

# Keratoconus associated with limbal vernal keratoconjunctivitis in African patients

TR Carmichael<sup>1</sup>, GJ Ben-Simon<sup>2</sup> and A Chopamba-Kamba<sup>3</sup>

Department of Ophthalmology, University of the Witwatersrand, 7 York Road, Parktown, 2193 South Africa  
<carmichaeltr@medicine.wits.ac.za>

## Abstract

*Objectives* - To evaluate conditions predisposing to keratoconus or associated with keratoconus in African patients. To document associated complications such as corneal hydrops and corneal vascularisation.

*Design* - Prospective study undertaken over a two year period.

*Setting* - St John Eye Unit of Chris Hani Baragwanath Hospital, Soweto, South Africa.

*Subjects* - African patients presenting with keratoconus were included.

*Outcome measures* - Associated conditions, for example, vernal keratoconjunctivitis (vernal) and type, eye rubbing, vascularisation of the cornea, corneal hydrops, visual acuity.

*Results* - There was a preponderance of males (28 patients, 62%) among the 45 patients studied. Thirty-three (73%) of the patients were aged between 10 and 29 years. Seventy eyes (72.8%) showed severe keratoconus and in 40 eyes (47%) the visual acuity was 6/60 or worse. The commonly associated condition was limbal vernal keratoconjunctivitis which was found in 29 patients (64%) and was significantly commoner in patients under the age of 20 years. Vernal was associated with male gender, but not significantly so. Acute hydrops was seen in three eyes and central scarring from previous hydrops was present in 30 eyes. Corneal hydrops was found to be nearly twice as com-

mon if vernal was present but this was not statistically significant. Eye rubbing was significantly associated with vernal with an odds ratio of 33.6 (Confidence Intervals 4.74 - 314) which was highly significant. Corneal vascularisation was found to be commoner in patients of 20 years or older but this was not statistically significant.

*Conclusions* - Vernal keratoconjunctivitis was found to be commonly associated with keratoconus in the African patients studied. Eye rubbing might play a role in the pathogenesis of the keratoconus or vernal in these patients. Appropriate and careful management of vernal keratoconjunctivitis and meticulous visual rehabilitation might improve the visual prognosis in this group of young adults.

## Introduction

Vernal keratoconjunctivitis (Vernal, Spring catarrh) occurring in the limbal form has been previously reported in African patients<sup>1,2</sup>. An association between keratoconus and vernal keratoconjunctivitis has been reported<sup>3-5</sup> but this link has not been described in African patients. In fact, diseases associated with keratoconus have not been described from Africa and the present study was undertaken to elucidate possible associations with keratoconus by studying a group of African patients with keratoconus of varying severity.

<sup>1</sup> MB BCh FCS PhD (Med)

<sup>2</sup> MD

<sup>3</sup> MB BCh FCS

Many different conditions have been associated with keratoconus and these associations as well as other aspects have been the subject of several extensive reviews<sup>6-8</sup>. Corneal hydrops has been associated with allergic conditions of the eye where it has been suggested that the constant rubbing might cause breaks in Descemet's membrane and result in corneal hydrops<sup>9-11</sup>. Again the importance of allergies in hydrops in the African patient has not been reported. It was our impression that the keratoconus seen at St John Eye Hospital (St John) was particularly severe and occurred at a young age and we wondered about the associations between keratoconus, corneal hydrops, vernal and eye rubbing in our patients.

Corneal vascularisation following on episodes of corneal hydrops might prejudice future corneal grafting and this sequel has been described<sup>12</sup>.

To define the associations between keratoconus, vernal and other conditions a study was undertaken to attempt to improve the outcome in these patients.

### Patients and methods

Forty five patients with keratoconus were studied at St John Eye Hospital during 1998 and 1999. Each patient had a full slit-lamp examination and a standard data sheet was used to document the findings. The usual demographic data were recorded. Anterior segment photography was used to record typical or unusual findings.

We were particularly interested in associated conditions (vernal keratoconjunctivitis, and complications such as corneal hydrops and scarring) but were also concerned about the poor visual acuities of some of these young patients caused by the keratoconus itself.

The cases were included as having a diagnosis of keratoconus where there was evidence of at least two of the following three clinical signs; central conical corneal protrusion, positive Munson's sign and central corneal thinning (unless there was previous hydrops).

Severity of keratoconus was assessed using

the average of the two principal meridian keratometry (K) readings;

mild	<48 D
moderate	48-54 D
severe	>54 D

The keratoconus was also classified as severe where either meridional K reading was over 60 D, or where irregular astigmatism was so severe as to make readings impossible, where there was acute hydrops or a scarred down cornea from a previous episode of hydrops.

The diagnosis of vernal keratoconjunctivitis depended on typical signs and symptoms and was categorised into palpebral, limbal and mixed as follows;

Palpebral	papillae > 1 mm on tarsal conjunctiva with no infiltration
Limbal	gelatinous involvement of the limbus, limbitis - brownish hyperpigmentation around the limbus and/or Horner-Trantas dots
Mixed	both palpebral and limbal involvement

Two patients (males aged 28 and 42 years) were included where they had no signs of active vernal but gave a clear history of vernal including itchy eyes requiring repeated visits to the hospital for drops during childhood.

Any associated eye rubbing was documented in a way similar to that used by Cameron<sup>5</sup>.

not at all	- 0 times/day
rarely	- 1 to 4 times/day
occasionally	- 5 to 10 times/day
frequently	- >10 times/day

The presence of neovascularisation of the cornea was noted as;

Peripheral	- just onto the cornea (1 mm)
Mid-peripheral	- between 1 mm and the central 5 mm
Central	- encroaching onto the central 5 mm of cornea

The visual acuity was noted and whether spectacles, contact lenses were used or whether corneal grafting had been performed.

Data were entered into a database in MS

Access for analysis. To further examine the associations between vernal and other factors in these keratoconus patients, odds ratios were calculated using Epi Info (Version 6, CDC, Atlanta, Georgia). The program also calculates confidence intervals at the 95% level, Chi square tests with uncorrected *p* values and *p* values corrected by the Mantel-Haenszel and Yates methods. The program also performs the Fisher Exact Test where required.

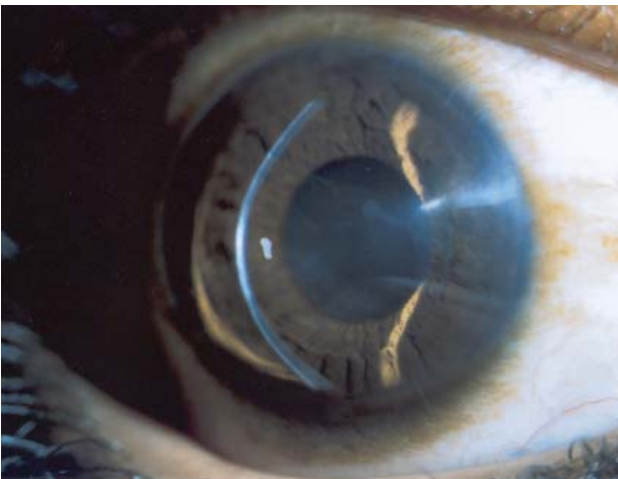
The study was approved by the Ethics Committee of the University of the Witwatersrand.

### Results

Of the 45 cases of keratoconus there were 28 males (62%) and 17 females and their ages ranged between 5 and 45 years with a mean of 22 years (standard deviation 10.1). There were only three patients aged less than ten years and only nine patients aged 30 years or older. The remaining 33 patients (73.3%) were aged 10-29 years.

#### Severity of keratoconus

The keratoconus in the study patients tended to be severe (see Figure 1).



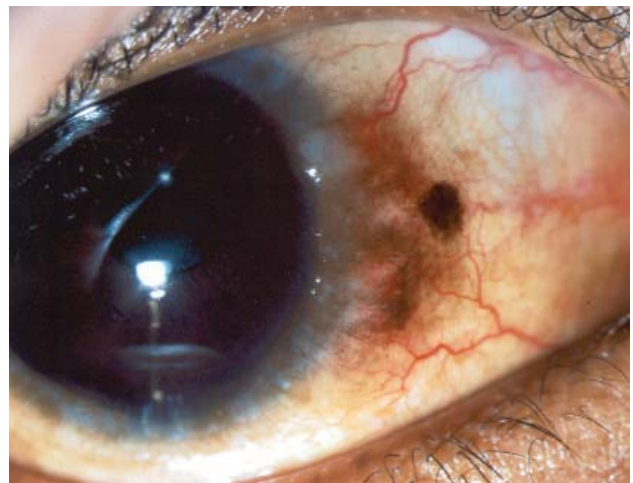
**Figure 1.** Severe keratoconus with central corneal thinning and protrusion

The assessment of severity depended on the keratometry readings and these measurements could not be obtained in four patients (eight eyes), two of whom were mentally retarded children. Ten eyes had received corneal grafts

and two were normal with no keratoconus. Of the remaining 70 eyes, 51 (72.9%) showed severe keratoconus, 8 (11.4%) moderate and 11 (15.7%) showed mild keratoconus.

#### Vernal keratoconjunctivitis and corneal hydrops

Vernal keratoconjunctivitis was found in 29 of the 45 patients (64.4%) and this was of the limbal type with a variable upper tarsal papillary conjunctival response depending on the activity and current treatment (see Figures 2-5).



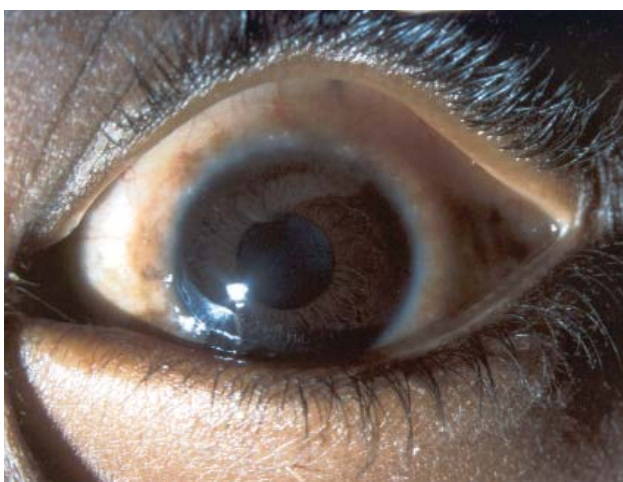
**Figure 2.** Limbal vernal keratoconjunctivitis with pigmentation of conjunctiva and gelatinous plaques



**Figure 3.** Tarsal conjunctiva from case in Figure 2 showing injection/inflammation with a papillary response

Purely palpebral vernal was not seen in this group of patients. Signs of vernal were commoner in patients under the age of twenty years with 18 of 21 patients having vernal in this age group while 11 of 24 aged twenty or older

showed signs. Limbitis was also commoner in the younger age group with four of the six cases of active limbitis occurring in this group of under 20 year olds. The keratoconus patients under twenty years were more predominantly male with 16 of 21 being male while in those aged twenty years or older there were 12 males and 12 females in the group.

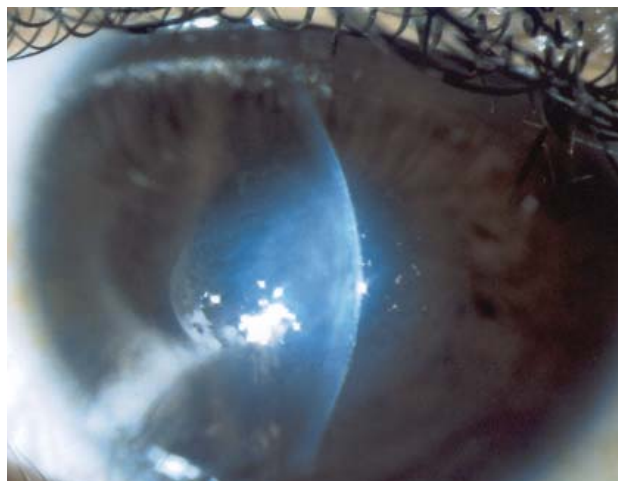


**Figure 4.** Nine year old male with typical limbitis and Horner-Trantas dots



**Figure 5.** Tarsal conjunctiva from case in Figure 4 showing a papillary response but only mild injection

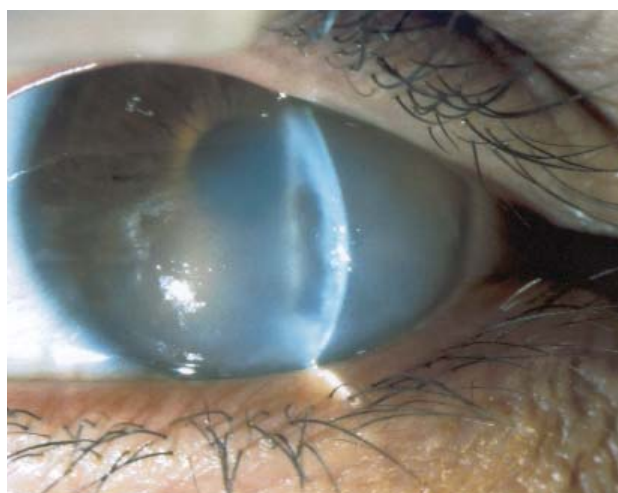
Thirty-three eyes showed evidence of acute corneal hydrops (three eyes, see Figure 6 for an example) or stromal corneal scarring from previous episodes of hydrops (30 eyes, see Figure 7). Sometimes the corneal hydrops can lead to stromal clefts with a lake of aqueous within the stroma (see Figure 8). Corneal hydrops was not associated with gender or a particular age group.



**Figure 6.** Acute corneal hydrops with a thickened oedematous central cornea



**Figure 7.** Under high magnification a split in Descemet's membrane can be seen with retraction of the edges resulting in scarring and opacification of the cornea



**Figure 8.** A lake of aqueous can be seen in the stroma in this patient with acute corneal hydrops

*Eye rubbing*

Of 39 patients questioned, six reported frequent eye rubbing (>10 x per day), nine reported occasional eye rubbing (5-10 x per day) while 13 reported rubbing their eyes rarely (1-4 x per day). Eleven denied rubbing their eyes. It can be seen that eye rubbing was seen almost entirely in the vernal group (Table 1).

**Table 1.** Eye rubbing in vernal and non-vernal patients (numbers of patients)

Eye rubbing	Vernal	non-Vernal	Total
Frequent (>10x)	6	0	6
Occasional (5-10x)	8	1	9
Rare (1-4x)	11	2	13
Not at all	2	9	11
	27	12	39

*Medication*

Fifteen of the 29 vernal patients were receiving anti-allergic eyedrops (antihistamine or mast cell stabilizers or mild steroids like fluorometholone) while only one of 16 non-vernal patients were using anti-allergic eyedrops. In both groups patients who had recently had corneal grafts were on topical steroids.

*Visual acuity*

There were 84 eyes in which the visual acuity was obtained (Table 2) and in 57 (68%) a best corrected visual acuity was obtained. In 40 eyes (47%) the visual acuity was 6/60 or worse and in 70% it was worse than 6/18, the level at which corneal grafting is usually indicated.

**Table 2.** Visual acuities in eyes with keratoconus

Visual status	Number of eyes (corneal grafts)			%
	Best corrected	Uncorrected	Total	
6/60 - HM	24 (2)	16	40	47
6/24 - 6/36	12	7 (4)	19	23
6/18 or better	21 (4)	4	25	30
			84	100

**Note:** HM is hand movement vision, two patients (four eyes) were excluded as the patients were mentally retarded and could not have visions measured and another two eyes were excluded which were normal (no keratoconus). The corneal graft eyes within the group are shown in brackets.

*Corneal vascularisation*

There was no association of vascularisation of the cornea and vernal. Twenty of 53 eyes with vernal showed vascularisation compared with five of 16 eyes without vernal. Vascularisation of the cornea seemed to be more a function of age. If patients under 20 years are compared with those 20 years or older; in the younger age group, eight of 42 eyes (19.1%) showed vascularisation while in the older group 17 of 48 eyes (35.4%) showed vascularisation (Table 3). There were no associations between patient gender or severity of keratoconus and corneal vascularisation.

**Table 3.** Vascularisation and position of vascularisation by age group (number of eyes)

Age (years)	Peripheral	Mid-peripheral	Central	Total
<20	4	1	3	8
20 and over	7	5	5	17
				25

*Associations with vernal keratoconjunctivitis using odds ratios*

Vernal keratoconjunctivitis was commoner in patients under twenty years of age. Eighteen of the 21 patients aged under twenty years had vernal compared with 11 of 24 patients over nineteen years. This was significant with an odds ratio of 7 (confidence intervals 1.4 - 41) with corrected *p* value of < 0.05 with Yates correction factor. In this group of patients, vernal was associated with male gender, but not significantly so. Nineteen of the 28 male patients had vernal compared with ten of 17 females. This gave an odds ratio of 1.5 (confidence interval 0.36 - 6.19) which was not statistically significant.

An increased likelihood of hydrops existed if vernal was present in this series of keratoconus patients. Of the 58 eyes with vernal, 24 showed hydrops or previous hydrops (scars) compared with nine of the 32 eyes without vernal. This association meant that there was an odds ratio of 1.8 (confidence interval 0.65 - 5.09) of an episode of hydrops in the presence of vernal.

This was, however, not statistically significant.

A history of eye rubbing was significantly commoner in vernal patients, as might be expected, with 24 of the 29 patients reporting eye rubbing of varying frequencies compared with only two of 16 patients without vernal. The odds ratio associated with rubbing was 33.6 (confidence intervals 4.74 - 314) with  $p$  value  $<0.0001$  using Yates correction factor.

Of the patients with vernal, five of 58 eyes had grafts compared with five of 32 who did not have vernal. This gave an odds ratio of 0.51 (confidence interval 0.11 - 2.27) indicating it was less common to have a graft in the presence of vernal. This was not statistically significant and the Fisher Exact Test also showed no significance.

Fifteen patients of the 29 with vernal were using anti-allergic medication (eyedrops) while only one of 16 without vernal was using this medication. Thus, keratoconus patients with vernal were significantly associated with medication use with an odds ratio of 16 (confidence interval 1.76 - 370) with corrected  $p$  value  $<0.01$  using Yates correction factor. There was no association of vascularisation of the cornea and vernal. Twenty of 53 eyes with vernal showed vascularisation compared with five of 16 eyes without vernal. This gave an odds ratio of 1.33 (confidence interval 0.35 - 5.21) which was not significant. Vascularisation of the cornea seemed to be more a function of age. If patients under 20 years were compared with those 20 years or older, in the younger age group, 8 of 42 eyes (19.1%) showed vascularisation while in the older group 17 of 48 eyes (35.4%) showed vascularisation (Table 3). This gave an odds ratio of 2.33 (confidence interval 0.8 - 6.91) which was not statistically significant.

Severe keratoconus was not particularly associated with vernal in this study. When eyes with grafts or unmeasurable eyes were excluded, thirty of 46 eyes with vernal showed severe cones while 21 of 26 eyes without vernal showed severity. This gave an odds ratio of 0.45 (confidence interval 0.12 - 1.58) which was not significant.

## Discussion

There was an excess of male patients (62%) in this study and this was mostly due to the larger number of young males (under twenty years of age). Patients were seven times as likely to have vernal if they were under twenty years of age as twenty years or older. One might infer that the excess males was because of the association of male gender with vernal and there was a 1.5 times odds ratio for vernal with male gender but this was not significant with the numbers in the study. Vernal<sup>1,13,14</sup> and keratoconus associated with vernal or atopic conditions<sup>3-5</sup> have been described as having a male predominance but keratoconus itself is probably best thought of as having no ethnic or gender preponderance<sup>8</sup>.

The mean age of this group of keratoconus patients was 21.9 years. Most (73%) were in their second or third decades. This would be in keeping with the perception that in keratoconus, corneal thinning begins at the time of puberty with progression occurring over the next two decades<sup>6</sup>. A similar age distribution to our patients has been described in their series of 48 patients with vernal and keratoconus by Khan *et al* from Pakistan<sup>4</sup>.

Keratoconus tended to be severe with 73% of measurable eyes showing severe cones. The visual acuities confirmed the severity of the cases with 70% having a visual acuity of under 6/18, the usual level where corneal grafting might be suggested. Khan *et al*<sup>4</sup> found 66% of their patients to have an acuity worse than 6/18, a similar result in a similar developing population. It was gratifying to note that the visions in our grafted patients, although not always best corrected, were mostly better than 6/60.

The overwhelming association with keratoconus in this study was with the limbal type of vernal keratoconjunctivitis which was found in 29 of the 45 patients (64%).

Severe keratoconus was not particularly associated with vernal in this study and the odds ratio of 0.45 shows rather that the keratoconus was less likely to be severe in the presence of

vernal although with the small numbers this was not significant.

Although no association between vascularisation of the cornea and vernal was found, there was a greater than two times risk of vascularisation if the patient was 20 years or over. This suggests that corneal vascularisation is a function of duration of disease and might result from the vernal disease or its complications found to be significantly commoner in the younger age group.

Eye rubbing has been implicated as causing keratoconus<sup>15</sup> in a case-control study and it was felt that the atopy was causative only in that it resulted in the eye rubbing. In our patients eye rubbing was strongly and significantly associated with vernal, as might be expected, and might have played a role in the development of keratoconus in those patients. The keratoconus in the vernal patients (who rubbed their eyes) was not more severe in this study.

Corneal hydrops, either acute or indicated by typical corneal scarring, was almost twice as common (1.8 times, not statistically significant) where vernal was present indicating perhaps that eye rubbing might be a causative factor in these patients. Patients reporting eye rubbing were virtually confined to the vernal group and this gave a very strong association (34 times) between eye rubbing and vernal which was statistically significant. It has been reported that in some children with vernal, corneal hydrops might be the presenting sign of keratoconus<sup>11</sup> and the authors suggest that keratoconus should be suspected if a child with vernal presents with corneal oedema and reduced vision.

Medical treatment in this group of patients was confined to topical steroids for corneal grafts which obviously would alleviate symptoms of allergy in the grafted eye, and anti-allergic eyedrops for about half the patients with vernal keratoconjunctivitis. Corneal grafts were interestingly found to be less common (0.5 odds ratio, not significant) in the presence of vernal and it might be that ophthalmologists are less likely to do corneal grafts where there is active

anterior segment inflammation.

It appears that complex relationships exist between keratoconus, vernal keratoconjunctivitis and eye rubbing as well as with corneal hydrops and vascularisation. These overlapping entities might be depicted diagrammatically as shown in Figure 9.

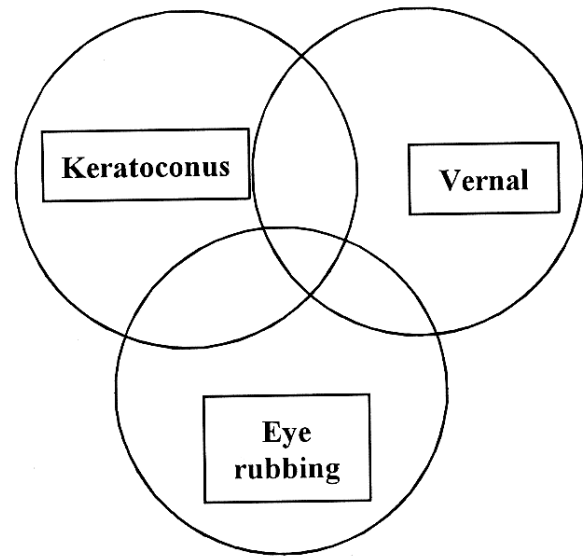


Figure 9

Correct management of vernal keratoconjunctivitis might reduce eye rubbing and prevent the development of keratoconus in some patients. All patients should have adequate access to visual rehabilitation through spectacles, contact lenses or corneal grafting.

**References**

1. Dahan E, Appel R. Vernal keratoconjunctivitis in the black child and its response to therapy. *Brit J Ophthalmol* 1983 **67** 688 - 692.
2. Sandford-Smith JH. Vernal eye disease in Northern Nigeria. *Trop Geogr Med* 1979 **31** 321 - 328.
3. Rahi A, Davies P, Ruben M, Lobascher D, Menon J. Keratoconus and coexisting atopic disease. *Brit J Ophthalmol* 1977 **61** 761 - 764.
4. Khan MD, Kundi N, Saeed N, Gulab A, Nazeer A. Incidence of keratoconus in spring catarrh. *Brit J Ophthalmol* 1988 **72** 41 - 43.
5. Cameron JA, Al-Rajhi AA, Badr IA.

- Corneal ectasia in vernal keratoconjunctivitis. *Ophthalmology* 1989 **96** 1615 - 1623.
6. Krachmer JH, Feder RS, Belin MW. Keratoconus and related noninflammatory corneal thinning disorders. *Surv Ophthalmol* 1984 **28** 293-322.
  7. Ihalainen A. Clinical and epidemiological features of keratoconus. Genetic and external factors in the pathogenesis of the disease. *Acta Ophthalmol* 1986 **64** (Supplement 178) 3 - 64.
  8. Rabinowitz YS. Keratoconus. *Surv Ophthalmol* 1998 **42** 297 - 319.
  9. Karseras AG, Ruben M. Aetiology of keratoconus. *Brit J Ophthalmol* 1976 **60** 522 - 525.
  10. Tuft SJ, Gregory WM, Buckley RJ. Acute corneal hydrops in keratoconus. *Ophthalmology* 1994 **101** 1738 - 1744.
  11. Rehany U, Rumelt S. Corneal hydrops associated with vernal conjunctivitis as a presenting sign of keratoconus in children. *Ophthalmology* 1995 **102** 2046 - 2049.
  12. Rowson NJ, Dart JKG, Buckley RJ. Corneal neovascularisation in acute hydrops. *Eye* 1992 **6** 404 - 406.
  13. Neumann E, Gutmann MJ, Blumenkrantz N, Michaelson IC. A review of four hundred cases of vernal conjunctivitis. *Am J Ophthalmol* 1959 **47** 166 - 172.
  14. Tabbara KF. Ocular complications of vernal keratoconjunctivitis. *Can J Ophthalmol* 1999 **34** 88-92.
  15. Bawazeer AM, Hodge WG, Lorimer B. Atopy and keratoconus: a multivariate analysis. *Brit J Ophthalmol* 2000 **84** 834 - 836.