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Research Article

Prevalence of Keratoconus and Keratoconus Suspect among a sample of Iraqi Children with Refractive Errors: A Cross-Sectional Study

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Abstract

Background: Keratoconus (KC) is a chronic, bilateral, non-inflammatory degenerative condition with severe consequences. ***Objective***: To assess the prevalence of KC and Keratoconus Suspect (KCS) in a pediatric population with astigmatic error ≥1 diopter (D) and non-axial myopia. ***Methods***: Between March and October 2022, a cross-sectional study was done with a group of 6–18-year-old kids with an astigmatic error of ≥1 D or non-axial myopia who went to the pediatric ophthalmology clinic at Ibn Al-Haitham Teaching Eye Hospital in Baghdad, Iraq, for regular checkups. All patients got a thorough eye examination and corneal imaging using the Corneal Tomography System (CSO) Sirius equipment and Scheimpflug technology. ***Results***: The majority of patients were females aged 110–14 years (55%). The frequencies of KC and SKC were 13.5 and 119.6%, respectively. The proportion of KC was substantially higher for those above the age of 14. Patients with KC exhibited considerably larger cylinder and axis measurements. Participants with inferior cones and an asymmetric Bow Tie exhibited greater rates of KC (51.2% and 29.4%, respectively). Except for Pachy-Thin and corneal volume mean values, all other metrics were considerably greater in KC and KCS patients than in control patients. ***Conclusions***: The high prevalence of KC and KCS emphasizes the importance of this issue and the necessity for a systematic strategy for screening in pediatric age groups with refractive error.

Keywords: Keratoconus, Pediatric, Prevalence, Refractive errors.

انتشار القرنية المخروطية والقرنية المخروطية المشتبه بها بين عينة من الأطفال العراقيين ذوي الأخطاء الانكسارية: دراسة مقطعية

الخلاصة

الخلفية: القرنية المخروطية (KC) هي حالة تنكسية مزمنة وثنائية وغير التهابية لها عواقب وخيمة. **الهدف**: تقييم انتشار KC والقرنية المخروطية المشتبه بها (KCS) في الأطفال الذين يعانون من خطأ الاستجماتيزم ≤1 الديوبتر (D) وقصر النظر غير المحوري. **الطريقة**: بين مارس وأكتوبر 2022 ، أجريت دراسة مقطعية مستعرضة مع مجموعة من الأطفال الذين تتراوح أعمارهم بين 6 و 18 عاما والذين يعانون من خطأ الاستجماتيزم ≤1 D أو قصر النظر غير المحوري الذين ذهبوا إلى عيادة طب عيون الأطفال في مستشفى ابن الهيثم التعليمي للعيون في بغداد، العراق، لإجراء فحوصات منتظمة. خضع جميع المرضى لفحص شامل للعين وتصوير القرنية باستخدام نظام التصوير المقطعي للقرنية (CSO) ومعدات Sirius وتقنيةScheimpflug . **النتائج**: كانت غالبية المرضى من الإناث الذين تتراوح أعمارهم بين 110-14 سنة (55 ٪). كانت ترددات KC و SKC 13.5 و 119.6٪ على التوالي. كانت نسبة KC أعلى بكثير بالنسبة لأولئك الذين تزيد أعمارهم عن 14 عاما. أظهر المرضى الذين يعانون من KC قياسات أكبر بكثير للأسطوانة والمحور. أظهر المشاركون الذين لديهم مخاريط سفلية و عنق غير متماثلة معدلات أكبر من KC 51.2٪ و 29.4٪ على التوالي). باستثناء قيم Pachy-Thin ومتوسط حجم القرنية، كانت جميع المقاييس الأخرى أكبر بكثير في مرضى KC و KCS مقارنة بالمرضى الضابطين. **الاستنتاجات**: يؤكد الانتشار المرتفع ل KC و KCS على أهمية هذه المشكلة وضرورة وجود استراتيجية منهجية للفحص في الفئات العمرية للأطفال الذين يعانون من خطأ انكساري.

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INTRODUCTION

Keratoconus (KC) is a chronic, bilateral, non-inflammatory disorder characterized by progressive steepening, thinning, and apical scarring of the cornea, resulting in the cornea bugling into a cone-like shape [1]. The disease typically starts in adolescence and continues after that. The recognizable regional variation in the prevalence of KC reflects the contribution of genetic makeup and environmental and socioeconomic factors to its causation. A prevalence of 0.04% was reported in the USA [2], with a higher figure of 0.76% reported from an adult Iranian population [3]. A prevalence of 7% was reported in the pediatric population from Egypt who suffered from allergic conditions [4]. A systematic review showed that the pooled prevalence from 15 countries was 1.38 per 1000 [5]. Major risk factors cited in the literature include male gender, eye rubbing, family history of keratoconus, allergy, asthma, and eczema [5]. While the exact etiology is unknown, genetic, environmental, biochemical, and biomechanical factors are thought to play a role [6]. Keratoconus is usually an asymmetrical condition; one eye may develop clinical KC before the other. Nonetheless, pediatric KC is more aggressive, with a higher rate of progression than adult KC due to the dynamic nature of the young cornea [7]. On the other

hand, diagnosing KCS clinically is more challenging. The diagnosis is based on the evaluation of corneal morphology using topography, tomography, aberrometry, and biomechanical techniques [8]. The major consequences of KCS are the progression to overt KC, the impact on quality of life through impaired vision, and the future implications of possible surgical interventions like LASIK [1]. Irregular astigmatism along with myopia causes a significant impact on the quality of vision [9]. There is no doubt about the costs associated with diagnosis and treatment. Despite the identifiable risk factors for KC, preventive measures aim toward early diagnosis and treatment to slow the progression of the disease. The most applied screening tests include corneal topography and tomography. Genetic screening applies to patients with a strong family history, despite it being costly [10]. Despite the negative impact of KC/KCS on visual abilities and quality of life, its regional variations and risk factors remain poorly understood. Few studies have explored the occurrence of KC and KCS in the pediatric age group, specifically in individuals with astigmatic error and myopia. There is a dearth of literature in the local setting that accurately estimates the magnitude of the problem. The results may inform policymakers of the burden of KC/KCS to guide preventive measures. We undertook this study to determine the prevalence of KC and KCS among an otherwise asymptomatic pediatric population with refractive errors in a tertiary eye center in Iraq.

METHODS

Study design and setting

This was a prospective cross-sectional study in the pediatric ophthalmology clinic at Ibn Al Haitham Teaching Eye Hospital from March 2022 to July 2022. The study involved 100 patients aged 6–18 who presented to the eye clinic for refractive error management.

Inclusion criteria

This study included all children aged 6 to 18, regardless of gender. Children with astigmatism greater than 1D or non-axial myopia were eligible to participate. Based on A-scan measurements, we excluded children with axial or lenticular myopia. All children aged 6–18 years, both male and female, were included in this study. All patients with astigmatism >1D or non-axial myopia (axial or lenticular myopia had been excluded by A-scan) are invited to participate in this study.

Exclusion criteria

Any patient with one of the following conditions was excluded from the study: axial myopia and lenticular myopia, history of previous intraocular surgery, history of trauma or any ocular disease (glaucoma, cataract, corneal diseases, uveitis), and history of systemic diseases like Down syndrome or diabetes mellitus.

Ethical consideration

The study abides by the ethical guidelines set forth by the World Medical Association's Helsinki Declaration for Human Studies. The study was approved by the Arab Board of Health Specialties and Ibn Al-Haitham Teaching Hospital of Ophthalmology with reference number 6370. Informed consent was obtained from the parents or guardians of the patients.

Data collection and outcome measurement

Patients were randomly selected from the list of outpatient clinics, whether presented for the first time or follow-up. The participants were selected from a pool of patients attending pediatric ophthalmology clinics for various complaints. An average of 150 patients attend different clinics each day for consultation. The investigator, who is a registrar in the clinic, selected cases in one of the weekdays based on her roster. Screening for inclusion criteria was made on the list of registered patients for that day. Patients who fit the criteria were invited to participate in the study. Five patients were selected by simple random sampling from the variable list of patients fulfilling the inclusion criteria. The investigator explained the study to the patient’s guardian, ensured confidentiality of the collected data, and that participation was voluntary. The potential participant was then given the data collection form, which included age and gender and surgical and medical history.

Eye examination

The patients' visual acuity was checked using the Snellen chart, as well as their best corrected visual acuity (BCVA) and cycloplegic refraction. The retinoscope was also used to measure their initial refractive error and look for early signs of KC. All pediatric age groups routinely undergo visual function examinations with the retinoscope. A retinoscope can easily detect the scissoring reflex, one of the early signs of KC. We performed a slit lamp biomicroscopy examination of the anterior segment to detect the presence or absence of biomicroscopic signs of KC, such as apical thinning, Fleischer's ring, Vogt's striae, and apical scars. We also examined the posterior segment using a +90 D condensing lens-assisted slit lamp.

Diagnosis of KC

Sirius tomography (CSO Florence, Italy) was used to image both corneas while sitting properly. A single optometrist took topographical photos and scans without knowing the patient's diagnosis. The topography employs a Scheimpflug camera to measure the radius of curvature of the steep and flat corneal meridians on a 3 mm diameter of the center section of the cornea. Scanning was repeated for any patients with abnormal topographical images. All of the patients' scanning records were reviewed by two cornea specialists who evaluated each patient's tomography scan. Sirius returned the following parameters: A) Symmetry index front (SIF), measures

vertical asymmetry; positive values indicate an inferior hemisphere steeper than a superior one and vice versa; B) Symmetry index back (SIb), keratoconus vertex front and back (KVf and KVb), represents the highest point of ectasia on anterior and posterior elevation maps of anterior and posterior corneal surfaces, respectively; C) Baiocchi-Calossi-Versaci index (BCV) front, back, and total; D) Root mean square values per unit area in Higher values indicate an uneven corneal surface.

Case definition

The case definition of KC and KCS was based on two main criteria: Sirius tomography maps and Sirius final analysis. A diagnosis of keratoconus was made when two or more abnormal tomography findings were found: an inferior isolated steep cone or asymmetric bow tie with inferior steepness; an I-S ratio (inferior point to superior point ratio) of more than 1.4; a posterior elevation of more than 20 µm; and K Max > 49 D and Km > 47.2 D [11]. A diagnosis of KCS was considered when only one of the following tomographic criteria was found: Shape map abnormalities (cone-like), posterior elevation 18-20 m, anterior elevation 13-15 m, or pachymetry thickness 470-500 m were considered for a diagnosis of KCS [12].

Statistical analysis

Data was entered and analyzed using SPSS-28 (Statistical Packages for Social Sciences, version 28). Data were presented as frequency, percentage, mean, standard deviation, and range (minimum-maximum values). More than two group mean differences were tested using an ANOVA test. The difference in proportions was tested using the chi-square test (c2-test) and Fisher's exact test. The significance level was set as $p<0.05$.

RESULTS

Table 1 shows that most patients aged 10–14 years were females (55%). The main presenting complaints were blurred vision and photophobia. Regarding diagnosis, 15% (95% CI: 10.0-19.0) had KC, and 17.5% (95% CI: 12.0-22.0) were diagnosed as KCS.

Table 1: Characteristics of the study sample (*n*=200)

Characters		*n*(%)
Age (year)	6-9	32(16)
	10-14	124(62)
	15-18	44(22)
Mean age (range) (year)	12.20±2.68 (7-17)	
Sex	Male	90(45)
	Female	110(55)
Symptoms	Blurred vision	141(70)
	Photophobia	55(28)
	Glare	2(1.0)
	Headache	2(1.0)
Visual acuity impairment (Snellen VA)	Mild	22(11)
	Moderate	77(38.5)
	Sever	101(50.5)
Diagnosis	Normal	135(67.5)
	Keratoconus suspect	38(17.5)
	Keratoconus	27(15.0)

Values are expressed as frequency(%), range, and mean±SD.

In Table 2, despite not being statistically significant, the proportion of KC was higher among those older than 14 years (27.3%) and who suffered other symptoms (headache).

Table 2: Distribution of case definition by sociodemographic variables

Characters		Status (*n* = 200)			*p-value*
		Normal	KCS	KC	
Age (year)	6-9	26(81.3)	4(12.5)	2(6.3)	0.062*
	1014	85(68.5)	23(18.5)	16(12.9)	
	> 14	24(54.5)	8(18.2)	12(27.3)	
Gender	Male	60(66.7)	16(17.8)	14(15.6)	0.972#
	Female	75(68.2)	19(17.3)	16(14.5)	
Symptoms	Blurred vision	96(68.1)	19(13.5)	26(18.4)	0.004*
	Photophobia	37(67.3)	16(29.1)	2(3.6)	
	Others	2(50)	0(0.0)	2(50)	
Visual acuity impairment (Snellen VA)	Mild	17(77.3)	4(18.2)	1(4.5)	0.150*
	Moderate	50(64.9)	10(13)	17(22.1)	
	Sever	68(67.3)	21(20.8)	12(11.9)	

Values are expressed as frequency (%). * Chi square test; # Fishers' exact test.

Table 3 illustrates the distribution of mean refractory measurement among individuals with KC status. The results indicate a significant increase in the mean (SD) of the cylinder and axis among patients with KC. Despite it being non-significant, the mean (SD) of the sphere was also higher among KC patients. Table 4 shows the mean distribution of CSO. There was a significantly higher proportion of KC among those with inferior cone and asymmetric bow tie, 51.2% and 29.4%, respectively.

Table 3: Mean refractive error classification among the three study groups

Objective Cycloplegic Refraction	Normal (*n*=135)	Keratoconus suspect (*n*=38)	Keratoconus (*n*=27)	*p*-value ANOVA
Sphere	-2.44±2.69	-2.59±2.46	-3.06±2.97	0.693
Cylinder	-2.53±1.43	-3.35±1.28	-5.99±3.07	0.0001
Axis	95.76±69.73	75.09±51.22	99.10±50.28	0.202

Data were presented as Mean±SD.

Except for pachy thin (µm) and corneal volume, all parameters' mean values were significantly higher among KCS and KC patients compared to normal patients.

Table 4: Mean values for CSO Sirius tomography screening indices for examined eyes

Topographic Imaging		Normal (*n*=135)	Keratoconus suspect (*n*=38)	Keratoconus (*n*=27)	*p*-value
Inferior Cone	No	129(82.2)	20(12.7)	8(5.1)	0.0001*
	Yes	6(14)	15(34.9)	22(51.2)	
Asymmetric Bow Tie	No	112(75.2)	22(14.8)	15(10.1)	0.0001*
	Yes	23(45.1)	13(25.5)	15(29.4)	
I-S Ratio		0.30±0.37	1.20±1.27	3.15±2.18	0.0001#
Posterior Elevation (µm)		11.2±7.23	29.8±23.3	60.1±29.3	0.0001#
K maximum (D)		46.1±2.25	51.4±4.49	63.4±11.4	0.0001#
K mean (D)		42.9±4.50	46.1±3.0	52.3±5.73	0.0001#
Pachy thin ((µm)		513±52.1	432±60.9	381±67.7	0.0001#
Topography cylinder (D)		-2.3±1.07	-3.4±1.26	-6.4±3.22	0.0001#
Sim-k1 (D)		42.7±1.38	45.3±2.82	49.4±9.85	0.0001#
Sim-k2 (D)		44.5±1.72	48.3±6.11	58.0±8.57	0.0001#
Corneal volume (mm^3)		54.7±4.09	49.8±7.86	52.2±4.02	0.0001#
Anterior chamber depth (ACD) (mm)		3.18±0.32	3.12±0.45	3.27±0.68	0.377#
Anterior elevation (µm)		6.41±3.99	16.8±7.79	60.3±28.2	0.0001#

Values are expressed as frequencies, percentages, and mean±SD. * Fishers' exact test; # ANOVA test. Abbreviations: Pachy thin: pachymetry thinnest location; I-S ratio: inferior to superior surface ratio.

DISCUSSION

Keratoconus is a preventable disease that leads to visual impairment when it progresses. Early diagnosis and identification need a combination of diagnostic approaches to quantify the incidence of this disease. Our study identified a high prevalence of KC/KCS among children with refractive errors. This result could highlight the need for a more vigilant approach among children visiting ophthalmic clinics. The prevalence of 13.5 and 19% for KC and KCS in our study, respectively, is higher than those reported from Nepal at 11.3% [13], Gambia at 0.9% [14], Italy at 0.77% [15], and Egypt at 7% [4]. On the other hand, studies showed a higher prevalence of KC in Turkey (26.2%) [16] and Brazil (22.5%) [17] and 20% [18] as well. Genetic makeup could explain the high prevalence of KC in this study; Middle Eastern people have demonstrated a higher genetic predisposition to acquire KC/KSC [19]. Exposure to high levels of UV radiation triggers eye rubbing and, hence, the development of KC/KCS [20]. The difference in the associated condition and diagnostic criteria could also account for the variation in prevalence. For instance, relying solely on a clinical examination without topography or tomography could lead to a lower identification rate. In most low-prevalence countries, patients primarily present with allergic eye conditions that cause corneal thinning; in these countries, the predisposing factor is the allergic condition rather than refractive errors. However, our patient suffers severe visual impairment and refractive errors. Such bulging of the lens/cornea makes it susceptible to thinning; hence, the development of KC/KCS disease. We didn't find a significant association between age and the prevalence of KC/SKC, which contradicts other studies reported in Brazil [17], Turkey [16], and Iran [18]. Nonetheless, an Egyptian study found that older age is associated with a higher prevalence of the disease [4]. Different diagnostic methods have been described in the literature to diagnose KC. Initially, the diagnosis relied on clinical criteria derived from slit lamp examination. Subsequently, it evolved into a more computerized process, analyzing parameters from topography and topographical tests, until advanced machine learning models were recently introduced. Serdarogullari *et al*. recommended that all patients with 2D or more astigmatism should undergo corneal topography screening for early diagnosis of KC [19]. Safarzadeh and Nasiri [20] concluded that multiple indices obtained with CSO Sirius are useful in distinguishing eyes in variable stages of keratoconus from normal eyes. These parameters include pachymetric thickness, anterior and posterior corneal power (BCVf and BCVb), and the posterior corneal elevation. The thinnest corneal thickness and posterior corneal elevation seem to be the best indices in differentiating keratoconus suspect from normal eyes [20]. These results are similar to those from our study, which showed that the KCS group had significantly different values for the pachymetric thinnest location and posterior elevation. The mean

value for the pachymetric thinnest location in the keratoconus suspect group was 381.07±67.79 µm in comparison to the normal group, which was 513.08±52.14 µm; the mean value of posterior elevation in the keratoconus suspect group was 60.13±29.34 µm, while in the normal group it was 11.21±7.23 µm ($p<0.001$). As KC is a progressive disease affecting vision, early diagnosis and treatment are vital to reduce the burden of this disease and preserve the vision of the patients. This requires a collaborative approach to increase awareness among the population about the risk factors and symptoms of KC and the application of advanced methods of diagnosis. Avoiding rubbing eyes, preventing and treating atopy and allergies, and undergoing genetic counseling and screening are considered necessary activities to halt the prevalence of KC/KCS.

Study limitations

We identified some limitations in this study that might affect the interpretation of the results. First, information about risk factors like family history and urban-rural dwelling was not gathered in this study. Nonetheless, there is no identifiable variation between urban and rural areas that may confound the results. Second, a larger sample size would have offered a better characterization of the severity of the disease. The scarcity of cases attending pediatric clinics necessitates a longer duration study. Finally, the samples collected from a single referral eye center may not accurately represent the population, which could lead to a generalization of the results. However, serving as a referral center provides a pool of cases.

Conclusion

The high prevalence of KC and KCS highlights the significance of this problem and the need for a systematic approach to screening this prevalent condition among pediatric groups with refractive error.

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Conflict of interests

No conflicts of interest were declared by the authors.

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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