



# EPIDEMIOLOGY OF PHYLECTENULAR KERATOCONJUNCTIVITIS: RISK FACTORS AND ETIOLOGIES

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Article History: Received: 25.03.2023

Revised: 30.04.2023

Accepted: 04.05.2023

## Abstract

**Purpose:** To investigate the risk factors and etiologies involved in the development of Phlyectenular Keratoconjunctivitis (PKC) at Sirte University, the Ibsen teaching Hospital Libya.

**Methods:** Patients with PKC were recruited from the Ibsen teaching Hospital between Jan 1st and Jun 31st 2022. Patients underwent complete ophthalmologic examinations with 4 laboratory tests and investigations: 1) Tuberculin test, 2.) Throat Swabs, 3) Stool Analysis, and Conjunctival Swabs. Patients with any ocular diseases, use ocular medication, or history of previous surgeries or trauma were excluded.

**Results:** Fifty patients with PKC were included; with age range: 3- 19 years (SD 5.09). There were 37 females (74%), and 13 males (26%). Lesion limbus location distributions were as follows: temporal in 26 cases (52%), nasal in 16 cases (32 %), inferior 3 cases (6 %), and superior 5 cases (10 %). Tuberculin test was positive in 4 cases (8%) with mean age  $7.25 + 4.19$  (range: 3-12 years), and, 3 cases were females (75%). Throat swab was positive in only 4 cases (8%) with mean age  $8.67 + 1.53$  (range: 7-10 years), 3 cases were males (75%). Stool Analysis was positives for intestinal parasites in 14 cases (28%), their mean age was  $11.38 + 5.68$  years (range: 3-19). Hymenolepis nana was detected in 11 cases (78.57%) of which 9 were female (64.28%), and Ascaris was detected in 3 male cases (21.43%). conjunctival swab was positive for staphylococci in 30 cases (60%) with a mean age of  $10.33 + 4.92$  years and 22 were females (73.33 %).

**Conclusion:** In this study, conjunctival bacteria appeared to first risk factor for developing PKC followed by intestinal parasitic infestations. Two infections that may require further attentions to reduce the incident of PKC.

**Keywords:** Phlyectenular Keratoconjunctivitis; Risk Factors, Etiology, Sirte, Libya.

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## 1. INTRODUCTION

Phlycten is an inflammatory keratoconjunctival condition with an extremely widely variable etiology.<sup>1, 2</sup> Nonetheless, it may have a serious progressive course affecting the visual acuity if it creeps over the visual field. Early diagnosis and treatment are safe haven for vision.<sup>3</sup> Many tools have been introduced for that purpose however it remains an important task to select the most accurate and the most reliable one for early management.<sup>4</sup>

In this study, we investigated the risk factors and etiologies involved in the development of Phlyectenular Keratoconjunctivitis (PKC) at Sirte University Hospital, Libya. The present work aims to highlight the tools an ophthalmologist can use for early detection and treatment of such a condition.

## 2. PATIENTS AND METHODS

This is a prospective case series at a single-center, Ibsen teaching hospital, at Sirte University Hospital, Libya. Patients presenting at the outpatient clinics with PKC between Jan 1<sup>st</sup> and Jun 31<sup>st</sup> 2022 were

included. The study protocol was revised and approved by the Institutional Review Board (The Department of Ophthalmology Scientific Committee, Sirte University) and followed the tents of the declaration of Helsinki.

### • Study Population:

**Inclusion Criteria:** Patients older than 18 years patients with bulbar, limbal or corneal PKC.  
**Exclusion Criteria:** Patients with diabetes mellitus, previous intraocular surgery, history of ocular trauma, concomitant ocular disease, current or history of use of systemic or topical medications.

### • Baseline Evaluation:

The patient including: age, sex, occupation if any, residence with special attention to the socioeconomic state were recorded. Careful history taking to report any medical history, previous ophthalmic history of similar condition or related ophthalmic problems, and hypersensitivity to any drug. Then full ophthalmological examination was done including: best corrected visual acuity (BCVA) measurements using Snellen chart, refraction

measured by auto-refractometer, anterior segment examination using slit lamp, intraocular pressure (IOP) measurement using Goldmann applanation tonometer, fundus examination using binocular indirect ophthalmoscope, and indirect slit lamp biomicroscopy (+90 volk lens) for detailed evaluation of macula.

#### **Conjunctiva and Cornea Examination for the PKC Phlycten:**

- 1) Exact location site, size measurements, and shape description.
- 2) The surrounding area and the amount and shape of invading and surrounding vascularization.
- 3) The lesion surface: intact or ulcerated.
- 4) Presence or absence: conjunctivitis (type of discharge), corneal involvement, and any associated anterior segment pathology.
- 5) Eyelid margin examination: to reveal any associated blepharitis or meibomian gland dysfunction.
- 6) Fluorescein stain: for detection of any surface ulcerations or corneal involvement.
- 7) A colored digital photograph was taken for documentation of the lesion and follow up of the patients.

#### **• Laboratory Investigation:**

- 1) Tuberculin test to detect Tuberculosis.
- 2) Throat swab: to detect any bacteria.
- 3) Stool analysis to detect any parasites.
- 4) Conjunctival swab to detect any bacteria.

#### **• Medical Treatment:**

1. All patients were treated for one week with an antibiotic-corticosteroid combination; Optidex-TT eye drops (tobramycin + Dexamethasone,) three times daily during day hours (JamJoom pharma SA) and Maxitrol (Alcon-couvreur) ointment was given at bed time.
2. In cases of corneal involvement, additional treatment in the form of Cornel gel (Minafarm) eye ointment was given t.d.s.
3. In cases of associated conjunctivitis: antibiotic drops were added (chloramphenicol or ofloxacin) with replacement of Maxitrol ointment by Fuscidic acid ointment at bed time (fucithalamic Leo/Egy Drug) (Leo Pharmaceutical).

#### **• Study Outcome Measures:**

1. Primary Outcome Measures: Assessing the risks involved in the development of PKC.
2. Secondary Outcome Measures:
  - a) Descriptive analysis of the PKC patients' demographics.
  - b) Assessment of the different tests value in PKC etiology detections.
  - c) Assessment of any associated systemic illness.

#### **STATISTICAL ANALYSIS:**

The collected data was organized, tabulated, and statistically analyzed using statistical package for the Social Sciences (SPSS) software statistical computer package version 12 (IBM Corp., Armonk, NY, USA). Data was summarized using mean and standard deviation in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. For quantitative data, the range, mean and standard deviation were calculated. The difference between two means was statistically analyzed using the students (t) test. For qualitative data, the number and percent distribution was calculated. Significance was adopted at  $p < 0.05$  for interpretation of results of tests of significance. P value  $> 0.05$  is considered non-significant. P value  $< 0.05$  is considered significant. P value  $< 0.01$  is considered highly significant.

### **3. RESULTS**

Fifty patients with PKC were included in this study. The mean patients age range: 3- 19 years (SD 5.09). The male to female ratio in all groups was 1:3 (Males 13 (26%), females 37(74%)). Right eye was involved in 35 cases (70%) and the left eye involved in 15 cases (30%). Corneal ulceration was demonstrated by fluorescein stain, in 3 cases (6%). All patients showed clinical clearance after one week of treatment and those with corneal ulcer were cured after two weeks. No associations were found with frank illness during the study period.

#### **Phlycten Distribution Location was as follows:**

- 1) Temporal limbus in 26 cases (52%).
- 2) Nasal limbus in 16 cases (32 %).
- 3) Inferior limbus 3 cases (6 %).
- 4) Superior limbus 5 cases (10 %).

#### **Laboratory Test Results:**

##### **1-Tuberculin Test:**

It was positive in 4 cases (8%) whose age mean age was  $7.25 \pm 4.19$  (range:3-12 years), 3 were females (75%) and only one male (25%).

##### **2-Throat Swab:**

It was positive in only 4 cases (8%). Their mean age was  $8.67 \pm 1.53$  (range: 7-10 years), 3 were males (75%), and only one female (25%).

##### **3-Stool Analysis:**

Two causative types of intestinal parasites were found in 14 cases (28%), their mean age was  $11.38 \pm 5.68$  (range:3-19 year). Hymenolepis nana was detected in 11 cases (78.57%); 9 were female (64.28%) and 2 males (14.28 %). The second parasite detected was Ascaris in 3 cases (21.43%) and cases were males.

##### **4- Conjunctival Swab:**

Conjunctival swab was positive for staphylococci in 30 cases (60%). Positive conjunctival swabs were found in 22 females (73.33%). The mean age was  $10.33 \pm 4.92$  (range: 3-19 years).

#### **Comparison between different laboratory methods:**

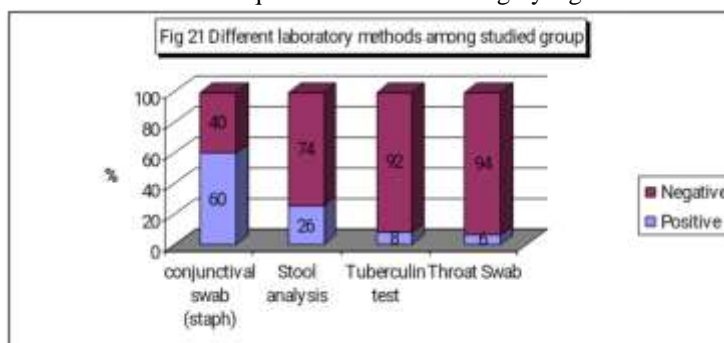
**Table 1** and **Figure 1** show the comparison between the different methods used to detected risk facts and/or etiologies for the development of PKC. It

appears that conjunctival swabs followed by stool analysis are the most useful methods to reveal the etiology of PKC.

**Table (1):** Comparison between different laboratory methods among studied group

	Positive	Negative	P value
Conjunctival swab (staph)	60%	40%	< 0.01
Stool analysis	26%	74%	
Tuberculin test	8%	92%	
Throat Swab	6%	94%	

P value for chi square test. P < 0.01: highly significant.



**Figure 1:** Bar Chart Showing: Different Laboratory Methods Among Studied Group.

#### 4. DISCUSSION

PKC is a nodular affection characterized by the formation of a small, circumscribed lesion at the corneal limbus. Duke-Elder referenced accounts of the condition in the Greek, Arabic, French, and English literature. He described the pitiable position of these children: "During the day the child hides away in a dark corner, burying his face in his hands; and during the night he curls up under the blankets."<sup>5</sup> Phlyctenulosis occurs mainly in children and young adults as a result of a hypersensitivity reaction of the conjunctiva or cornea to bacterial products. It can lead to discomfort, extreme photophobia, tearing, and blepharospasm. In severe cases involving the cornea, it may result in ulcers, scarring, vascularization, and even perforation. Disturbance in vision is related to the degree of scarring and to the location of the scarring relative to the visual axis.<sup>6</sup>

PKC has been associated in the past with poor, undernourished, sickly children, with tuberculosis strongly implicated. In our work the average age of all cases around 3-19 years. It is found most commonly during the first and second decades of life in children living in crowded, impoverished quarters.<sup>7, 8</sup> considering sex privilege; all observers report a higher incidence (60% to 70% of reported cases) in girls than in boys. This is in agreement with the present work where number of female patients (37=74%) exceeded their male sibilants who were just 13 (26%).

**Fritz et al.**<sup>9</sup> studied 346 Alaskan native children with corneal scarring apparent in 143 cases. The

involvement was bilateral in 112 cases (78%) and unilateral in 31 (22%). **Sorsby**<sup>10</sup> reported that PKC occurs more often in spring and summer than in late autumn or winter. In our work the majority of our cases 42 were collected during the period from July to the end of September with only 8 cases were from Sept. to Dec.

Never the less, there is some debate about the pathophysiology and causes of PKC. A clear analogy exists between phlyctenules of the conjunctiva and bacterids of the skin. Bacterids are nodules in the skin that are comparable histologically, and in their allergic origin, to phlyctenules of the conjunctiva and cornea. Although the tuberculid is the most common bacterid, dermatologists describe other types, such as monilia and trichophytid. That results from sensitization to proteins from organisms other than the tubercle bacillus. The organism is not present in the id reaction, which is a hypersensitivity to organisms present elsewhere in the body. The tubercle bacillus has not been found in the phlyctenular lesion itself.<sup>11, 12</sup>

Although the precise mechanism by which phlyctenules are produced has not been determined, it is assumed from clinical evidence that the patient has been sensitized to an offending antigen in the past. **Thygeson**<sup>13</sup> reported the relationship between PKC and tuberculoprotein. Thygeson believed that the incidence of Phlyctenulosis on a worldwide basis appeared to parallel the incidence of tuberculosis. The occurrence of Phlyctenulosis in a child should be considered a warning of impending clinical tuberculosis. In our work we failed to demonstrate

statistically significant correlation with tuberculosis only 4 (8%) of our cases tested positive for TB.

PKC is now accepted as a morphologic expression of delayed hypersensitivity to diverse antigens. The condition is one of several corneal disorders that arise as an expression of altered immune mechanisms.<sup>14</sup> In the United States, where the rate of positive tuberculin test results is relatively low, PKC may occur in adults as well as in children and it is likely to occur in patients free of tuberculosis. With tuberculosis, this sensitization presumably occurred as part of a bacteremia from an early infection in the lungs or lymph glands.<sup>15</sup>

For non-tuberculosis phlyctenular keratoconjunctivitis caused, for example, by *Staphylococcus*, the antigen probably comes from the pathogenic staphylococci that inhabit the lid margins of all people from time to time. The attack of phlyctenular keratoconjunctivitis may be precipitated by the presentation of the antigen to the sensitized ocular tissue, either by the bloodstream in the event of a recrudescence of a focus of infection elsewhere or by an exogenous inoculation of bacteria into the conjunctival sac from the lid margin.<sup>16</sup> This is in agreement with the present study where conjunctival swab showed statistically significant staphylococcal positive swabs 24 cases (48%). Hypersensitivity to Intestinal parasites was the next most common positive factor where 11 cases (22%) were tested positive for *Hymenolepis nana* and 2 cases (4%) for *Ascaris* and that was in agreement with **Hussien et al.**<sup>17</sup>

Incidence of complications was very low where only 3 cases showed superficial ulceration which responded to a cover of steroids and use of soothing ointment. No cases of steroid-induced complication were recorded. Of special interest, is the high association with blepharitis, where 10 cases (20%) were reported. They just required treatment with systemic tetracycline, a finding cited by many other authors.<sup>17</sup>

#### **Data Availability Statement**

The authors confirm that the data supporting the findings of this study are available within the article [and/or] its supplementary materials.

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