

Vernal Keratoconjunctivitis Clinical Features and Complications in 123 Patients in Gaza Strip

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ABSTRACT

Objectives: This study was conducted to assess the clinical features and to detect ophthalmic complications of vernal keratoconjunctivitis in a group of patients who were treated in the Jordanian field hospital in the Gaza strip.

Methods: This was a prospective hospital-based study conducted on patients with vernal keratoconjunctivitis at the Jordanian Field hospital in the Gaza strip between 15 March and 23 May 2012. Vernal keratoconjunctivitis diagnosis was made clinically. Ophthalmic examination included visual acuity using Snellen chart, eyelids, conjunctivae, anterior segment, dilated fundus to assess the retina and optic discs, and intra-ocular pressure measurement using slit lamp biomicroscopy.

Results: During the study period 1,753 patients attended the eye clinic, 123 (7%) of them were vernal keratoconjunctivitis sufferers. Out of the 123 patients 72 (58.5%) were males and 51(41.5%) were females with a male to female ratio of 1.4: 1. Their age ranged between four and 20 years with an average of 9.9 years. Moderate and severe vernal keratoconjunctivitis were seen in 55 (44.7%) patients. Of the moderate and severe forms mixed vernal keratoconjunctivitis was the commonest type seen in 25/55 (44.5%) patients, followed by limbal and palpebral, 20/55 (36.4%) and 10/55 (18.2%) patients, respectively. Severe vernal keratoconjunctivitis was seen in 31 (25.2%) patients: 16 (13%) patients of mixed type, 9 (7.3%) of limbal type, and 6 (4.9%) of palpebral type. One patient had Horner-Trantas dots that involve limbal and bulbar conjunctiva.

Conclusion: Young age presentation and male predominance agree with that reported in literature but the male to female ratio was less. The commonest type was mixed followed by limbal and palpebral and this is different from that found in previous studies. Blepharoptosis and conjunctival inclusion cysts were seen more frequently. More representative sample over longer duration with collaboration of other local hospitals is needed to determine the true incidence, clinical features, complications, and seasonal variations of vernal keratoconjunctivitis in the Gaza strip.

Key words: Giant papillae, Horner-Trantas dots, Jordanian field hospital, Vernal keratoconjunctivitis.

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Introduction

The Jordanian Field Hospital in Gaza Strip was established in January 2009 upon the order of his Majesty King Abdullah Bin Al-Hussein the

Second. The aims of this hospital were to mitigate the suffering and to provide free field medical services to about 1.5 million Palestinians under military siege from the Israeli forces in

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Gaza strip. The hospital provides free medical services to all age groups in all specialties including ophthalmology. We have eight outpatient eye clinic sessions and one operation list per week that cover all aspects of ophthalmology.

Vernal keratoconjunctivitis, which is an immunologically mediated hypersensitivity reaction to environmental antigens,⁽¹⁾ is relatively common in the warm dry climate regions as Middle East.⁽²⁾ It is a chronic recurrent bilateral conjunctival disorder with seasonal variations that primarily affects young children with male predominance and usually remits or subsides in the majority of cases before the end of the second decade.⁽³⁾ The peak incidence of exacerbation occurs over late spring and summer.⁽⁴⁾ The exact mechanism of vernal keratoconjunctivitis is not fully understood at the time being,⁽⁵⁾ but there is a possibility of type I and IV hypersensitivity reactions involvement with vasoactive mediators release.⁽⁶⁻⁷⁾

There are three types of vernal keratoconjunctivitis, palpebral, limbal, and mixed, Fig. 1a, b, and c respectively.

Patients present with intense itching, foreign body sensation, photophobia due to keratopathy, and thick ropy mucoid discharge. Severe palpebral (tarsal) vernal keratoconjunctivitis is characterized by giant papillae, more than 1 mm in size, which has the appearance of cobblestones, while severe limbal vernal keratoconjunctivitis is associated with gelatinous perilimbal conjunctival papillary hypertrophy with Horner-Trantas dots,⁽⁴⁾ which are desquamated epithelial cells and degenerated eosinophils located at the top of the hypertrophied papillae, Fig. 1b.⁽³⁾

Keratopathy is a serious complication of vernal keratoconjunctivitis and usually seen in patients with giant papillae.⁽⁴⁾ It can be simple and transient like punctate epithelial erosions, or severe and sight threatening like epithelial macro-erosions, plaques and shield ulcers, subepithelial scars, pseudogerontoxon (arcus juvenilis), and keratoconus.^(8,9)

Severe form of vernal keratoconjunctivitis may adversely affect the school performance in affected children due to severe itching, photophobia and blurring of vision if not appropriately treated.⁽¹⁰⁾

Management includes prevention of exacerbation by avoiding exposure to environmental allergens (pollens), preservative-free artificial tears, and mast cell stabilizers eye drops few weeks before the beginning of spring season and to be continued usually till the end of summer.⁽⁴⁾ Short and intense courses of topical corticosteroids eye drops are needed in severe form with close monitoring of intraocular pressures, lens clarity to prevent steroid induced-glaucoma and complicated cataract.⁽¹¹⁾ Immune-modulating agents like cyclosporine A ophthalmic emulsion or oral was found to be a promising and a safe alternative to steroids in severe and refractory forms of vernal keratoconjunctivitis.^(8,12,13) Topical anti-metabolites in low dose, Mitomycin C, was found to be effective and safe alternative to steroid in controlling acute exacerbation of severe vernal keratoconjunctivitis.^(14,15)

The work of Gaza/18 mission was carried on during late spring and early summer seasons where patients with vernal keratoconjunctivitis suffering were at peak.

The aim of this study was to assess the clinical features and to detect ophthalmic complications of vernal keratoconjunctivitis in a group of patients who were treated in the Jordanian field hospital (Gaza/ 18) in Gaza strip and to review the literature.

Methods

This is a prospective hospital-based study conducted on 123 patients with vernal keratoconjunctivitis at the Jordanian Field hospital in the Gaza strip over 70 days between 15 March and 23 May 2012. Vernal keratoconjunctivitis diagnosis was made based on symptoms of itching, photophobia, burning sensation, and ropy mucoid discharge and clinical findings of conjunctival hyperemia, presence of large- or giant papillae of the upper palpebral conjunctivae and/ or limbal papillary hypertrophy with or without Horner-Trantas dots. Vernal keratoconjunctivitis was graded on a scale of 0-3 using Bleik *et al*⁽¹⁶⁾ grading system and classified as 0= no symptoms or signs, 1= mild symptoms or discomfort, mild conjunctival hyperemia, 0.2mm or less papillary size, punctate keratitis involving 1 quadrant of the cornea, 1-2 Horner - Trantas dots, and limbal edema

Table I: Age and gender distribution of vernal keratoconjunctivitis according to severity.

Age group(year)	Males			Females		
	Mild	Moderate	Severe	Mild	Moderate	Severe
0- 5	2 (1.6%)	3(2.4%)	0(0.0%)	6(4.9%)	1 (0.8%)	0(0.0%)
6- 10	12 (9.8%)	10(8.1%)	13 (10.6%)	9 (7.3%)	3(2.4%)	5(4.1%)
11- 15	16 (13%)	4(3.3%)	6(4.9%)	11 (8.9%)	0(0.0%)	2 (1.6%)
> 15	5(4.1%)	0(0.0%)	1 (0.8%)	7(5.7%)	3(2.4%)	4(3.3%)
Total	35(28.5%)	17(13.8%)	20(16.3%)	33(26.8%)	7(5.7%)	11(8.9%)

Table II: Age and gender distribution of severe vernal keratoconjunctivitis.

Age group (year)	Males 20(64.5%)				Females 11(3.2%)			
	Palpebral	Limbal	Mixed	Total	Palpebral	Limbal	Mixed	Total
0- 5	0 (0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0 (0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
6- 10	0 (0.0%)	8(25.8%)	6(19.4%)	14(45.2%)	1(3.2%)	1(3.2%)	3(9.7%)	5(16.1%)
11-15	1 (3.2%)	0(0.0%)	4(12.9%)	5(16.1%)	1(3.2%)	0(0.0%)	2(6.5%)	3(9.7%)
> 15	1(3.2%)	0(0.0%)	0(0.0%)	1(3.2%)	2 (6.5%)	0(0.0%)	1(3.2%)	3(9.7%)
Total	2 (6.5%)	8(25.8%)	10(32.3%)	20(64.5%)	4(12.9%)	1(3.2%)	6(19.4%)	11(3.2%)

involving less than 90° of limbal circumference, 2= moderate discomfort that does not interfere with daily routine, moderate conjunctival hyperemia, 0.3- 1 mm (large) papillary size, punctate keratitis involving 2 quadrants of the cornea, 3-4 Horner- Trantas dots, and limbal edema involving more than 90° and less than 180° of limbal circumference, and 3= severe symptoms with disruption of daily routine activity and patient staying at home most of the time, severe conjunctival hyperemia, more than 1 mm (giant) papillary size, punctate keratitis involving 3 or more quadrants of the cornea, more than 4 Horner- Trantas dots, and limbal edema involving more than 180° of limbal circumference.

Ophthalmic examination included visual acuity using Snellen chart for children who were above 5 years of age, eyelids, conjunctivae, anterior segment, dilated fundus to assess the retina and optic discs, Goldmann appanator to measure intra-ocular pressure for cooperative patients using slitlamp biomicroscopy. Intra- ocular pressure measurement was done before, during and after treatment with topical steroid or supratarsal Triamcinolone acetonide injection. Patients were diagnosed as keratoconus if they had bulging of the lower eyelid in down gaze (Munson sign), Fig. 2b, fundus oil- droplet red reflex by direct ophthalmoscope, or Vogt's striae on slit- lamp biomicroscopy. Other diagnostic methods like retinoscopy, placido disc, keratometer, corneal topography, and skin allergen prick test were not available in the hospital during the study period.

All patients were treated with topical sodium cromoglicate 4% eye drops as a mast cell stabilizer, artificial tears, antihistamine eye drops, with or without topical steroids. Fluorometholone 0.1% eye drops were used in moderate vernal keratoconjunctivitis, and prednisolone acetate 1% eye drops or supra- tarsal Triamcinolone acetonide injection for severe form.

Patients who were not inhabitant of the Gaza strip, patients who wear contact lens, patient with bacterial, viral or toxic conjunctivitis, phlyctenulosis, and patients who had pre-existing eye disease like congenital cataract or glaucoma were excluded from the study.

Royal Medical Services of Jordan Ethics Committee approved the study. The data were analyzed descriptively by the use of Microsoft Excel Worksheet 2007.

Results

During the 70 days rotation 1,753 patients were seen, 123 (7%) of them were vernal keratoconjunctivitis sufferers. Out of the 123 patients 72 (58.5%) were males and 51 (41.5%) were females with a male to female ratio of 1.4: 1. The age ranged between 4 and 20 year with an average of 9.9 years.

Table I shows age and gender distribution of vernal keratoconjunctivitis according to severity. Moderate and severe vernal keratoconjunctivitis was seen in 55 (44.7%) patients. Of the moderate and severe forms mixed vernal keratoconjunctivitis was the commonest type seen in 25/55 (44.5%) patients, followed by limbal type in 20/55 (36.4%) patients, and the

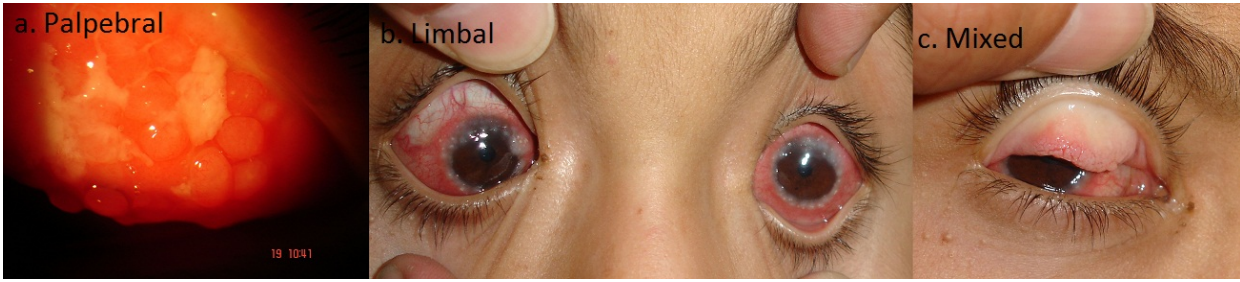


Fig. 1: Types of vernal keratoconjunctivitis: a. Palpebral, b. Limbal, and c. Mixed



Fig. 2: Vernal keratoconjunctivitis complications: a. Blepharoptosis, b. Keratoconus, Munson's sign, and c. Conjunctival inclusion cysts



Fig. 3: Horner- Trantas dots that involve limbal and part of bulbar conjunctiva in severe limbal vernal keratoconjunctivitis

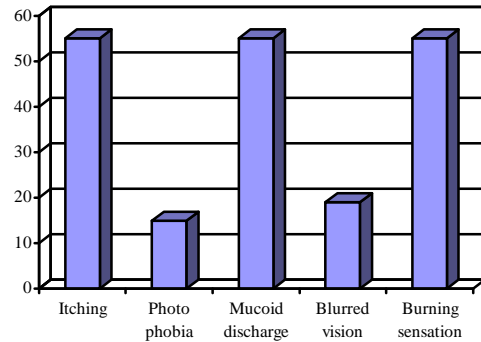


Fig. 4: Symptoms of moderate and severe vernal keratoconjunctivitis

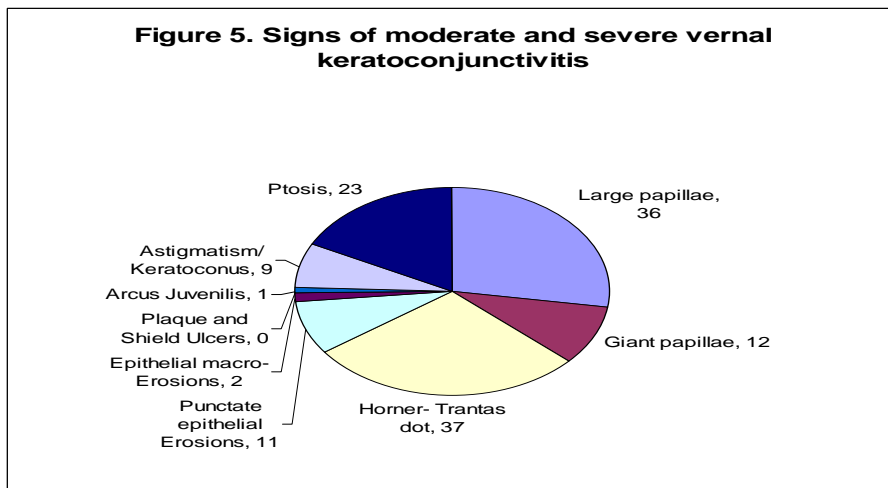


Fig. 5. Signs and complications of moderate and severe vernal keratoconjunctivitis

least type was palpebral in 10/55 (18.2%) patients. Bilateral severe vernal keratoconjunctivitis was seen in 27 (22%) patients and unilateral in 4 (3.3%) patients. Severe vernal keratoconjunctivitis was found in the right side in 31 (25.2%) patients and in the left side in 27 (22%) patients. Severe form was seen in 16 (13%) patients of mixed type, 9 (7.3%) of limbal type, and 6 (4.9%) of palpebral type. One patient with severe limbal vernal keratoconjunctivitis had Horner-Trantas dots that involve limbal and part of bulbar conjunctiva, Fig. 3. Two cases of severe mixed type were twin girls and 3 patients were from same family, 2 sisters and one brother.

All patients with moderate and severe forms had itching, mucoid discharge, and burning sensation, Fig. 4. Giant papillae were seen in 12 (9.8%) patients three of them had mixed type, while large papillae were seen in 36 (29.3%) patients. Horner-Trantas dots were found in 37 (30.1%) patients 19 of them had mixed type.

Table II shows age and gender distribution of severe vernal keratoconjunctivitis according to type.

At presentation bilateral superior corneal punctate epithelial erosions were seen in 9 (7.3%) patients and unilateral in two (1.6%) patients. One patient had bilateral macro-erosions and one had unilateral. Shield ulcer was not seen in any of the patients. One patient had bilateral pseudogerontoxon. Nine (7.3%) patients had bilateral keratoconus and one of them had history of penetrating keratoplasty. Twenty-three (18.7%) patients had asymmetrical bilateral blepharoptosis, Fig. 2a and 4 (3.3%) patients had bilateral blepharitis, Fig. 5. Two (1.6%) patients with long standing vernal keratoconjunctivitis had limbal conjunctival inclusion cysts, Fig. 2c.

All patients with severe vernal keratoconjunctivitis received short intensive course of prednisolone acetate 1% eye drops, one drop four times per day for one week then if Trantas spots disappeared the prednisolone acetate 1% stopped and changed to Fluorometholone 3 times per day, and 4 (3.3%) patients with severe palpebral type received supra-tarsal Triamcinolone acetonide 40mg/ml injection. None of the patients received immunomodulators as a steroid-sparing agents.

None of the patients had lens opacity or increased intraocular pressure before, during or after treatment. Follow up period ranged between one week and two months with an average of 43 days.

DISCUSSION

Vernal keratoconjunctivitis is a conjunctival allergic disease that is more common in warm dry climate.⁽³⁾ The climate in Gaza strip is tropical with hot and humid summer which makes it one of the regions that are prevalent with this disease. Allergic conjunctival disease is one of the commonest diseases that are usually seen in ophthalmology clinic, for example a study performed in Yemen revealed that this disease was the second most common exceeded only by refractive errors.⁽²⁾ In a survey of vernal keratoconjunctivitis in Palestinians in East Jerusalem⁽¹⁷⁾ the annual incidence was 10% while in our study the incidence was 7% and this could be due to the short duration of our study. This disease is characterized by seasonal variations with a peak incidence of exacerbations in late spring and early summer and this study was conducted during this time of the year which explains the high percentage of moderate and severe forms of vernal keratoconjunctivitis (44.5%). The majority of patients affected were children in the first and second decades of life with an average age of 9.9 year and this agrees with other studies in literature.^(1-3,5,7-17) Although the males predominate in this study but the male to female ratio was lower than that reported in literature. In our study it was 1.4: 1 while in other studies it ranged between 2:1 and 4:1.^(1,2,5,7-17)

The presenting symptoms were itching which is the sine qua non for the diagnosis, foreign body sensation, photophobia, mucoid discharge, and blurring of vision that affected their ability to prepare for end of semester exams that coincided with the period of the study that encouraged them to seek immediate management to improve their school performance, Fig. 4.⁽¹⁰⁾

In contrary to other studies where the commonest type was limbal followed by palpebral and mixed, our study showed that the most common type of vernal keratoconjunctivitis was mixed type followed by limbal and the least was palpebral.^(1,2,7,8,10-17) However, the limbal

type was the least frequent in females and this is in contrast to Leonardi *et al*⁽¹⁾ finding where the limbal form was the most frequent in female patients. The right eye was affected more frequently than the left eye and this might be explained by the excessive rubbing of the right eye by the right hand as all patients were right-handed.

Mild vernal keratoconjunctivitis was almost the same in males and females groups with 11-15 years age group being more frequently affected. In the moderate type males (13.8%) were more commonly affected than females (5.7%) and the commonest affected age group in males was 6-10 years (8.1%). Males had almost twice severe vernal keratoconjunctivitis than females and the commonest affected age group in males was 6-10 years while in females it was in two age groups, 6-10 and above 15 years.

Severe vernal keratoconjunctivitis was seen in 25.2% of patients and this was higher than that reported in literature.⁽²⁾

Although the disease resolved around puberty in most of the cases,^(7,18) which might be due to hormonal factors, but severe form was seen frequently in females above the age of 15 years in our study and this agrees with Leonardi *et al* study.⁽¹⁾

Horner- Trantas dots, which are found in the limbal and mixed types along the limbus, were seen as frequently as large papillae while giant papillae were seen in about one tenth of the studied group. One case had Horner- Trantas dots that involved the bulbar conjunctiva and this finding is rarely seen in patients with vernal keratoconjunctivitis, Fig. 3.

The presence of family history of vernal keratoconjunctivitis in 3 members of one family and twins suggests genetic factors and complex immunological mechanisms with the involvement of local conjunctival IgE- and non IgE- mediated mechanisms like eosinophils and chemotactic factors. Montan *et al*⁽¹⁹⁾ suggested genetic and environmental factors when they noticed that the prevalence of vernal keratoconjunctivitis was increased in Northern Europe by the immigrant children of Asian and African origin.

Superior punctate epithelial erosions of the cornea, which are usually seen in patients with

palpebral vernal keratoconjunctivitis due to mechanical irritation by the tarsal giant papillae that may lead to toxic effect of inflammatory mediators released by the mast cells,^(3,4) were not that common in the studied group (8.9%) and this might be due to the lower incidence of giant papillae in this study. Coalescence of the punctate epithelial erosions of the cornea leads to macro-erosions that may cause shield ulcer.⁽³⁾ Macro- erosions of the cornea was seen in 1.6% of the cases and because of early presentation and the intensive management of these cases none of them developed shield ulcer. Pseudogerontoxon is a peripheral degenerative corneal opacity seen in patients with chronic limbal vernal keratoconjunctivitis;⁽²⁰⁾ this was found in a 16-year old female patient with chronic mixed vernal keratoconjunctivitis. Keratoconus has been associated with atopy and eye rubbing. In case of vernal keratoconjunctivitis this may be due to vigorous knuckle rubbing forces on the normal peripheral cornea which exposes the thinner weakened cone apex to higher intra-ocular pressure distending forces that may tend to promote corneal ectasia.⁽²¹⁾ Keratoconus was seen in 7.3% of patients and this was less than that reported in literature. This can be explained by the poor facilities for diagnosis of mild keratoconus.⁽²²⁾

Bilateral asymmetrical blepharoptosis was found in 18.7% and this might be due to levator aponeurosis disinsertion secondary to excessive rubbing and giant papillae, mechanical ptosis as a result of giant papillae, blepharospasm in patients with keratopathy, and steroid induced ptosis as these patients use intensive topical steroid courses and sometimes Triamcinolone acetonide supratarsal injection that can cause degenerative muscle changes.⁽²³⁻²⁵⁾

Limbal conjunctival inclusion cysts were seen in two cases with long standing vernal keratoconjunctivitis. Suzuki *et al*⁽²⁶⁾ claimed that infiltration and inflammatory cell contribute to the development of conjunctival inclusion cysts in vernal keratoconjunctivitis. While Lee *et al*⁽²⁷⁾ presumed that the formation of the conjunctival inclusion cysts was secondary to chronic irritative friction caused by giant papillae in patients with long standing vernal keratoconjunctivitis.

Severe vernal keratoconjunctivitis needs to be treated aggressively with short intensive courses of topical steroids or supr- tarasal steroid injection and if not properly controlled and monitored steroid induced- glaucoma, cataract, and keratitis may occur.^(2,3) Luckily none of our patients developed glaucoma, cataract, or infection during the treatment and this may be due to close follow up and monitoring of intra-ocular pressure. Saleh *et al.*⁽²⁾ relate the development of steroid- related complications in Yemen to non- compliance of the patients and their families and the prolonged unsupervised self- prescription of topical steroids.

Because of severe itching, photophobia, and blurring of vision, vernal keratoconjunctivitis sufferers have poor school performance,⁽¹⁰⁾ and this disease affect the life style of the patients adversely. For example, they have to avoid environmental conditions that exacerbate the itching such as dust and sunlight, and they have to use eye drops regularly that cost them a lot of money every month.

There were limitations for this study: First, history of atopy was not included in the study. Second, due to limitations of facilities in this hospital visual assessment in preschool children was not possible. Third, diagnostic methods like retinoscopy, Placido disc, keratometer, and corneal topography to properly assess astigmatism and keratoconus and skin allergen prick test to detect allergy to pollen were not available in the hospital. Fourth, the study period was about 10 weeks and to properly determine the true incidence of the disease a longer duration is needed. Fifth, the hospital is located in the Northern part of Gaza strip, so most of the patients attended the clinic were from the Northern area and because of difficulty in transportations due to scarcity of fuel, less patients were seen from the Southern part of Gaza strip. Finally, the follow up period was not long enough to detect topical steroid- related complication.

Conclusion

Although clinical picture, young age presentation, and male predominance were the same as that reported in literature, there were differences in male to female ratio and frequency of vernal keratoconjunctivitis types. The

commonest type was mixed followed by limbal and the least was palpebral. Complications encountered were almost the same as other previous studies apart from higher incidence of blepharoptosis and conjunctival inclusion cysts. More representative sample over longer duration with collaboration of other local hospitals is needed to determine the true incidence, clinical features, complications, and seasonal variations of vernal keratoconjunctivitis in Gaza strip. Family history of vernal keratoconjunctivitis suggests genetic and environmental factors that need to be thoroughly investigated.

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