including race, socioeconomic, and geographic limitations, which prevent generalization to the larger population. Further large-scale, multicenter studies are needed to understand prevalence in the general population.

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