

Corneal topographic changes in young patients with chronic allergic eye disease

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Running title: Corneal topographic changes in young patients with chronic allergic eye disease.

Abstract

Purpose: Evaluate the changes in corneal topography in patients with chronic eye allergy by using pentacam.

Patients and methods: This is a cross sectional case control study on 50 patients with chronic eye allergy and 50 normal individuals who were recruited over one year from March 2019 to February 2020. Each case was subjected to history taking, complete ophthalmic examination and corneal topography.

Results: Patients with chronic eye allergy have a statistically significant higher K max and elevation back. Complicated keratoconus cases have higher Kmax, Km and elevation back and lower thinnest point, ARTmax and corneal volume. No significant differences were found among groups as regards astigmatism power, thinnest location displacement and angle of anterior chamber. keratoconus (KC)in allergic patients was more associated with vernal keratoconjunctivitis (VKC), long duration of rubbing and systemic atopy.

Conclusion: Assessment of corneal topography by pentacam could be used in patients with chronic allergic eye disease for early diagnosis and management of keratoconus.

Key words: Eye allergy, Topography, Pentacam, Keratoconus.

INTRODUCTION

Chronic allergic eye disease has become a common ocular problem, it affects about 20% of the population all over the world¹. It is a collection of common symptoms that affects conjunctiva and cornea, classified to VKC, atopic keratoconjunctivitis [AKC], Seasonal allergic conjunctivitis, perennial allergic conjunctivitis, drug induced conjunctivitis and giant papillary conjunctivitis².

Corneal disease in patients with chronic eye allergy ranges from superficial punctate keratitis, shield ulcer, corneal neovascularization, corneal plaque, lipid infiltration, viral, bacterial or fungal keratitis, keratoconus [KC], hydrops to corneal opacification. Superficial punctate keratitis is the commonest corneal complication of VKC³.

The changes in corneal thickness are one of the most important chronic allergic eye diseases complications. It may result from corneal stromal cell apoptosis or induced by the activation of matrix-degrading enzymes, particularly members of the matrix metalloproteinase [MMP] family and decreased proteinase inhibitors and authors proved that

interleukin [IL]-6, tumor necrotic factor [TNF]- α and MMP-9 are overexpressed in the tears of patients with keratoconus that indicate the pathogenesis of keratoconus may be caused by chronic inflammation⁴.

Excessive eye rubbing causes release of inflammatory mediators. Both rubbing and corneal injury in allergic conjunctivitis (AC) patients have been known as possible causes of KC progression⁵.

Keratoconus (KC) is a progressive non-inflammatory ectatic disorder of the cornea. It is characterized by cone-like steepening of the cornea with irregular stromal thinning, resulting in a cone-like bulge (protrusion) and severe visual loss⁶.

Corneal topography is a non-invasive exploratory technique to analyze both qualitatively and quantitatively the morphology of the cornea⁷.

The Pentacam is a cornea and anterior segment tomography device, based on a rotating Scheimpflug camera. Its optical cross-sectional analysis that helps in imaging of anterior and posterior

corneal surfaces which provides us with a full pachymetric map and many other data such as corneal aberrometry and densitometry that allow early detection of ectasia⁸. In this study we assess the changes in corneal topography in patients with chronic eye allergy in comparison to normal individuals in the same age group.

PATIENTS AND METHODS

This study is a cross sectional case control study that conducted to investigate the changes in topography of the cornea in patients with chronic eye allergic diseases by using pentacam at Mansoura ophthalmic center, Mansoura University, Egypt. Our study was conducted for a duration of one year from March 2019 to February 2020. this study was conducted on 92 eyes with chronic eye allergy (divided in to 2 groups; allergic conjunctivitis (AC) with complicated keratoconus or keratoconus suspect group (group 1: n 37) and AC normal topography group (group 2: n 55) and 94 normal eyes without allergy (group 3: control group), of the same age (7-20 years old).

In this study we exclude patients with corneal opacity, corneal dystrophy or degenerative changes, previous corneal surgery, ocular trauma and contact lens wearers.

After approval from the institutional review board (IRB) NO: MS.18.12.418 of Mansoura Faculty of Medicine and obtaining an informed written consent from the participants or the legal guardian, all cases were subjected to full history taking and ophthalmic examination including Visual acuity assessment (Best corrected visual acuity using landolt's visual acuity chart or Snellen chart, Patient refractive error using autorefractometer:(Autoref –keratometer RK-3 canon). Examination of Anterior segment by using slit lamp biomicroscopy and posterior segment examination.

Automatically rotating scheimpflug camera (pentacam oculus Wetzlar.Germany) was used to investigate corneal topography include corneal front (CF) average of diopter

power of flat and steep meridians(Km), CF power of astigmatism, corneal back elevation, thinnest point(TP) ,TP displacement, the point of highest diopter value of the cornea [K max], Maximum Ambrosio rational of thickness (ART max) , Belin/Ambrosio Enhance ectasia total d deviation(D), angle of anterior chamber and Corneal volume.

Statistical analysis

Data were analyzed using the Statistical Package of Social Science (SPSS) program for Windows (Standard version 21). The normality of data was first tested with one-sample Kolmogorov-Smirnov test.

Qualitative data were described using number and percent. Continuous variables were presented as mean \pm SD (standard deviation) for normally distributed data and median (min-max) for non-normally distributed data. We used the following tests; Chi square test: Compare qualitative variables, Student t test: Compare two means (parametric), Mann Whitney test: Compare two medians (non-parametric), Pearson correlation: Correlate continuous data (parametric) and Spearman correlation: Correlate continuous data (non-parametric). For all mentioned statistical tests done, the threshold of significance is fixed at 5% level. The results were considered significant when $p \leq 0.05$.

RESULTS

The mean age in the group 1(Allergic with keratoconus/ suspect) was 13.54 ± 3.79 years, in the group 2(Allergic without keratoconus/ suspect) was 11.87 ± 2.93 while in the group3 (Control normal group) it was 13.2 ± 3.72 years. Most of subjects in the group 1 (62.2%) and group 3 (54.3%) were females while in group (2) the majority of subjects were males (50.9%). No significant differences were detected between the studied groups regarding age or gender (Table1).

Table (1): Sociodemographic data among studied groups.

Demographic data	Group (1) (n=37)	Group (2) (n=55)	Group (3) (n=94)	Test of significance		
				P1	P2	P3
Age (years)						
Mean ± SD	13.54±3.79	11.87±2.93	13.20±3.72	t=0.465 p=0.643	t=1.51 p=0.133	t=1.77 p=0.080
Gender						
Male	14 (37.8%)	28 (50.9%)	43 (45.7%)	χ ² =0.675 P=0.411	χ ² =0.371 P=0.542	χ ² =1.52 P=0.217
Female	23 (62.2%)	27 (49.1%)	51(54.3%)			

Group (1): Allergic with keratoconus/ suspect

Group (2): Allergic without keratoconus/ suspect

Group (3): Control normal group

t: student t test, χ²: Chi square test,

p1: compare allergic with keratoconus/ suspect with control normal group

p2: compare allergic without keratoconus/ suspect with control normal group

p3: compare allergic with keratoconus/ suspect with allergic without keratoconus/ suspect

The mean duration of disease was longer in group (1) (5.91±2.27) than in group (2) (3.25±1.30). Most of patients in group (1) were diagnosed as vernal kerato-conjunctivitis (VKC) 73% while most of them in group (2) had seasonal allergic conjunctivitis (AC) 41.8%. In group (1) 35.1% of

patient have systemic atopy while in group (2) only 5.4% have systemic atopy. There were statistically significant differences between the studied groups as regards duration, type of allergy and association with systemic atopy (**table2**).

Table (2): Duration and severity of disease among the studied groups.

Duration of disease	Group (1) (n=37)	Group (2) (n=55)	Test of significance
Mean ± SD	5.91±2.27	3.25±1.30	t=5.58 p≤0.001*
Min-Max	2.00-10.00	2.00-7.00	
Systemic atopy			
No	24 (64.9%)	52 (94.5%)	MC P=0.001*
Dermatitis	3 (8.1%)	0 (0%)	
Bronchial asthma	6 (16.2%)	1 (1.8%)	
Allergic rhinitis	4 (10.8%)	2 (3.6%)	
Type of allergy			
VKC	27 (73.0%)	22 (40.0%)	χ ² =20.78
Seasonal AC	0 (0%)	23 (41.8%)	p≤0.001*
Perennial AC	10 (27.0%)	10 (18.2%)	

MC: Monte Carlo test, *significant p ≤0.05

Statistically significant differences were detected between group 1(Allergic with keratoconus/ suspect) and 2(Allergic without keratoconus/ suspect) also among group (1) and group 3(control group) as regards the mean KM and RM, while no significant differences were detected between

groups regarding the mean values of astigmatism power. There were no statistically significant differences between group (2) and (3) regarding the mean values of Rm and KM (Table 3).

Table (3): Corneal front topography among the studied groups.

Corneal front	Group (1) (n=37)	Group (2) (n=55)	Group (3) (n=94)	Test of significance		
				P1	P2	P3
CF RM				t=2.389	t=0.313	t=2.157
Mean ± SD	7.58±0.60	7.81±0.36	7.79±0.33	p=0.018*	p=0.754	p=0.034*
CF KM				t=5.105	t=1.148	t=4.376
Mean ± SD	44.81±2.65	42.88±1.52	43.13±1.08	p≤0.001*	p=0.253	p≤0.001*
CF ASTG				Z=0.930	Z=1.683	Z=1.413
Median	2.95	0.80	1.50	p=0.352	p=0.092	p=0.158
(Min-Max)	(-5.50-6.40)	(-5.50-5.00)	(0.09-3.80)			

CF: Corneal front, **RM:** average of radius of curvature of flat and steep meridians, **KM:** average dioptric power of flat and steep meridians, **ASTG:** astigmatism power **Z:** Mann Whitney test.

There were statistically significant differences between allergic groups and Control normal group as regard the median elevation back, as well as the mean values of K MAX. There were statistically significant differences between group (1) and (2) as well as group (1) and (3) as

regards the mean values of the TP while no statistically significant differences were found between group (2) and group (3) regarding it. No statistically significant differences were found among the studied groups as regards the median values of displacement of the TP on either X or Y (**Table 4**).

Table (4): Elevation back, KMAX, thinnest point and displacement thinnest location of among studied groups.

	Group (1) (n=37)	Group (2) (n=55)	Group (3) (n=94)	Test of significance		
				P1	P2	P3
Elevation back						
Median	10.00	6.00	5.00	Z=5.34	Z=2.25	Z=3.46
(Min-Max)	(2.00-75.00)	(-3.00-19.00)	(-6.00-15.00)	p≤0.001*	p=0.024*	p=0.001*
K MAX				t=8.25	t=2.78	t=5.24
Mean ± SD	48.54±4.65	44.90±1.75	44.18±1.35	p≤0.001*	p=0.006*	p≤0.001*
TP				t=6.17	t=0.505	t=4.91
Mean ± SD	488.62±85.87	550.43±28.84	548.22±23.27	p≤0.001*	p=0.614	p≤0.001*
Displacement of TP on x						
Median	0.40	0.20	0.25	Z=0.441	Z=-0.654	Z=-0.044
(Min-Max)	(-1.20-1.70)	(-1.40-1.10)	(-1.40-1.30)	p=0.659	p=0.513	p=0.965
Displacement of TP on y						
Median	-0.21	-0.30	-0.30	Z=0.561	Z=0.00	Z=0.863
(Min-Max)	(-1.18-0.90)	(-1.09-1.90)	(-1.10-0.70)	p=0.575	p=1.00	p=0.388

TP thinnest point

Statistically significant differences were found between group (1) and (2) as well as between group (1) and (3) regarding Belin/Ambrosio D value, ART MAX and corneal volume (p<0.05) while no significant differences were found

between group (1) and other groups in the mean values of AC angle. Still statistically significant differences were found between group (2) and (3) regarding ART MAX while no significant differences were found between them in the mean

values of other parameters (table 5).

Table (5): ART MAX, D Corneal volume and AC angle among studied groups.

Variables	Group (1) (n=37)	Group (2) (n=55)	Group (3) (n=94)	Test of significance		
				P1	P2	P3
ART MAX				t=5.16	t=3.34	t=6.65
Mean±SD	336.03±106.46	464.04±76.98	420.97±74.3	p≤0.001*	p=0.001*	p≤0.001*
D				χ ² =75.13	χ ² =0.002	χ ² =54.93
Normal	6(16.2%)	51(92.7%)	87(92.6%)	P≤0.001*	P=0.969	P≤0.001*
Abnormal	31(83.8%)	4(7.3%)	7(7.4%)			
Corneal				t=2.71	t=0.062	t=3.17
volume				p=0.008*	p=0.950	p=0.002*
Mean±SD	59.21±3.61	61.35±2.79	61.31±4.12			
AC angle				t=0.440	t=0.395	t=0.604
Mean±SD	37.33±4.24	38.12±7.16	37.73±4.85	p=0.661	p=0.693	p=0.547

ARTMax Maximum ambrosio relation thickness.

DISCUSSION:

Many studies were done to assess the relationship between eye itching, atopy and keratoconus which was first reported in 1937. following investigators confirmed this relationship. However, others denied it⁹.

This study was conducted to evaluate changes of corneal topography in young patients with chronic allergy by using The Pentacam Scheimpflug imaging in examination of 100 subject (50 nonallergic and 50 allergic) attending to Mansoura university Ophthalmic Center.

In this study the mean age was 13.54±3.79 years in kc and suspest group and 11.87±2.93 in AC without KC or suspect group, while in the normal control group it was 13.20±3.72 years (table 1) like a study by Deonarain et al. (2019)¹⁰, who found no significant differences in the mean age and sex distribution between the keratoconus and non-keratoconus groups but on the contrary with a study by Gautam et al. (2015)¹¹, in which the average age of presentation of the patients with VKC was 10.9 (SD 4.9), with early presentation in limbal VKC (8.4±4.3) and late presentation in palpebral VKC (13.4±5.0)¹¹.

Most of subjects in the AC with kc and suspect group were females (62.2%), while in the AC without KC or suspect group the majority of subjects were males (50.9%) (table 1) unlike studies by Gautam et al. (2015)¹¹ and Totan et al. (2001)¹⁵ who found male predominance in VKC and keratoconus.

In current study most of KC and suspect patients had VKC (table 2). This result was in agreement with Totan et al. (2001)¹⁵, Lapid-Gortzak et al. (2002)¹², using video keratography (VKG), and Barreto et al. (2007)¹³, using slit-scanning topography, have compared the topographic pattern of eyes with VKC with that of normal eyes, and reported that subjects with VKC have more abnormal topographic patterns of the cornea than controls.

In our study 35.1% of KC and suspect group had systemic atopy while only 5.4% of AC without KC or suspect group had it (table 2). This confirms the association between KC development and atopy presence. Similarly in the Keratoconus CLEK study¹⁴, 53% of KC subjects had a history of atopy. On the other hand, Totan et al. (2001)¹⁵, denied this association in their study about incidence of Keratoconus in VKC patients.

The mean duration of the disease in KC and suspect group was 5.91±2.27 years and in AC without KC or suspect group was 3.25±1.30 (table 2). This signifies that long duration of rubbing is a very serious risk factor for development of KC. Comparable results were reported by Totan et al. (2001)¹⁵, Dantas et al. (2005)¹⁶.

According to our results, the mean values of Km were significant higher and thinnest point was significant lower in KC and suspect group than other groups (table 3&4). This is in agreement with the study conducted by Barreto et al. (2007)¹³, about Slit-scanning topography in VKC. They

found that sagittal curvature came out to be significantly higher, thinner corneal thickness and higher pachymetric index in VKC compared with the control group. The same results were obtained by Mazzotta et al. (2018)²¹.

No significant differences between AC without KC or suspect group and control group regarding the mean values of Km, RM, astigmatism power or thinnest point displacement were found (table 3&4). Comparable results were reported by Ekinici et al. (2019)¹⁷, in their study about the topographic changes of the cornea in patients with VKC that there were no statistically significant difference between VKC group and control group in average of sagittal curvature, K1, K2, and Km while on contrary they found statistically significant difference in The median value of astigmatism power among studied groups also Birjees Hakak et, al. (2018)¹⁸, found VKC patients had much higher astigmatism in comparison to the general population.

In addition, the current result showed the median elevation back and Kmax were significant higher in allergic groups than control group (table4). These findings were consistent with what was reported by Wang et al. (2012)¹⁹, who found much higher corneal elevation values in posterior surface in AC patients than in normal subjects. Similarly, Jafarinasab et al. (2015)²⁰, found that the mean values of maximum posterior elevation and were significantly higher in KC and KC-suspect eyes than in control eyes. Mazzotta et al. (2018)²¹, also agreed with our result as they found that allergic patients with eye rubbing and elevated inflammatory mediators in tears have more rapid KC progression, indicated by higher K MAX and thinner corneal thickness.

The present work also found that patient with complicated KC had more abnormal Belin-Ambrosio D (BAD) value, lower ART max and corneal volume than other 2 groups (table 5). Awad et al. (2017)²², agreed with the results and found that the keratometric reading, difference between the posterior elevation of the cornea and back difference elevation, and D measurement were significantly higher in eyes with KC than in normal eyes; and that the corneal thickness and ART max were significantly lower in eyes with KC than in normal eyes. Mannion et al.²³, also agreed with the result and showed significant decrease in corneal volume in the keratoconus group.

No significant differences were found between AC without KC or suspect subjects and normal subjects regarding BAD, corneal volume and anterior chamber angle (table 5). In agreement with that Zaky et al. (2020)²⁴, found no significant differences between children with VKC and normal groups regarding anterior chamber depth and corneal volume.

CONCLUSION:

The current findings suggested that assessment of corneal topography by pentacam for young patients with chronic eye allergy could be a helpful method for early diagnosis and treatment of keratoconus.

Recommendations:

Based on the results of the current study, it is recommended to perform further studies including larger number of patients from more than a single center.

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Ethics declarations

Conflict of interest

Heba Z. Ibrahim, Rasha M. Elzeini, Hanem M. Kishk, Ehab M. Nafie, all authors have no conflicts of interest that are directly relevant to the content of this review.

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