

Prevalence of keratoconus in patients with allergic conjunctivitis attending Kenyatta National Hospital eye clinic

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ABSTRACT

Objective: To determine the prevalence of keratoconus among patients with allergic conjunctivitis aged between 8 and 30 years, attending Kenyatta National Hospital eye clinic.

Methods: A cross sectional study of patients on follow up for allergic conjunctivitis. They were examined on the slit lamp, clinical signs of keratoconus were elicited, and then keratometry and corneal topography was done on each of them. The social demographic and clinical data was captured in a questionnaire. Descriptive analysis of the data was done to determine means, frequencies and proportions of the various variables. The relationship between the demographic characteristics of the patients, the duration and severity of allergic conjunctivitis, with keratoconus was assessed.

Results: Two hundred and forty six eyes of 123 patients were examined. Keratoconus prevalence was found to be 10.6% by clinical diagnosis, 14.6% by keratometry and 30.9% by topography. Majority of those diagnosed with keratoconus were aged 10 to 14 years (42.1%). The male: female ratio of those with keratoconus was 1.9:1, and among them 34.2% had moderate allergic conjunctivitis, and 42.1% had severe allergic conjunctivitis, which was statistically significant. Patients with allergy symptoms for more than 10 years formed the largest proportion of those with keratoconus (42.1%).

Conclusion: The prevalence of keratoconus in patients with allergic conjunctivitis was found to be high and the majority were male. Corneal topography diagnosed more patients with keratoconus, and therefore is highly recommended as part of the follow up investigations for all patients with allergic conjunctivitis. This will ensure early detection and management of the condition.

Key words: Keratoconus, Allergic conjunctivitis, Kenyatta National Hospital

INTRODUCTION

Keratoconus is a bilateral progressive disorder of the cornea, characterised by central or paracentral asymmetrical, non-inflammatory, corneal thinning and protrusion, assuming a conical shape. This induces irregular astigmatism, myopia and corneal scarring, which may cause mild to severe visual impairment. Onset is usually at puberty and the condition progresses up to the third or fourth decade. Progression may halt at any stage between mild to severe keratoconus.

The prevalence of keratoconus varies widely depending on geographical location, cohort of selected patients, diagnostic criteria used and ethnicity of patients. In the general population, it ranges from 0.3 per 100,000 as reported by Gorskova and Sevost'ianov in Russia, to 2,300 per 100,000 as reported in Central India by Jonas *et al*¹. In the USA, keratoconus is estimated to affect 1 in every 2,000 people², while in Denmark Nielsen *et al*³ reported the incidence of keratoconus of 1.3 per 100,000 per year, and a prevalence of 86 per 100,000.

Ethnicity has also been shown to influence the incidence and prevalence of keratoconus as demonstrated

by Cozma *et al*⁴ who found an incidence rate of 32.3 per 100,000 per year among Asians, and 3.5 per 100,000 per year among whites. It was also noted that the Asian patients were significantly younger at time of diagnosis than whites⁴. Keratoconus is associated with some genetic disorders, like Down's syndrome with a reported prevalence of 0.5% to 15% that is 10-30 fold of normal population. The hypothesis of hormonal involvement in keratoconus is supported by the fact that it generally begins at puberty and has also been shown to progress more during pregnancy⁵.

A strong association between allergic conjunctivitis and keratoconus has been proven in various studies. For instance, Bawazeer *et al*⁶ demonstrated that eye rubbing due to allergy was a major cause of keratoconus, whereas Lapid-Gortzak *et al*⁷ found corneal topography patterns consistent with keratoconus in 15% of children with VKC but none in those without. Totan *et al*⁸ found 26.8%, incidence of keratoconus among those with VKC which was associated with male gender, and mixed and palpebral forms of VKC. Similar findings were demonstrated by Shonja and Besharati⁹ who found an incidence of 28% in Iran.

Few studies have reported the prevalence of keratoconus in Africa. In Gambia, Wade *et al*¹⁰ found a prevalence of 0.9% of keratoconus, among patients with ocular allergy, where as in Rwanda, De Smedt *et al*¹¹ found 1.7% of the children had corneal astigmatism or keratoconus. Waweru and Bhajji¹² did a study on vernal keratoconjunctivitis as seen at KNH, and he found 3% of the patients had keratoconus. The lower prevalence reported in Africa, compared to the West and Asia, could be attributed to the different methods of diagnosis, because in Africa keratoconus was diagnosed by clinical signs, while in the west, corneal topography was used, which detects earlier signs of keratoconus. This has been demonstrated in some studies where the prevalence of clinically diagnosed keratoconus was found to be lower than when corneal topography was used^{8,13}. Keratoconus is best managed in the early stage for good visual prognosis. It is therefore necessary to have data demonstrating the importance of adopting corneal topography as a diagnostic tool in our set up.

MATERIALS AND METHODS

A hospital based cross sectional study was done at Kenyatta National Hospital eye clinic, where consecutive patients presenting for follow up for allergic conjunctivitis, were recruited into the study. The patients were aged between 8 to 30 years because keratoconus mostly develops between puberty and the 3rd decade of life¹⁴. Those with corneal ulcers, corneal scars from causes other than hydrops and those who did not complete the study were excluded. The patients were recruited from February 2016 to April 2016. Ethical approval had been obtained from Kenyatta National Hospital/University of Nairobi ethics and research board. Informed consent was obtained from all the adult patients participating in the study, and for those under the age of 18 years, consent was given by the parent/guardian while the child assented to the study.

Relevant history was taken from each patient, presenting visual acuity was recorded and clinical signs of keratoconus were demonstrated. Allergic conjunctivitis was graded according to severity as proposed by Bore and Ilako¹⁵. Clinical diagnosis of keratoconus was made if a patient had stromal corneal thinning by slit lamp evaluation accompanied by 1 or more of: Munson sign, irregular or crowded mires on hand held placido disc, scissoring on retinoscopy, or if they had stromal thickening due to hydrops. Diagnosis and grading of keratoconus using keratometry was done: mild keratoconus $K < 48D$, moderate keratoconus $K 48-54D$, severe keratoconus $K > 54D$. Corneal topographic was done on each patient, and diagnosis of keratoconus was made using the Pentacam derived Amsler-Krumeich staging.

Statistical analysis was done using the Statistical Package for Social Scientists (SPSS) version 20.0. Study population was described using socio-demographic and clinical characteristics by summarizing categorical

and continuous variables into percentages and means or medians respectively. Prevalence of keratoconus in allergic conjunctivitis was calculated as a percentage number of patients with 95% Confidence Interval (CI). Grade of keratoconus was correlated with the severity of allergic conjunctivitis using chi square test. Furthermore, presence of keratoconus was correlated with other variables such as age, sex, duration and severity of allergic conjunctivitis using chi square test for categorical variables and student's t test for comparison of means. All statistical tests were conducted at 5% level of significance (p value less or equal to 0.05).

RESULTS

The study had a response rate of 88%, and 246 eyes of 123 patients were examined (Figure 1).

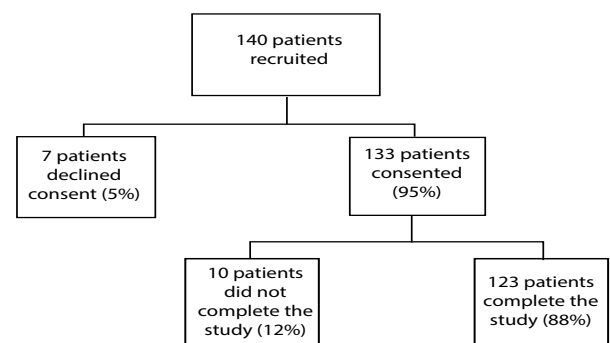


Figure 1: Flow chart of patients' recruitment

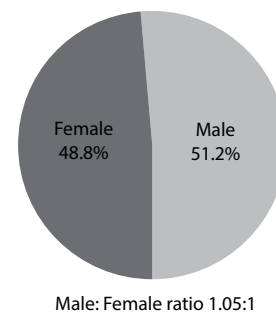


Figure 2: Distribution of patients by sex

Most patients were aged 10 to 14 years (33.3%). The mean age was 16 years (SD \pm 7), the range was 8-30 years. The median age was 14 years, and the mode 16 years (Figure 3).

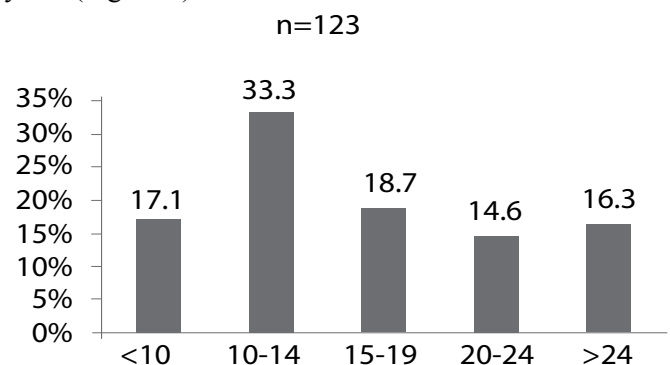


Figure 3: Distribution by age

The mean duration of allergy was 4.1 years with SD of 3.2 (Figure 4).

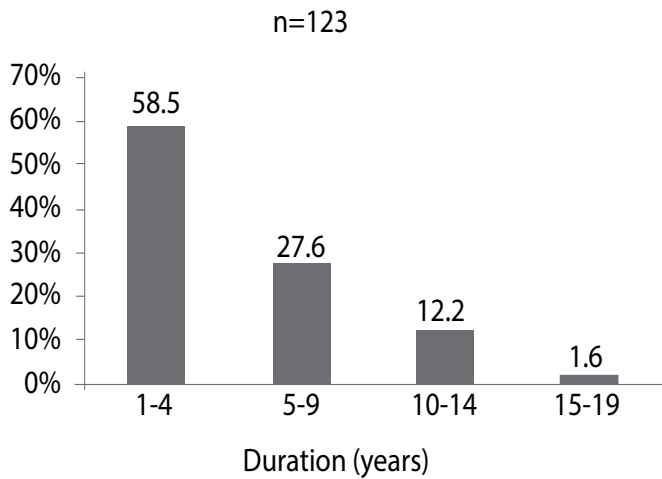


Figure 4: Duration of allergic conjunctivitis symptoms

Majority of the patients had mild allergic conjunctivitis, followed by moderate and severe (Figure 5).

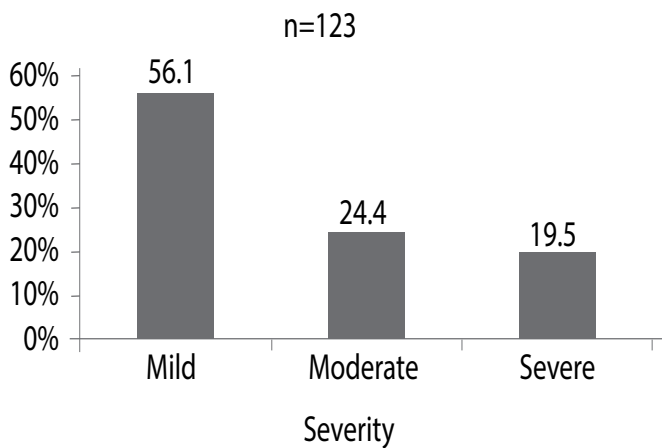


Figure 5: Severity of allergic conjunctivitis

The highest prevalence of keratoconus was diagnosed with topography, which was significant in comparison to clinical diagnosis and keratometry with p value <0.001 (Figure 6).

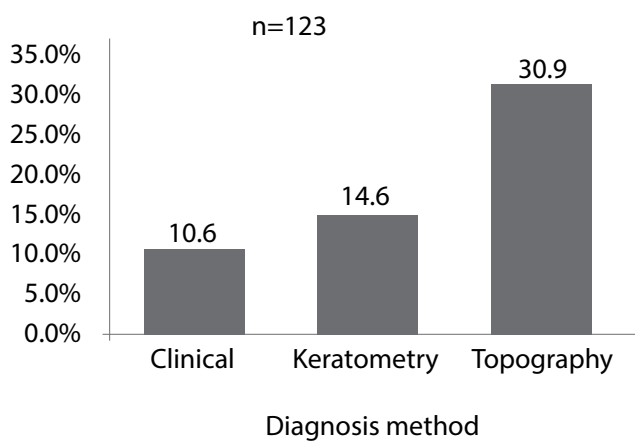


Figure 6: Prevalence of keratoconus

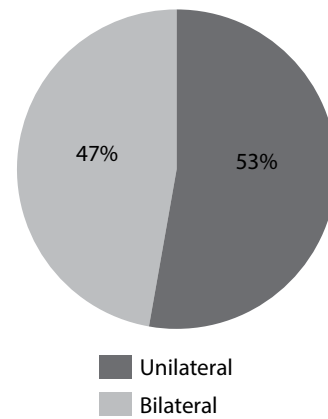


Figure 7: Keratoconus laterality

Most of the patients with keratoconus were between 10-14 years, followed by those aged 15-19 years. The mean age of the patients diagnosed with keratoconus was 14.9 SD 5.9 (Figure 8).

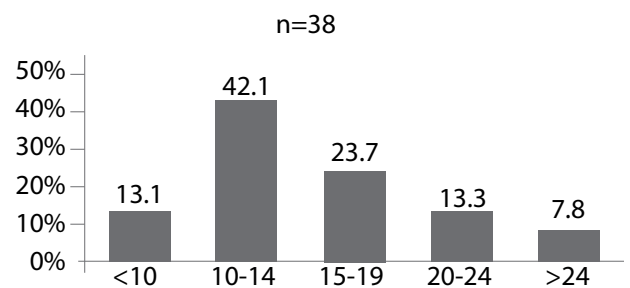


Figure 8: Distribution of patients with keratoconus by age

The proportion of patients with bilateral keratoconus increased with increase in age (Figure 9).

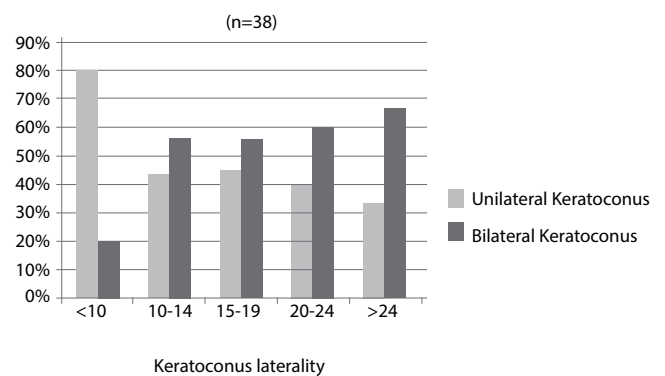


Figure 9: Distribution of keratoconus laterality by age

Table 1: Presenting visual acuity of all the eyes (246 eyes)

Presenting visual acuity	Keratoconus n (%)	No keratoconus n (%)
6/6-6/18	39 (17.5)	184 (82.5)
<6/18-6/60	9 (69.2)	4 (30.7)
<6/60-3/60	2 (100)	
<3/60	8 (100)	

Table 2: Keratoconus severity

Severity of keratoconus	Keratometry n=34 eyes n (%)	Topography n=54 eyes n (%)
Mild	4 (11.8)	18 (31)
Moderate	10 (29.8)	16 (27.6)
Severe	20 (58.8)	24 (41.4)

Thirteen eyes were diagnosed with keratoconus clinically, 3 of which had hydrops. Four of the eyes that were diagnosed clinically were found to have moderate keratoconus by keratometry, and 6 had severe keratoconus by keratometry. All the eyes that had keratoconus by clinical diagnosis, had severe keratoconus by corneal topography.

Table 3: Presenting visual acuity of the eyes with keratoconus (54 eyes)

Visual acuity	Mild keratoconus n (%)	Moderate keratoconus n (%)	Severe keratoconus n (%)
6/6-6/18	15(38.5)	14(35.9)	10(25.6)
<6/18-6/60	2(22.2)	3(33.3)	4(44.4)
<6/60-3/60	-	-	2(100)
<3/60	-	-	8(100)

All the patients with visual acuity less than 6/60 had severe keratoconus by topography.

Table 4: Factors associated with keratoconus

Variable	Corneal topography		OR (95% CI)	P value
	Keratoconus	No keratoconus		
Sex				
Male	25 (65.8%)	38 (44.7%)	2.4 (1.1-5.3)	0.031
Female	13 (34.2%)	47 (55.3%)	1.0	
Severity of AC				
Mild	9 (23.7)	60 (70.6)	1.0	
Moderate	13 (34.2)	17 (20.0)	5.1 (1.9-13.9)	0.002
Severe	16 (42.1)	8 (9.4)	13.3 (4.4-40.1)	<0.001
Allergies/asthma				
Yes	6 (15.8)	11 (12.9)	1.3 (0.4-3.7)	0.672
No	32 (84.2)	74 (87.1)	1.0	

Table 5: Association of duration of allergy with keratoconus

Duration of allergic conjunctivitis	Keratoconus	No keratoconus	OR (95% CI)	P value
Median (IQR)	5 (4-8)	2 (1-5)	-	0.001
Category, n (%)				
1-4 years	16 (22.2)	56 (77.8)	1.0	
5-9 years	13 (38.2)	21 (61.7)	2.2 (0.9-5.3)	0.088
>10	9 (53)	8(47)	5.3 (1.6-17.0)	0.006

The mean duration of allergy symptoms in patients with keratoconus was 5.8 years, SD 3.8.

DISCUSSION

Demographic characteristics: In this study, 246 eyes of 123 patients were examined (Figure 1). The male to female ratio was almost equal 1.05:1 (Figure 2), unlike in other similar studies where the male:female ratio was

higher. Shoja and Besharati⁹ found a male:female ratio of 1.7:1, and Totan *et al*⁸ found a ratio of 3:1. This could be attributed to the fact that all types of allergic conjunctivitis were examined in this study unlike in the other studies where they looked at patients with VKC, which has been found to affect males more than females.

The patients' ages ranged from 8 to 30 years with the majority aged between 10 to 14 years (33.3%). The mean age was 16 years SD 7 (Figure 3). This is comparable to the study by Totan *et al*⁸ and Shoja and Besharati⁹ whereby the mean age (SD) in their studies was 15.04 (6.11) and 13.07 (4.71) respectively. This can be attributed to the fact that allergic conjunctivitis mainly affects patients between the ages of 5-20 years with a peak at 11 to 15 years¹⁶. A similar age distribution has been demonstrated in several studies including that done by Waweru and Bhajji¹² at KNH.

Severity and duration of allergic conjunctivitis: Most of the respondents had symptoms of allergic conjunctivitis for duration of 1 to 4 years, with a mean duration of 4.1(SD 3.2) years (Figure 4). This duration is shorter by 1 year compared to what was found by Totan *et al*⁸ of 5.52 ± 4.16 years and Shoja and Besharati⁹ who found 5.12 ± 4.29 years. Allergic conjunctivitis was graded according to the criteria proposed by Bore and Ilako¹⁵ which takes into consideration conjunctiva signs, cornea and limbal involvement. Majority of the patients had mild allergic conjunctivitis (56.1%), whereas 24.4% had moderate allergy and 19.5% had severe allergy (Figure 5).

Prevalence of keratoconus: The prevalence of keratoconus was found to be 10.6% by clinical diagnosis, 14.4% by keratometry and 30.9% of the patients had keratoconus by topographic criteria (Figure 6). The difference in the prevalence found by corneal topography was statistically significant when compared to keratometry and clinical diagnosis, with a p value <0.001. This is because topography diagnosed eyes with early signs of keratoconus, which did not have evident clinical and keratometry changes. This difference in prevalence depending on the diagnosis method compares to what Totan *et al*⁸ found; 8.5% by slit lamp biomicroscopy, 18.4% by keratometry and 26.2% by corneal topography. It is also similar to what Dantas *et al*¹³ found in Brazil where the prevalence was 9.85% by clinical diagnosis and a higher prevalence of 22.5% by topographic diagnosis. Shoja and Besharati⁹ found a comparable prevalence of 28% in Iran after using topography to diagnose keratoconus.

This study found a higher prevalence of keratoconus by topography as compared to other studies, which could mean that the allergic conjunctivitis patients in our set up have a slightly higher prevalence of keratoconus than in other geographical regions, especially since Africa is considered as one of the regions with a higher prevalence of VKC. The topography diagnostic criteria should also be taken into account, and in this case the Pentacam

derived Amsler staging which was used, has been shown to have highly sensitive measures for early detection of ectatic corneal disorders¹⁷.

The prevalence of keratoconus by clinical diagnosis in other studies is lower compared to what our study found. In Rwanda, De Smedt *et al*¹¹, evaluated children with VKC, and found 1.7% had keratoconus. Waweru and Bhajji¹² also did an evaluation of patients with VKC at Kenyatta National Hospital and found 3% had keratoconus by clinical diagnosis. This can be attributed to the difference in clinical diagnostic criteria used, or the fact that the other two studies were generally evaluating all the clinical features in patients with VKC while this study concentrated on diagnosing keratoconus in patients with allergy, therefore picking more signs of keratoconus.

Of note is that, only two patients in this study had been diagnosed with keratoconus previously, while for the others this was the first time the diagnosis was made. This implies that most clinicians don't concentrate in looking for signs of keratoconus in patients with allergic conjunctivitis. It could also be attributed to limited resources for diagnosing keratoconus especially topography which was found to be more effective in diagnosing early keratoconus in this study.

Characteristics of patients diagnosed with keratoconus:

Among the patients who were diagnosed with keratoconus in this study, majority were aged 10 to 14 years followed by those aged 15 to 19 years and the reported mean age 14.9 ±5.9 (Figure 8). The mean age of patients with keratoconus in this study is comparable to the mean age found in other studies; Dantas *et al*¹³ found 13.9±4.3, Totan *et al*⁸ found 15.78 ±4.728, and Shoja and Besharati⁹ found 14.5 ±5.349. This is the same age group that forms the highest proportion of patients with allergic conjunctivitis, therefore the most likely to have keratoconus. Hormonal changes have also been postulated to have a role in pathogens on keratoconus which could also be one of the reasons why the incidence of keratoconus is high in the teenage years.

There was male predominance in those with keratoconus, a male: female ratio of 1.9:1 (Table 4). This has also been the case in the studies done by Totan *et al*⁸, M:F=2.7:1, and Shoja and Besharati⁹ M:F=1.8:1. Keratoconus has been associated with male sex in some studies, although the reasons are not well understood^{18,19}. However, not all studies are in consensus with the male predominance theory, as some have found equal sex distribution while others have found female predominance, as highlighted by Gordon-Shaag *et al*¹.

Among the patients diagnosed with keratoconus, 47% had unilateral, whereas 53% had bilateral keratoconus (Figure 7). The proportion of those with bilateral keratoconus increased with increasing age. This can be explained by the natural course of keratoconus where by it has been found to be a bilateral but asymmetrical condition. It therefore means that if a patient is diagnosed

with keratoconus in one eye they are likely to develop similar signs in the other eye at a later period as they get older.

In terms of keratoconus diagnosis and severity, clinical diagnosis picked 13 eyes, of which 3 presented with hydrops. The number of eyes diagnosed with keratoconus by keratometry was 34 and by topography 54 (Table 2). All the eyes diagnosed clinically were also picked by keratometry and topography. By keratometry, 6 of the clinically diagnosed eyes were graded as moderate and the rest as severe, whereas by topography, they were all graded as severe keratoconus. Clinical criteria picked the more advanced keratoconus in contrast to topography which picked more eyes with mild keratoconus (31%). This is not surprising because it has been proven that corneas with keratoconus exhibit topographic, tomographic and pachymetry changes way before slit lamp and clinically detectable signs¹⁹.

In this study, most of the eyes presented with a visual acuity better than 6/18 followed in proportion by those who presented with visual acuity worse than 6/18 but better than 6/60 (Table 1). Most of the patients with keratoconus presented with visual acuity better than 6/18 (72%). Majority of them had mild to moderate keratoconus. All the patients who had visual acuity worse than 6/60, had severe keratoconus (Table 3). This shows that visual performance is not clearly predictable in keratoconus and can present with wide variation¹⁷. It also emphasises on the importance of diagnosing keratoconus in its early stages in order to intervene before the vision is severely impaired especially in our set up where corneas for PKP are not readily available.

In this study, 23.7% of the patients with keratoconus had mild allergy, 34.2% had moderate allergy which was statistically significant, with a p value=0.002, and 42.1% had severe allergy, which was also statistically significant with a p value <0.001 (Table 4). This could be attributed to the fact that patients with severe allergies are likely to rub their eyes more therefore causing more trauma to their corneas and release more immune mediators into the tears, which has been postulated to have a role in the pathogenesis of keratoconus²⁰.

The mean duration of allergy symptoms among those with keratoconus was 5.8 ±3.6 (Table 5). This is slightly lower than that found by Totan *et al*⁸ 6.65 ±4.75 and Shoja and Besharati⁹ 7.65 ± 4.32. This implies that the patients in our set up may develop keratoconus much earlier than those of Turkey and Iran. Among the patients in this study, 53% of those who had allergy symptoms for >10 years had keratoconus compared to, 22.2% with symptoms for 1 to 5 years, and 38.2% with symptoms for 5 to 9 years, implying that the longer the duration of allergic conjunctivitis symptoms, the higher the proportion of those with keratoconus. This was statistically significant with a p value of 0.006 (Table 5). Patients with allergic conjunctivitis for more than 10 years were found to have a higher chance of developing KC. Emphasis should be put

on the follow up allergic conjunctivitis patients, to reduce both the severity and duration of the symptoms as they seem to have an impact on keratoconus.

Out of those diagnosed with keratoconus, 15% had other atopies (Table 4), but this association was not statistically significant in this study probably due to the sample size. However, the association between the two cannot be ruled out and more studies with larger sample size should be done to determine this.

CONCLUSIONS

The prevalence of keratoconus in patients with allergic conjunctivitis was found to be high and the majority were male. Corneal topography diagnosed more patients, especially those with mild keratoconus and good vision, compared to keratometry and clinical diagnosis. Long standing symptoms and moderate to severe allergic conjunctivitis were associated with a higher proportion of patients with keratoconus. Corneal topography is therefore recommended as part of the follow up investigations for patients with allergic conjunctivitis to ensure early detection and management of keratoconus. These patients can benefit from crosslinking which is known to slow down or stop keratoconus progression, thus reducing the need for keratoplasty. This is of great importance especially in our setup where corneal tissues are not readily available.

In areas with limited resources, all the patients on follow up for moderate or severe allergic conjunctivitis, or visual acuity of 6/18 or worse, should be referred to an ophthalmologist for corneal topography.

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