

## PENTACAM CORNEAL IMAGING IN PATIENTS WITH VERNAL KERATOCONJUNCTIVITIS

By

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### ABSTRACT

**Background:** Vernal keratoconjunctivitis (VKC) is known to be one of the most severe forms of ocular allergy with potential to cause corneal damage and permanent visual loss. Corneal involvement in VKC patients occurs in the form of superficial punctate keratitis, with superficial pannus, pseudogerontoxon, shield ulcer, astigmatism and keratoconus. Children with VKC have a high incidence of keratoconus and astigmatism and have more abnormal corneal topography patterns compared with normal eyes.

**Objective:** To study pentacam based corneal changes in patients with chronic vernal keratoconjunctivitis and finding out prevalence of keratoconus in those patients.

**Patients and Methods:** This study was a descriptive controlled clinical trial (30 patients) including all patients with chronic vernal keratoconjunctivitis. Pentacam was done for both eyes. This study conducted on 30 patients with 60 eyes admitted from Damanshour Eye Hospital and Al-Hussien and Sayed Galal University Hospitals during the period from January 2020 till January 2021 with age ranged from 9 to 17 years with mean  $\pm$  SD of  $13.53 \pm 2.87$ ; they were 14 females (46.7%) and 16 males (53.3%).

**Results:** There was a statistically significant increase in the level of K2 and K max in positive keratoconus eyes than negative keratoconus. There was a statistically significant decrease in thinnest location (TL) in eyes with positive keratoconus than eyes with negative keratoconus. Also, the changes in TL (TL < 490) was found higher in eyes with positive keratoconus than eyes with negative keratoconus. There was no statistically significant difference between eyes with positive keratoconus than eyes with negative keratoconus regarding Y coordinate deviation. There was a statistically significant increase in belin ambrosia display deviation (Bad-d) in eyes with positive keratoconus than negative keratoconus. There was statistically significant relation found between rubbing severity and positive keratoconus.

**Conclusion:** Vernal keratoconjunctivitis was fairly common among children, and proved to make certain changes in the corneal topography. Exposure to dust and family history were the major risk factors and rubbing of the eye is the major risk factor

**Keywords:** Vernal keratoconjunctivitis, Anterior chamber depth, Pentacam.

### INTRODUCTION

Vernal keratoconjunctivitis (VKC) is an allergic eye disease that especially affects young boys. The most common symptoms are itching, photophobia, burning, and tearing. The most common signs are giant papillae, superficial

keratitis, and conjunctival hyperemia (Buckley, 2012).

VKC mainly affects boys in their first decade of life and the sequelae of the disease may be responsible for permanent visual impairment. Despite its name, the disease can be frequently present all year round. Approximately 23% of patients

have a perennial form of VKC from disease onset and more than 60% have additional recurrences during the winter. Furthermore, in almost 16% of the cases, the seasonal (vernal) form evolves into a chronic, perennial inflammation after a mean of 3 years from disease onset, suggesting that the longer patients suffer from VKC, the more appropriate they are to develop a persistent form of the disease (Colby and Dohlman, 2011).

Keratoconus is a disorder characterized by progressive corneal steepening, most typically inferior to the center of the cornea, induced myopia, and both regular and irregular astigmatism. Eye rubbing is strongly associated with the development of keratoconus (Kansakar, 2011).

The prevalence of keratoconus in the general population varies in different series. A recent study that evaluated 4.4 million patients from a mandatory health insurance database found the estimated prevalence of keratoconus in the general population to be 1 out of 375 persons. Corneal Pentacam is useful to confirm the diagnosis of keratoconus and, in some cases, even to make the diagnosis of subtle cases without clinical manifestations (Simon, 2015).

The Pentacam (Oculus Optikgeräte GmbH, Wetzlar, Germany) has become a popular device for evaluating the anterior segment of the eye. Previous studies have shown excellent reproducibility of this device for the automated measurements of the anterior segment structures. The Pentacam system may be used for the diagnosis of keratoconus, monitoring post-surgical corneas. In addition to several reports on corneal thickness (CT) anterior and posterior corneal curvature

and elevation, anterior chamber depth (ACD) refractive errors (Marey *et al.*, 2017).

**The aim of this work was to study** Pentacam based corneal changes in patients with chronic vernal keratoconjunctivitis and finding out prevalence of keratoconus in those patients.

## PATIENTS AND METHODS

This study was descriptive controlled clinical trial (30 patients) including all patients with chronic vernal keratoconjunctivitis. Pentacam was done for both eyes.

**Inclusion Criteria:** Age between 9 and 17 years. Confirmed children with chronic VKC which they had more than one attack based on clinical data.

**Exclusion Criteria:** Non progressive keratoconus. Previous eye surgery. Coexistence of ocular pathology other than VKC.

This study conducted on 30 patients with 60 eyes admitted from Damanshour Eye Hospital and Al-Hussien and Sayed Galal University Hospitals in the period from January 2020 till January 2021 with age ranged from 9 to 17 years with mean  $\pm$  SD of  $13.53 \pm 2.87$ ; they were 14 females (46.7%) and 16 males (53.3%).

**All patients in the study were subjected to the following:** Informed consent. Full history taking with complete clinical ophthalmological examination: Visual acuity testing: (UCVA, BCVA, pinhole test). Diagnosis of VKC will be made on the basis of the typical clinical history of severe itching, redness, foreign body sensations with characteristic signs, including giant papillae on the upper

palpebral conjunctiva, limbal infiltrates, and eosinophilic concretions (Horner-Trantas' spots). Pentacam Scheimpflug system (Oculus, Inc., Wetzlar, Germany) assessment. K2 reading. K max. Thinnest location. Decentration of the TL on Y-coord. BAD – D. KC compatible or suspected.

**Statistical analysis:**

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution

Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Qualitative data were represented as frequencies and relative percentages. Chi square test ( $\chi^2$ ) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean  $\pm$  SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data) and the Mann-Whitney test. P value  $< 0.05$  was considered significant.

**RESULTS**

The demographic data of the cases male patient was 16 and female patient was 14 with mean age  $13.53 \pm 2.87$ . The age ranged from 9 to 17 years with mean

$\pm$  SD of  $13.53 \pm 2.87$ ; they were 14 females (46.7%) and 16 males (53.3%) (Table 1).

**Table (1): Demographic data of the studied patients**

		<b>No. = 30</b>
Age	Mean $\pm$ SD	$13.53 \pm 2.87$
	Range	9 – 17
Sex	Female	14 (46.7%)
	Male	16 (53.3%)

The incidence of keratoconus compatible 35.3% and the incidence of keratoconus suspect 8.3% and incidence

of negative keratoconus was 56.7% (Table 2).

**Table (2): Incidence of suspected and compatible keratoconus among the studied patients**

<b>Keratoconus</b>	<b>No.</b>	<b>%</b>
No	34	56.7%
kc compatible	21	35.0%
kc suspect	5	8.3%
<b>Total</b>	<b>60</b>	<b>100.0%</b>

There was no statistically significant difference found between negative keratoconus and positive keratoconus

cases regarding age and sex with p-value = 0.159 and 0.961 respectively (**Table 3**).

**Table (3): Comparison between cases with negative and positive keratoconus regarding age and sex of the studied patients**

Parameters		Groups	Negative keratoconus	Positive keratoconus
			No. = 17	No. = 13
Age	Mean±SD		12.88 ± 3.02	14.38 ± 2.53
	Range		9 – 17	10 – 17
Sex	Female		8 (47.1%)	6 (46.2%)
	Male		9 (52.9%)	7 (53.8%)

There was a statistically significant increase in the level of K2 and K max in positive keratoconus eyes than negative keratoconus eyes with p-value <0.001 and < 0.001 respectively. Also the table shows that there was statistically significant increase in the changes of K max in positive keratoconus eyes than negative keratoconus eyes with p-value = 0.018. The changes in K2 was found higher in eyes with positive keratoconus than eyes with negative keratoconus but did not reach statistically significant with p-value = 0.069.

There was a statistically significant decrease in TL in eyes with positive keratoconus than eyes with negative keratoconus with p-value < 0.001 also the changes in TL (TL < 490) was found higher in eyes with positive keratoconus than eyes with negative keratoconus with p-value 0.024. The table also shows that there was no statistically significant difference between eyes with positive keratoconus than eyes with negative

keratoconus regarding Y coord deviation and also changes in Y coord deviation with p-value 0.717 and 0.720. Finally the table shows that there was statistically significant increase in bad-d in eyes with positive keratoconus than eyes with negative keratoconus with p-value <0.001 and also the changes in bad-d were found higher in eyes with positive keratoconus than eyes with negative keratoconus with p-value < 0.001.

There was a statistically significant relation found between rubbing severity and positive keratoconus with p-value < 0.001.

There was a statistically significant increase in the number of eyes with inferior steeping in positive keratoconus eyes than negative keratoconus eyes with p-value < 0.001. Also the table shows that there was statistically significant increase in superior steeping in negative keratoconus superior steeping with p-value <0.001 (**Table 4**).

**Table (4): Comparison between eyes with negative and positive keratoconus regarding K2, Kmax, TL, Y coord deviation, bad-d, rubbing severity and inferior and superior steeping and inferior and superior steeping**

Parameters \ Groups		Negative keratoconus	Positive keratoconus	p-value
		No. = 34	No. = 26	
k2	Mean±SD	44.04 ± 1.81	46.21 ± 1.91	<0.00
	Range	41.1 – 46.7	42.7 – 50.1	
	<46	27 (79.4%)	15 (57.7%)	0.069
	>46	7 (20.6%)	11 (42.3%)	
k max	Mean±SD	44.42 ± 1.78	47.40 ± 2.75	<0.00
	Range	41.5 – 47.3	45.2 – 55.3	
	<49	34 (100.0%)	22 (84.6%)	0.018
	>49	0 (0.0%)	4 (15.4%)	
TL	Mean±SD	551.94 ± 33.70	513.15 ± 41.81	0.000
	Range	484 – 606	441 – 577	
	> 490	32 (94.1%)	19 (73.1%)	0.024
	<490	2 (5.9%)	7 (26.9%)	
Y coord	Mean±SD	-0.24 ± 0.20	-0.26 ± 0.17	0.717
	Range	-0.69 – 0.2	-0.79 – 0.07	
	< -0.5	32 (94.1%)	25 (96.2%)	0.720
	> -0.5	2 (5.9%)	1 (3.8%)	
Bad-d	Mean±SD	0.60 ± 0.51	2.90 ± 2.44	0.000
	Range	-0.74 – 1.39	1.12 – 10.8	
	<1	26 (76.5%)	0 (0.0%)	0.000
	>1	8 (23.5%)	26 (100.0%)	
Rubbing	Mild	6 (17.6%)	0 (0.0%)	0.00
	Moderate	20 (58.8%)	4 (15.4%)	
	Severe	8 (23.5%)	22 (84.6%)	
Steeping	Negative	22 (64.7%)	0 (0.0%)	0.00
	Superior	12 (35.3%)	0 (0.0%)	
	Inferior	0 (0.0%)	26 (100.0%)	

There was a statistically significant difference found between the three studied groups regarding K2 level and K max level with p-value < 0.001 and < 0.001 also the changes in K2 and K max was found higher in Kc compatible than suspected and negative KC cases with p-value = 0.014 and 0.019 respectively.

There was a statistically significant decrease in TL level in suspect and compatible KC than negative KC eyes with p-value = 0.001. Also the table shows that there was no statistically significant difference found between the three groups regarding Y coord deviation

with p-value = 0.904 while there was statistically significant increase in bad-d in suspect KC and compatible KC than negative KC eyes with p-value < 0.001.

The changes in TL was found higher in suspect KC and compatible KC than negative KC eyes but did not reach statistically significant with p-value = 0.069. The changes in Y coord deviation showed non-statistically significant difference between the three groups. Finally the changes in bad-d was found higher in suspect KC and compatible KC eyes than negative KC eyes with p-value < 0.001 (**Table 5**).

**Table (5): Comparison between cases with negative, suspected and compatible keratoconus K2, Kmax TL, Y coord deviation and bad-d**

Parameters		Groups	No	kc suspect	kc compatible	P-value
			No. = 34	No. = 5	No. = 21	
k2	Mean±SD		44.04 ± 1.81	45.40 ± 0.41	46.40 ± 2.08	0.00
	Range		41.1 – 46.7	44.9 – 45.9	42.7 – 50.1	
	<46		27 (79.4%)	5 (100.0%)	10 (47.6%)	0.014
	>46		7 (20.6%)	0 (0.0%)	11 (52.4%)	
k max	Mean±SD		44.42 ± 1.78	46.18 ± 0.62	47.69 ± 2.99	0.00
	Range		41.5 – 47.3	45.4 – 47.1	45.2 – 55.3	
	<49		34 (100.0%)	5 (100.0%)	17 (81.0%)	0.019
	>49		0 (0.0%)	0 (0.0%)	4 (19.0%)	
TL	Mean±SD		551.94 ± 33.70	507.80 ± 35.65	514.43 ± 43.85	0.001
	Range		484 – 606	479 – 570	441 – 577	
	> 490		32 (94.1%)	4 (80.0%)	15 (71.4%)	0.069
	<490		2 (5.9%)	1 (20.0%)	6 (28.6%)	
Y coord	Mean±SD		-0.24 ± 0.20	-0.28 ± 0.15	-0.26 ± 0.18	0.904
	Range		-0.69 – 0.2	-0.46 – -0.06	-0.79 – 0.07	
	< -0.5		32 (94.1%)	5 (100.0%)	20 (95.2%)	0.852
	> -0.5		2 (5.9%)	0 (0.0%)	1 (4.8%)	
Bad-d	Mean±SD		0.60 ± 0.51	2.10 ± 0.56	3.09 ± 2.68	0.00
	Range		-0.74 – 1.39	1.12 – 2.5	1.34 – 10.8	
	<1		26 (76.5%)	0 (0.0%)	0 (0.0%)	0.00
	>1		8 (23.5%)	5 (100.0%)	21 (100.0%)	

## DISCUSSION

A descriptive study was conducted on children with vernal keratoconjunctivitis to detect these corneal topographic changes. By using Oculus Pentacam, we examined 60 eyes of 30 patients as a VKC group with mean age 13.53 years with standard deviation (SD) of 2.87 years, male patients were 16(53.3%) and female patients were 14 (46.7%).

Our study has detected the keratoconus compatible cases were 35% and keratoconus suspected patients were 8.3%

Our results were comparable to that in *Kassahun et al. (2012)* in Ethiopia (5.2% of students between 11 and 15 years), South Africa (2.1% among school children aged 6–10 years), and *De Smedt et al. (2013)* in Rwanda (4%). In two separate cross-sectional studies from

Nigeria, VKC prevalence was 6.7% (age range between 4 and 15 years) in the first study *Ayanniyi et al. (2010)* and 2.9% (age 6–16 years) in the second one *Okoye et al. (2013)*. *Sethi et al. (2013)* in Saudi Arabia revealed that vernal catarrh was the most common ocular disorder, accounting for 35.6% of the cases with age range between 0–16 years. Also, *Marey et al. (2017)* found that the prevalence rate in the age group of 6–9 years old, it is found to be 72.7% in mild cases and 73.7% in severe cases. These rates are 2.3% and 5.3%, respectively, when we trace the prevalence in the older age group of 13–14 years old.

The difference in the prevalence rate between studies was due to the different age groups of patients included. The prevalence was also affected by the temperature of the study area; high

prevalence was observed in high-temperature areas with tough climate, such as in Saudi Arabia, and was not observed in the moderate climates of Jordan, East Jerusalem, and Gaza. In this study, the low to moderate prevalence rate is compatible with local temperature in the Nile Delta, and with the wide age range of the included children.

In the current study, there were non-statistically significant differences between children with vernal keratoconjunctivitis (VKC) regarding age and sex ( $p=0.159$  and  $0.961$  respectively).

In agreement with our results, some studies have not found differences in the prevalence between genders as in *Li et al. (2013)*. Also, *Ahmed et al. (2019)* found that males represented 63.3% and females 36.7% among the VKC cases, making a male to female ratio of nearly 1.7:1. However, there was no significant difference in sex distribution between normal and VKC children.

On the other hand in the study by *Khaled and Liu (2020)*, males (81%) were more affected than females (19%). Similar male predominance was found in *Salman et al. (2010)*, another study at Nigeria, the number of affected boys was almost double that of girls, making a male to female ratio of 1.8: 1. *Ayanniyi et al. (2010)*, which is very similar to *De Smedt et al. (2013)* in Rwanda and *Zicari et al. (2013)* in Italy, where male to female ratio was 2.4:1 *Zicari et al. (2013)* and 3.3:1 *Leonardi et al. (2015)*, respectively.

There was a male predominance, with ~74% of the cases being males, whereas only ~26% of the cases belonged to the female sex in India *Awargaonkar et al. (2014)*. Similarly, a study was done in

Pakistan in which males represented 88% of the cases in their early years *Shaikh and Ovais (2013)*. In Yemen, the results were a little different, with a male: female ratio of 3.1: 1. Other studies done by *Leonardi et al. (2015)*, *Bonini et al. (2014)*, and *Kansakar et al. (2011)* observed male predominance in patients under 20 years of age, among whom the male: female ratio was 4: 1–3: 1, whereas the ratio in those who were older than 20 years of age was nearly 1:1.

In our study, there was a statistically significant increase in the power of K2 and K max in positive keratoconus eyes than negative keratoconus eyes with  $p$ -value  $<0.001$  and  $< 0.001$  respectively. Also the table shows that there was statistically significant increase in the changes of K max in positive keratoconus eyes than negative keratoconus eyes with  $p$ -value = 0.018. The changes in K2 was found higher in eyes with positive keratoconus than eyes with negative keratoconus but did not reach statistically significant with  $p$ -value = 0.069

In the study done by *Ekinici et al. (2019)*, who compared the topographic corneal changes in patients with vernal keratoconjunctivitis to a control group, they found that no statistically significant difference was found in K1, K2, Km values, whereas the difference of K max values was found statistically significant. When values of keratometry above 48D are accepted as pathological, K2 and Kmax values" ratio of being above 48D was found significantly high compared to the control group. Whereas in the average of sagittal curvature, no statistical difference was detected between groups. However, when the values above 47D are

accepted as pathological, 5 eyes of 81 were accepted as pathological.

In the study of *Barreto et al. (2015)* conducted, sagittal curvature came out significantly high compared to the control group ( $p < 0.05$ ). These data showed that keratometry values might increase in the patients diagnosed with VKC.

This increase in the keratometric values might be explained as the result of microtrauma in corneal structure caused by frequent rubbing occurs due to intense itching. In our study we examined a much larger study group than in *Ekinici et al. (2019)* who examined only 41 patients and this might be the reason for difference results.

In our study, there was a statistically significant decrease in TL in eyes with positive keratoconus than eyes with negative keratoconus. Also, the changes in TL ( $TL < 490$ ) were found higher in eyes with positive keratoconus than eyes with negative keratoconus.

In the study conducted by *Nawaz et al. (2012)*, they evaluated corneal topographic characteristics of patients with vernal keratoconjunctivitis (VKC) and compared the corneal topographic indices in VKC subjects with normal subjects. Central corneal thickness was found to be significantly decreased in VKC subjects compared to normal subjects. Central corneal thickness was even more significantly reduced in VKC subjects with suspected keratoconus like topography.

The same as in *Ondas and Keles (2014)* who evaluated central corneal thickness in VKC patients comparing with normal person and found that the CCT

significantly decreased in VKC subjects compared to normal subjects.

In our study there was a statistically significant increase in the number of eyes with inferior steeping in positive keratoconus eyes than negative keratoconus eyes with  $p$ -value  $< 0.001$ . Also the study shows that there was statistically significant increase in superior steeping in negative keratoconus .

In agreement with our results, *Barreto et al. (2015)* found that anterior and posterior elevation peaks, elevation color patterns, central curvature, thinnest pachymetry, and pachymetric index differed significantly between VKC and control group.

Another study in Italy done by *Leonardi et al. (2015)* showed that 68.5% were affected by the tarsal form, 20.4% by the mixed form, and only 11.1% by the limbal type. In Asian countries like India, the isolated limbal form was present in 12.6%, whereas the isolated palpebral form was seen in 15.6% (*Saboo et al., 2013*). In Karachi, the palpebral form was observed in 58% followed by the mixed type in 26% and the limbal in 16% (*Sultan et al., 2015*).

The study also showed that there was no statistically significant difference between eyes with positive keratoconus than eyes with negative keratoconus regarding Y coordinate deviation and also changes in Y coordinate deviation with.

The study showed that there was a statistically significant increase in BAD-D in eyes with positive keratoconus than eyes with negative keratoconus and also the changes in Bad-d was found higher in

eyes with positive keratoconus than eyes with negative keratoconus.

### CONCLUSION

Vernal keratoconjunctivitis is fairly common among children and proved to make certain changes in the corneal topography. Exposure to dust and family history were the major risk factors and rubbing of the eye is the major risk factor

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## متابعة التغيرات التي تحدث في القرنية للمرضى المصابين بالتهاب الموسمي للملتحمة والقرنية بجهاز البنتكام

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**خلفية البحث:** يعرف التهاب القرنيه والملتحمة الربيعى بأنه أحد أشكال حساسية العين مع احتمال التسبب فى تليف القرنيه وفقدان البصر الدائم تحدث اصابه القرنيه فى مرضى الرمى الربيعى فى شكل التهاب القرنية النقطة السطحى مع التهاب القرنيه السطحى الذى ينتج عنه نمو أوعية دموية دقيقة على سطح القرنية وتبييض حواف القرنية وقرحة القرنية والاستجماتيزم والقرنية المخروطية و يعانى الاطفال المصابون بالرمى الربيعى بالقرنية المخروطية والاستجماتيزم ولديهم أنماط تضاريس غير طبيعیه للقرنيه مقارنة بالعيون الطبيعية.

**الهدف من البحث:** دراسة تغيرات القرنية القائمة على البنتكام فى المرضى الذين يعانون من التهاب القرنية والملتحمة الربيعي المزمن ومعرفة مدى انتشار القرنية المخروطية فى هؤلاء المرضى.

**المرضى وطرق البحث:** كانت هذه الدراسة عبارة عن تجربة إكلينيكية وصفية مضبوطة (٣٠ مريضاً) بما فى ذلك جميع المرضى المصابين بالتهاب القرنية والملتحمة الربيعي المزمن. وتم إجراء البنتكام لكثا العينين. وأجريت هذه الدراسة على ٣٠ مريضاً لديهم ٦٠ عيناً تم قبولهم فى مستشفى دمنهور للعيون ومستشفى الحسين وسيد جلال الجامعي خلال الفترة من يناير ٢٠٢٠ حتى يناير ٢٠٢١. وتراوحت أعمارهم بين ٩ إلى ١٧ عاماً، وكانوا ١٤ إناث (٤٦.٧٪) و ١٦ ذكور (٥٣.٣٪).

**نتائج البحث:** كانت هناك زيادة ذات دلالة إحصائية فى مستوى K2 و K-max فى عيون القرنية المخروطية الإيجابية من القرنية المخروطية السلبية و كان هناك انخفاضاً ذا دلالة إحصائية فى أنحف مكان فى العين مع القرنية المخروطية الموجبة من العين مع القرنية المخروطية السلبية. وقد وجدت أن التغيرات فى

أنحف مكان (أنحف مكان > ٤٩٠) أعلى في العيون ذات القرنية المخروطية الموجبة مقارنة بالعيون ذات القرنية المخروطية السلبية. ولم يكن هناك فرقا ذا دلالة إحصائية بين العيون ذات القرنية المخروطية الموجبة من العيون وذات القرنية المخروطية السلبية فيما يتعلق بانحراف إحداثيات Y و كانت هناك زيادة ذات دلالة إحصائية في انحراف عرض بيلين اللطيف في العين مع القرنية المخروطية الموجبة من القرنية السالبة. وقد وجدت علاقة ذات دلالة إحصائية بين شدة الاحتكاك والقرنية المخروطية الإيجابية.

**الاستنتاج:** كانت الملحمة القرنية الربيعية شائعة إلى حد ما بين الأطفال، وثبت أنها تحدث بعض التغييرات في تضاريس القرنية. كان التعرض للغبار والتاريخ العائلي من عوامل الخطر الرئيسية وفرك العين هو عامل الخطر الرئيسي.

**الكلمات الدالة:** إتهاب القرنية، الملحمة الربيعي، عمق الحجرة الأمامية، البنتكام.