Corneal topographic patterns and factors associated with keratoconus among patients presenting with ocular allergy at a tertiary hospital in northern Tanzania

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ABSTRACT

Objective: To determine the corneal topographic patterns and factors associated with keratoconus among patients presenting with ocular allergy.
Method: This was a hospital-based cross-sectional study conducted among patients aged 5–30 years with ocular allergy. Data collection included questionnaires, slit-lamp examination, retinoscopy, and corneal topography. Keratoconus was diagnosed using clinical signs and a steep K > 47.2D on topography. Topographic patterns were also recorded. Data were analysed using STATA v17, with descriptive statistics and multivariable analysis; p-values < 0.05 were considered statistically significant.
Results: A total of 270 participants (534 eyes) were enrolled, 61.9% of whom were male. Vernal keratoconjunctivitis was present in 60.7% of participants. Keratoconus prevalence was higher via corneal topography (19.3%) as compared to clinical signs alone (12.2%). Common topographic patterns among those with keratoconus included inferior steepening (26.9%), round (21.2%), symmetric bowtie (13.5%), and asymmetric bowtie with inferior steepening (13.5%). Significantly associated factors were aged >10 years (p = 0.001), allergy duration >5 years (p < 0.001), and chronic allergies: vernal keratoconjunctivitis and atopic keratoconjunctivitis (p < 0.001).
Conclusion: The prevalence of keratoconus is higher when diagnosed using topography compared to relying only on clinical signs. This highlights the need for screening all patients with ocular allergy for keratoconus, especially those with VKC and AKC, older age (>10 years) and longer duration of symptoms.

Key words: Keratoconus, Ocular allergy

INTRODUCTION

Ocular allergy is the inflammation of the conjunctiva due to immediate hypersensitivity reaction to environmental allergens[1]. Keratoconus (KC) in association with ocular allergy is thought to be due to chronic eye rubbing that leads to increase in levels of tear proteolytic enzymes and decreased concentration of protease inhibitors, which results in altered corneal collagen configuration and eventually thinning and protrusion[2,3].

The overall prevalence of keratoconus globally is estimated to be 1.38 per 1000 population[4]. Among patients with ocular allergy the prevalence of KC ranges (1.7-10.6%) in East African countries[5,6].

Complications of KC include progressive myopia, astigmatism, corneal thinning, hydrops and scarring, thus leading to decreased visual acuity and poor quality of life[3].

Corneal topography is a diagnostic tool for keratoconus, even before it is clinically visible[7] ,enabling early diagnosis and timely management. A steep K>47.2 diopters is suggestive of keratoconus[8].

Although keratoconus is also associated with systemic conditions such as Down syndrome and connective tissue disorders[3,9], this study hypothesized a strong association between keratoconus and ocular allergy particularly its chronic forms. Despite the growing incidence of ocular allergy in Tanzania[10], there is limited data on fundamental knowledge of its extent, corneal topographic patterns, and factors that contribute to the development of keratoconus among these patients. This study aimed to address this gap and thus providing data that will help in better management of these patients.

MATERIALS AND METHODS

Study design and population

This was a hospital-based cross -sectional study that was conducted from October 2023 to May 2024 at Kilimanjaro Christian Medical Centre (KCMC) in the Eye Department. KCMC is a tertiary and a teaching hospital found in Northern Tanzania.

The study included patients aged 5 to 30 years who were diagnosed with ocular allergy and attended the eye clinic at KCMC.This age range was chosen because most patients under 5 years old have difficulty cooperating during topography, and keratoconus typically develops during puberty and adolescence, with progression up to the age of 30 years[11]. Consent to collect data was obtained from patients aged 18 years and above, and from parents or guardians for those below 18 years.

Patients who did not meet the eligibility criteria, that is those who had undergone corneal transplant, corneal scar, corneal ulcer, dry eye syndrome were excluded because these conditions can significantly alter corneal curvature and surface regularity, thereby affecting the accuracy of corneal topography[9]. Also patients with other forms of corneal ectasia apart from keratoconus and patients unable to cooperate for corneal topography, other systemic conditions that are associated with keratoconus such as, Down's syndrome, Ehlers-danlos syndrome, osteogenesis imperfecta[3,12] were excluded.

Study procedure

Consecutive sampling technique was applied during this study. Patients of interest were identified at the eye clinic, then demographic characteristics (age, sex, residency) were documented for every patient. Visual acuity testing was then performed using Snellen chart. Structured interviews using a questionnaire with closed-ended questions were conducted.

This helped to attain symptoms that were used to differentiate types of ocular allergy, duration of symptoms, other atopies (asthma, allergic rhinitis and eczema). Ocular examination using slit-lamp biomicroscopy was then performed, during which various signs were identified to differentiate between different types of ocular allergy.

Types of ocular allergy were classified using Leonard classification system[13] and categorized into acute and chronic types. Acute being Perennial Allergic Conjunctivitis (PAC) and Seasonal Allergic Conjunctivitis (SAC) and chronic being Vernal Keratoconjunctivitis (VKC) and Atopic Keratoconjunctivitis (AKC). Also, different signs of keratoconus observed on slit lamp bio microscopy were documented i.e., Munson's sign, apical scarring, Fleischer's ring, Vogt's striae and Rizutti's sign (using a pen torch) were documented. Clinical diagnosis of keratoconus was made by the presence of one or more of these signs.

Refraction using a retinoscopy was done to identify scissoring sign and refractive errors (hyperopia, myopia, astigmatism and myopic astigmatism). Best Corrected Visual Acuity (BCVA) was graded according to WHO grading system that is 6/6-6/12 (normal vision), 6/18-(mild visual impairment), 6/24-6/60 (moderate visual impairment), 5/60-3/60 (severe visual impairment) and <3/60 (blindness).

Corneal topography was then performed using (Zeiss Atlas 9000 Corneal topography system). Steep K, Flat K were documented. Also, corneal topographic patterns were categorized according to Rabinowitz- as Round (R), Oval (O), Symmetric Bowtie (SB), Superior Steepening (SS), Inferior Steepening (IS), Asymmetric Bowtie with Superior Steepening (ABSS), Asymmetric Bowtie with Inferior Steepeining (ABIS) and Irregular(I)[8].

A Steep K > 47.2 D and with at least one clinical sign of keratoconus was considered as clinical keratoconus. A steep K > 47.2D with absence of clinical signs was considered of subclinical keratoconus[8.]

Keratoconus was also graded according to severity using Amsler Krumeich grading system by using a steep K. Grade I- steep K <48D, Grade II- Steep K <53, Grade III- Steep K 53-55D, Grade IV-Steep K>55D[9,14].

Data analysis

Data was analyzed using STATA (Stata Corp LLC, College Station, Texas, USA) version 17. Descriptive statistics were carried out, whereby categorical variables were summarized using frequency and percentages and numeric variables were summarized using mean with Standard Deviation (SD) and median with Interquartile Range (IQR).

A modified poisson was used to assess the factors associated with keratoconus. A univariate analysis was done to obtain the Crude Prevalence Ratio (CPR) while a multivariable analysis was done to obtain Adjusted Prevalence Ratio (APR). Variables with a P-value of < 0.05 were considered statistically associated with keratoconus.

Ethical considerations

Ethical clearance was sought from the Institutional Review Board of Kilimanjaro Christian Medical University College Research and Ethics Review Committee (KCMU-CREC) and granted with No. PG 84/2023.Only file numbers were used to maintain confidentiality when completing the questionnaires.

RESULTS

This study included 270 individuals (534 eyes). Median age among study participants was 11 years IQR (8,15), 61.9% were male. The largest subgroup consisted of those with VKC, accounting for 60.7% (Table 1).

Table 1: Social-demographic and clinical characteristics of study participants (N=270)

Variable	Frequency (n)	(%)
Age of the participant in years		
≤ 10	122	45.2
11-30	148	54.8
Median (IQR)	11 (8,15)	
Sex		
Female	103	38.1
Male	167	61.9
Residence		
Rural	110	40.7
Urban	160	59.3
Duration of ocular allergy		
≤ 5	183	67.8
6-10	59	21.9
> 10	28	10.4
Type of ocular allergy		
SAC	77	28.5
PAC	17	6.3
AKC	12	4.4
VKC	164	60.7
Other atopies		
None	223	82.6
Asthma	4	1.5
Allergic rhinitis	28	10.4
Eczema	13	4.8
Either atopies	2	0.7
Refractive error status		
Emmetropia	169	62.6
Myopia	16	5.9
Hyperopia	1	0.4
Astigmatism	35	13
Myopic astigmatism	49	18.1

Figure 1, shows proportion of those with keratoconus, out of 270 study participants, the proportion of keratoconus by clinical diagnosis alone was 12.2% (33/270) and this increased by topography to 19.3% (52/270). Among the 52 participants with keratoconus, 44 had bilateral and 8 unilateral making a total of 96 eyes with keratoconus. In regards to Best Corrected Visual Acuity (BCVA) of eyes with keratoconus, those with BCVA between 6/6-6/12 were 45.8% (44/96) and those with BCVA of <3/60 were 12.5%(12/96) as shown in figure 2.

Figure 1: Proportion of keratoconus among patients with ocular allergy by clinical diagnosis and topography

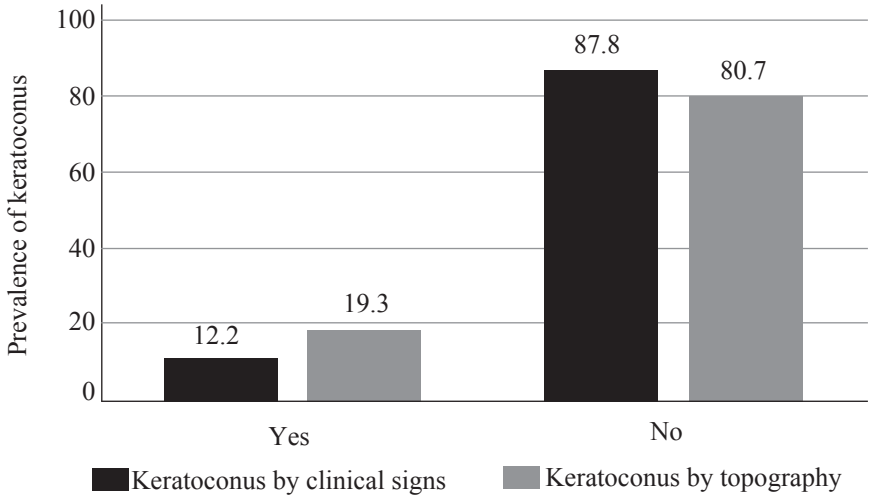


Figure 2: Best corrected Visual Acuity (BCVA) among the study participants' eyes with keratoconus (N=96)

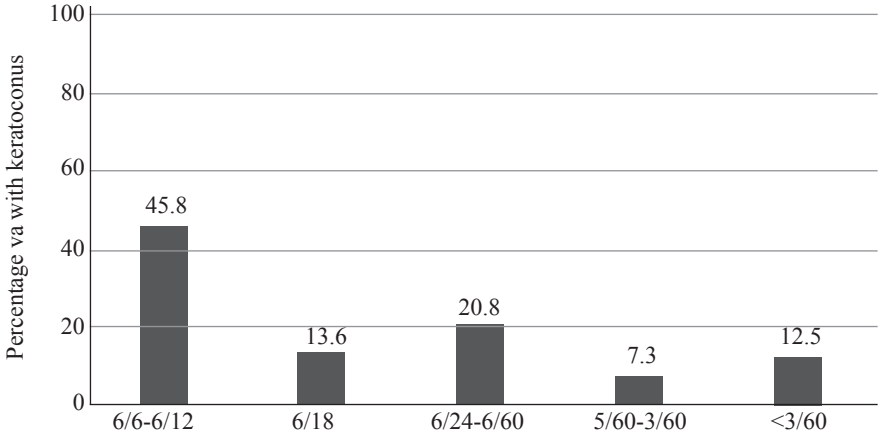


Figure 3 shows the distribution of keratoconus severity according to the Amsler Krumeich grading system. The highest proportion was observed in grade 4, with 44% (42/96).

Figure 3: Distribution of grades of keratoconus by severity (N=96 eyes)

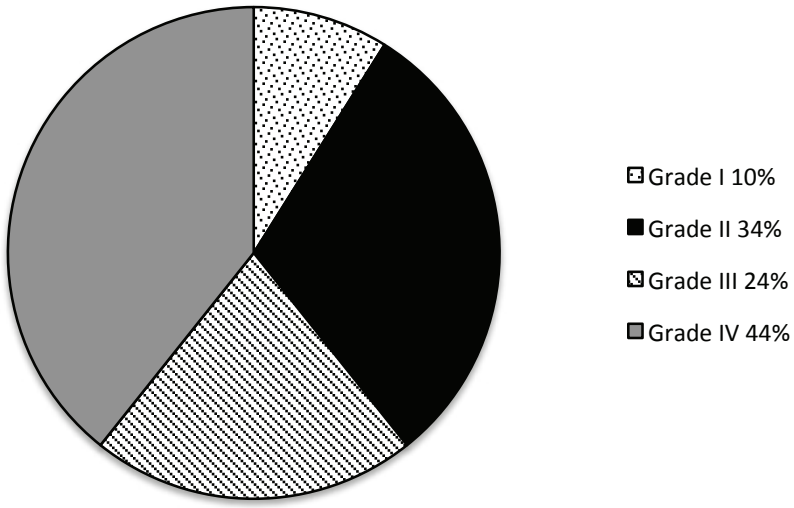
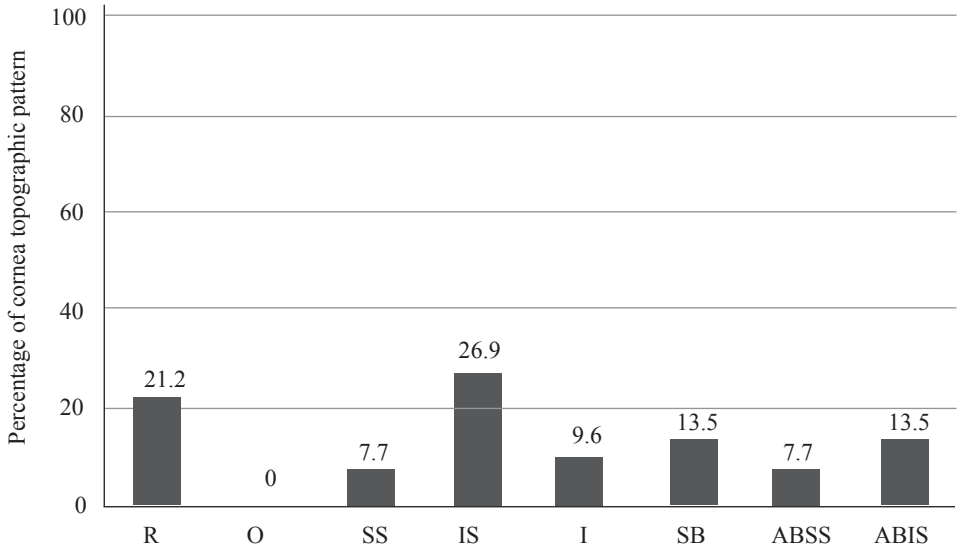


Figure 4, shows the distribution of different corneal topographic patterns in Keratoconus patients. the most prevalent corneal topographic patterns were Inferior Steepening (IS) by 26.9% (14/52), Round by 21.2% (11/52), Symmetric Bowtie (SB) by 13.5% (7/52) and Asymmetric Bowtie with Inferior Steepening (ABIS) also by 13.5% (7/52).

Figure 4: Corneal topographic patterns among the study participants with keratoconus (N=52)



R-*Round, **O**-Oval, **SS**-Superior steepening, **IS**-inferior steepening, **I**-Irregular, **SB**-Symmetric Bowtie, **ABSS**-Asymmetric Bowtie with Superior Steepening, **ABIS**- Asymmetric Bowtie with Inferior Steepening

Table 2 summarizes the factors associated with keratoconus among participants with ocular allergy. In the adjusted analysis, age of the participant, duration of ocular allergy, and type of ocular allergy were statistically significant factors.

Participants aged 10 years or younger were 0.35 times as likely to have keratoconus compared to those older than 10 years (APR = 0.35; 95% CI: 0.17–0.71; p = 0.001). Those with acute forms of ocular allergy were 0.26 times as likely to have keratoconus compared to participants with chronic forms (APR = 0.26; 95% CI: 0.14–0.49; p < 0.001). Participants with a duration of ocular allergy of 5 years or less were also 0.26 times as likely to have keratoconus compared to those with allergy lasting more than 5 years, after adjusting for age and type of ocular allergy (APR = 0.26; 95% CI: 0.14–0.49; p < 0.001).

Table 2: Factors associated with keratoconus among participants with ocular allergy

Variable	CPR (95%CI)	P-value	APR (95%CI)	P-value
Age of the participant in years				
≤10	0.25 (0.12-0.50)	<0.001	0.35 (0.17-0.71)	0.001
>10	Ref		Ref	
Sex				
Female	0.72 (0.42-1.23)	0.231		
Male	Ref			
Duration ocular allergy in years				
≤5	0.18 (0.10-0.31)	<0.001	0.26 (0.14-0.49)	<0.001
>5	Ref		Ref	
Type of ocular allergy				
Acute	0.28 (0.14-0.57)	<0.001	0.26 (0.13-0.50)	<0.001
Chronic	Ref		Ref	
Atopies				
No	Ref			
Yes	0.86 (0.43-1.71)	0.673		

DISCUSSION

In this study the proportion of keratoconus among patients with ocular allergy was 12.2% by clinical diagnosis and raised to 19.3% by corneal topography. Clinical diagnosis relies on observable symptoms and signs that are mostly observed in advanced cases of keratoconus. On the other hand, corneal topography can identify subtle changes in corneal shape that may not be apparent during a routine clinical examination.

Similarly, other studies showed that the prevalence of keratoconus (KC) increased when diagnosed by topography. A study done in Malaysia showed that the prevalence of KC increased from 10.3% to 11.5% among patients with VKC[15]. Another study done in India among patients with VKC:11.2% had KC by corneal topography, none clinically[16].

Studies done in Kenya and Egypt differed dramatically from clinical to topography diagnosis that is; (10.6% to 30.9%) and (7% to 27%) respectively as compared to our study[16,17]. This difference could be explained by different diagnostic criteria of keratoconus by topography; for instance, a study done in Egypt used two criteria, which are steep K > 47.2 and I-S asymmetry >1.2D. Also, the results could have been overestimated due to variances in the expertise of healthcare providers interpreting clinical signs on topography.

A study conducted in Italy demonstrated a significantly lower prevalence of KC among VKC patients (0.77%) compared to our own findings[18]. This low prevalence might be attributed to the inclusion criteria, which required a minimum follow-up period of 12 months and the use of cyclosporine eye drops by all participants during this period. Additionally, racial and geographic disparities could contribute to the observed differences, as it has been shown in different studies that higher rates of keratoconus are typically reported in tropical regions as compared to European countries .

Of note, in our study, the majority of participants' eyes, 44%, with keratoconus were in grade 4. This could be due to the absence of effective screening programmes for early detection of keratoconus among patients with ocular allergies which result in a higher proportion of advanced cases by the time patients are diagnosed. Many of which in this category require corneal transplant. These findings were similar to the study done in Kenya whereby the majority of the participants, 58.8%, had severe keratoconus[6].

Among patients with ocular allergy diagnosed with keratoconus, inferior steepening was most prevalent (26.9%), followed by round, symmetric bowtie, asymmetric bowtie with inferior steepening (21.2%,13.5% and 13.5%) respectively. It has been speculated that the most pattern found in early forms of keratoconus are inferior steepening[8]. Round pattern is found in more severe forms of keratoconus[9]. A similar study conducted in India showed the frequencies of various corneal topographic patterns were as follows: round (R) 17.11%, Asymmetric Bowtie with Inferior Steepening (AS-IS) 17.11%, and Symmetric Bowtie (SB) 38.16%. The discrepancy primarily lies in the slightly higher percentage of symmetric bowtie patterns. And this could be due to the fact that the patients included in their study had early stages of KC, as all the participants with KC were diagnosed by topography, none clinically[16].

Another study done in Israel showed the most prevalent patterns were asymmetric bowtie with superior steepening (36.25%), asymmetric bowtie with inferior steepening (31.25%), and symmetric bowtie (18.75%)[19]. The difference in these studies can be explained by the fact that the study only enrolled patients with VKC; other types of ocular allergy were not studied.

In our study, age was an independent risk factor for the development of keratoconus; those aged <10 years were less likely to have keratoconus ((P-value < 0.001) compared to those aged 10 years. This can be explained by the fact that studies have shown most of the patients develop keratoconus at puberty. This is due to hormonal changes during puberty and adolescence that influence corneal remodeling and may contribute to the onset of keratoconus in susceptible individuals. This study is similar to a study done in Kenya, where most of the patients diagnosed with keratoconus were aged 10-14 years (42.1%), followed by those aged 15-19 years (23.7%); the mean age of the patients diagnosed with keratoconus was 14.9 SD 5.9[6]. It is also similar to another study done in Egypt, a case-control study where the mean age of patients with KC was 11.2 ± 3.7 years for the cases[17].

Participants with a duration of ocular allergy of <5 years were less likely to have keratoconus compared to those with duration of ocular allergy >5 years (P-value < 0.001). This could be due to individuals with shorter durations of ocular allergy having experienced less cumulative inflammatory damage to the cornea compared to those with longer durations, thereby reducing their risk of developing keratoconus. A study done in India[16] revealed similar results, whereby the odds of having keratoconus increased significantly in those with allergy duration of more than 6 months, and this was statistically significant (p < 0.0001). In another study done by Salam Wani *et al*[20] the mean duration of illness in eyes with a KC pattern was 6.7 years, and in eyes with severe KC and astigmatism was 8.5 years and 5.7 years, which is more compared to eyes with non-KC pattern. It was also similar to a study done in Kenya where the mean duration of allergy symptoms in patients with keratoconus was 5.8 years[6]. However, it is important to note that these two studies did not show association by univariate and multivariate analysis.

In this study, those with acute forms of ocular allergy were less likely to have keratoconus compared to those with chronic forms (P-value < 0.001); this is probably due to the fact that chronic inflammation is believed to play a role in the pathogenesis of keratoconus. The more severe the allergic response, the higher the levels of inflammatory mediators released in the eye. These mediators can potentially contribute to the thinning of the cornea over time, which is a characteristic feature of keratoconus. This study was comparable to a study done in Kenya where those with severe forms of ocular allergy had 13.3 odds of developing keratoconus compared to those with mild-moderate forms of ocular allergy (p < 0.001). It is also similar to a study done in Egypt whereby 65.9% of VKC had KC[17]. Comparing our study to others was challenging because most previous studies focused exclusively on patients with VKC rather than encompassing all types of ocular allergies. Therefore, there is a need for further research that includes all forms of ocular allergy.

Study limitation

This study employed a cross-sectional design, which limits the ability to establish temporal relationships, highlighting the need for further evidence from prospective research. Additionally, as a hospital-based study, the findings may not be fully representative of the general population.

CONCLUSION

In this study, we found there was an increase in the proportion of keratoconus in patients with ocular allergy when diagnosed by topography as compared to when we rely only on clinical signs. Also, corneal topographic patterns that were mostly found in KC patients included inferior steepening, round, symmetric bowtie and asymmetric bowtie with inferior steepening. Factors that were significantly associated with the development of keratoconus were age >10 years, long duration of allergy and chronic forms of ocular allergy. This highlights that, while clinical examination remains important, it may miss mild or subclinical cases. This may lead to delays in diagnosis and timely management of such patients, increasing the risk of complications.

RECOMMENDATIONS

To incorporate early corneal topography screening for patients with ocular allergy, particularly those over 10 years of age, with a long duration of allergy, and those experiencing chronic forms such as VKC and AKC.

This will help in early diagnosis, timely management such as corneal collagen crosslinking to arrest progression of the disease, thus reducing the number of complications and need for corneal transplant.

Authors contributions

I Ndyanabo L. (lead author) conceptualized the study, designed the methodology, and conducted data collection. I also performed the statistical analysis, drafted and revised the manuscript. Muna. EJ and Mndeme FG contributed in supervising the clinical aspects of data collection and provided critical insights during data interpretation and contributed to manuscript editing. All authors read and approved the final version of the manuscript.

Disclosure

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