Title

Case Series: Unbiased Deep Sequencing Analysis of Acute Infectious Conjunctivitis in an Ambulatory Eye Center in Berkeley, California.

Journal

Optometry and Vision Science, 100(4)

Authors

Yeung, Sze
Coulter, Adrienne
Roufail, Mareena
et al.

Publication Date

2023-04-01

DOI

10.1097/OPX.0000000000002010

Peer reviewed

HHS Public Access

Author manuscript

Optom Vis Sci. Author manuscript; available in PMC 2024 April 01.

Published in final edited form as:

Optom Vis Sci. 2023 April 01; 100(4): 276–280. doi:10.1097/OPX.0000000000002010.

Case Series: Unbiased Deep Sequencing Analysis of Acute Infectious Conjunctivitis in an Ambulatory Eye Center in Berkeley, California

Kuniyoshi Kanai, OD,
University of California, Berkeley, School of Optometry, Berkeley, California

Meredith Whiteside, OD,
University of California, Berkeley, School of Optometry, Berkeley, California

Michel Wong, OD, MS,
University of California, Berkeley, School of Optometry, Berkeley, California

Tammy La, OD,
University of California, Berkeley, School of Optometry, Berkeley, California

Maryam Nassiri, OD,
University of California, Berkeley, School of Optometry, Berkeley, California

Sam Lee, OD,
University of California, Berkeley, School of Optometry, Berkeley, California

Sze Kei Yeung, OD,
University of California, Berkeley, School of Optometry, Berkeley, California

Adrienne Coulter, OD,
University of California, Berkeley, School of Optometry, Berkeley, California

Kevin Ruder, BS,
Francis I. Proctor Foundation, University of California San Francisco, San Francisco, California

Cindi Chen, MS,
Francis I. Proctor Foundation, University of California San Francisco, San Francisco, California

David Liu, BS,
Francis I. Proctor Foundation, University of California San Francisco, San Francisco, California

Thomas Abraham, BS,
Francis I. Proctor Foundation, University of California San Francisco, San Francisco, California

Armin Hinterwirth, PhD,
Francis I. Proctor Foundation, University of California San Francisco, San Francisco, California

Thomas M. Lietmanb, MD,
Department of Ophthalmology, University of California San Francisco, San Francisco, California

Thuy Doan, MD, PhD,

Corresponding author: Thuy Doan, Thuy.Doan@ucsf.edu.

Francis I. Proctor Foundation, University of California San Francisco, San Francisco, California; Department of Ophthalmology, University of California San Francisco, San Francisco, California

Gerami D. Seitzman, MD
Francis I. Proctor Foundation, University of California San Francisco, San Francisco, California; Department of Ophthalmology, University of California San Francisco, San Francisco, California

Seasonal Conjunctivitis Outbreak Reporting for Prevention and Improved Outcomes (SCORPIO) Study Group

Abstract

Significance: Acute infectious conjunctivitis poses significant challenges to eye care providers. It can be highly transmissible and as etiology is often presumed, correct treatment and management can be difficult. This study utilizes unbiased deep sequencing to identify causative pathogens of infectious conjunctivitis, potentially allowing for improved approaches to diagnosis and management.

Purposes: To identified associated pathogens of acute infectious conjunctivitis in a single ambulatory eye care center.

Case Reports: This study included patients who presented to the University of California Berkeley eye center with signs and symptoms suggestive of infectious conjunctivitis. From December 2021 to July 2021, samples were collected from 7 subjects (ages ranging from 18 to 38 years old). Deep sequencing identified associated pathogens in 5 out of 7 samples, including human adenovirus D (HAdV), *Haemophilus influenzae*, *Chlamydia trachomatis*, and human coronavirus 229E (HCoV-229E).

Conclusions: Unbiased deep sequencing identified some unexpected pathogens in subjects with acute infectious conjunctivitis. HAdV was recovered from only one patient in this series. While all samples were obtained during the COVID-19 pandemic, only one case of HCoV-229E and no SARS-CoV-2was identified.

Infectious conjunctivitis is a common ocular disease affecting all ages and socioeconomic statuses, with outbreaks frequently occurring in the community, schools, military units, nursing homes, workplaces, and healthcare facilities.[1-4] Previous studies have reported that viruses cause 80% of all cases of acute conjunctivitis, with the remaining caused by bacteria, and to a lesser extent, fungi and protozoa.[5] Of those caused by viruses, human adenovirus (HAdV) is the most presumed cause of conjunctivitis.[6-8] Infectious conjunctivitis may be confused with non-infectious conjunctivitis (caused by allergy or irritants) since both conditions have overlapping signs and symptoms. The diagnosis of conjunctivitis is typically made through clinical evaluation alone, and confirmative microbiologic tests are rarely obtained unless there is high suspicion of a sexually transmitted disease. First-line providers often empirically manage presumed infectious conjunctivitis, leading to misdiagnosis and inappropriate treatment.

Errors in recognizing the etiology of infectious conjunctivitis can have a substantial impact. In the US, estimates indicate nearly $430 million/year may be spent in prescriptions and medical care for viral conjunctivitis.[9] There is also a societal cost. Excessive antibiotic

use increases the likelihood of ocular surface antibiotic resistance which can impact vision-threatening conditions such as corneal ulcers.[10] Patients incorrectly diagnosed with viral conjunctivitis may unnecessarily be quarantined and needlessly miss work or school. Conversely, if there is a failure to recognize an infectious etiology of conjunctivitis, the condition may be transmitted to others since appropriate hygiene protocols may not have been recommended. Thus, by understanding regional variances in etiologies of infectious conjunctivitis, better education and guidelines can be implemented to help decrease healthcare spending, reduce antibiotic resistance, and improve patient outcomes.

Seasonal Conjunctivitis Outbreak Reporting for Prevention and Improved Outcomes (SCORPIO) is an international, multi-center study that utilizes an unbiased approach, RNA deep sequencing, to identify and track the causes of conjunctivitis epidemics, worldwide. RNA-sequencing allows for the detection of any pathogen in a clinical sample, including bacteria, parasites, fungi, DNA and RNA viruses. The University of California Berkeley Eye Center is a participating site in SCORPIO and this study presents the results of a case series of participants who presented with signs and symptoms of acute infectious conjunctivitis.

METHODS

This research was reviewed by an independent ethical review board and conforms with the principles and applicable guidelines for the protection of human subjects in biomedical research. The research was approved by the University of California, Berkeley, and the University of California, San Francisco Institutional Review Board. No identifiable health information was included in this case report. Study informed consent was obtained from all participants. Samples were obtained from July 2021 through December 2021 at an urban university eye center.

Subjects were recruited from patients of any age presenting with signs and symptoms suggestive of acute infectious conjunctivitis for a duration of less than 14 days. Exclusion criteria were presumed non-infectious conjunctivitis, such as allergic conjunctivitis or medicamentosa. Prior use of topical antibiotics did not exclude the subject.

All subjects were queried about systemic and ocular symptoms. A slit lamp clinical examination confirmed signs of infectious conjunctivitis. External disease photographs were obtained. For sample collection, clinicians wore masks and gloves, and participants were masked. Samples were collected using three different sterile polyester swab applicators (Puritan, Guilford, ME). The inferior conjunctival fornix of each eye was swabbed separately. The final swab included sampling from both anterior nares. All swabs were immediately placed in DNA/RNA Shield (Zymo Research) and transferred to a −20°C freezer for storage until shipment to the University of California, San Francisco. Details of sequencing, library preparation, and bioinformatics analyses have been previously described.[11] Briefly, total RNA is extracted from conjunctival swabs and prepared for sequencing. Using a custom bioinformatics pipeline, low quality sequences and human sequences are removed. The remaining non-redundant, non-host sequences are aligned against the National Center for Biotechnology Information (NCBI) GenBank nucleotide database. To account for laboratory and environmental contaminants, background

subtraction using no-template (i.e., water) controls from the same sequencing run is performed. The pre-specified criteria for positive pathogen are 1) it is known to be a human pathogen and represent the most abundant reads after water background subtraction or 2) two or more unique reads covering separate regions in DNA virus genomes or 3) 1 or more unique reads matching RNA virus genomes.

RESULTS

Seven subjects were consented for study enrollment (Table 1). The average age was 25 years (range 19-38). 60% (4/7) were female. The average time until presentation was 5 days (range 3-13). 43% (3/7) presented on a topical antibiotic drop. Both eyes were affected in 71% (5/7) of cases. 86% (6/7) reported tearing. 71% (5/7) experienced purulent discharge and 29% (2/7) described itching. Pre-auricular lymphadenopathy was palpated in 29% (2/7). Sub-epithelial infiltrates and pseudo-membranes were not present in any participant. Representative clinical appearance is demonstrated in Figure 1. Unbiased deep sequencing identified a pathogen in 71% (5/7) of the participants (Figure 2). Bacterial etiologies were identified in 43% (3/7) and included two cases of *Haemophilus influenzae* and one case of *Chlamydia trachomatis*. 29% (2/7) of the samples demonstrated a viral pathogen including once case of HAdV-D, and one case of the commonly circulating human coronavirus 229E (HCoV-229E). In two of the participants, no associated pathogens were identified. One patient in this group was using topical antibiotics prior to the swabbing.

DISCUSSION

The present study utilized unbiased RNA deep sequencing to identify organisms associated with presumed acute infectious conjunctivitis in patients presented to the University of Berkeley eye clinic in Northern California, United States. While the sample size is small, the results suggest several important clinical implications.

Most cases of acute conjunctivitis are thought to be attributed to viruses, with HAdV the most likely etiology. Results of this study indicate a different pattern where HAdV was identified in a single case. It is estimated that 20 million cases of HAdV ocular infections occur every year in the United States (US).[12] Adenoviral species diversity varies by location.[13] HAdV is a known cause of epidemic keratoconjunctivitis. In particular, HAdV-D, the species isolated in this study, is associated with a severe form of epidemic keratoconjunctivitis. Potential explanations for the low number of adenoviruses isolated in this series include small sample size, the likelihood that infectious conjunctivitis etiology varies by season and region, and the possibility that the patient's immune response cleared the infection prior to swabbing.

Of the two viruses identified in this series, HCoV-229E RNA was detected in one patient with bilateral conjunctivitis. Notably, patient recruitment was performed during the SARS-CoV-2 pandemic, indicating that other coronaviruses, in addition to SARS-CoV-2, can be concurrently circulating in the community. HCoV-229E is an RNA virus first identified in the 1960s and known to cause upper respiratory illnesses.[14] HCoV-229E is believed to be the second most common cause of the common cold after rhinoviruses. While HCoV-229E

is an alphacoronavirus, unlike the other commonly circulating alphacoronavirus, HCoV-NL63, it is not commonly documented to be associated conjunctivitis.[15] In this study, HCoV-229E RNA was detected in both conjunctival samples. However, while HCoV-229E RNA was detected in the nasal sample, the patient denied any respiratory symptoms indicating this was likely the cause of a primary conjunctivitis. This patient's clinical course was typical for a viral conjunctivitis including bilateral conjunctival hyperemia that started in one eye and progressed to the other, tearing, conjunctival discharge upon awakening, and lack of improvement in symptoms after using unknown topical antibiotics for two days. On clinical examination, a mixture of papillary and follicular reaction was noted in both inferior palpebral conjunctivae.

H. Influenza was identified as the cause of infectious conjunctivitis in two participants. With the introduction of a vaccine against *H. influenzae* type b (Hib) in 1987, severe systemic complications, such as pneumonia, from Hib have dramatically declined. Yet, *H. influenzae* remains a commonly identified ocular surface pathogen. In the nationwide Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) study, *H.* influenzae was the most common ocular bacterial pathogen identified a patient population less than seventeen years-old.[16] In both cases of *H. influenzae* conjunctivitis, the patients reported recent flu-like symptoms. *H. influenzae* can occur regardless of age along with upper respiratory infections[17]; it is prudent to keep this pathogen in the conjunctivitis differential diagnosis, even in non-pediatric patients.

Identification of the sexually transmitted strain of *Chlamydia trachomatis* as a cause of acute conjunctivitis in this series was surprising. This participant's ocular symptoms and clinical examination was like other participants. Clinical examination revealed a mild follicular conjunctivitis, mild injection, and a lack ocular discharge. As the examiner did not suspect a sexually transmitted disease and diagnosed the patient with viral conjunctivitis, urogenital symptoms and recent sexual history were not queried. Appropriate treatment for chlamydia conjunctivitis requires systemic antibiotics and an incorrect clinical assumption of viral conjunctivitis in this setting could have serious systemic sequelae. The Center for Disease Control has reported a steady increase in the rate of chlamydial infection over the last 20 years in the US, making it the most common notifiable sexually transmitted disease in the US.[18]

In two patients, no associated pathogen was identified. This illustrates the challenge of microbial confirmation in presumed cases of infectious conjunctivitis. In one patient, it is possible the pathogen was successfully treated secondary to the use of topical antibiotics (polymyxin B 10,000 units/ml and trimethoprim 1mg/ml) prior to study presentation. Alternatively, conjunctivitis in these two subjects could have been secondary to a resolving viral conjunctivitis or a non-infectious cause such as allergy or toxicity.

While the results of our samples differ from previously expected causes of presumed infectious conjunctivitis, it is worth noting the diagnostic value of unbiased deep sequencing in the setting of infectious disease surveillance. RNA-sequencing is an unbiased, or hypothesis-free, method of pathogen detection. Prior studies have demonstrated high agreement with RNA-sequencing and pathogen-directed polymerase chain reaction

testing[11,19,20] and better performance of RNA-sequencing over traditional cultures.[21] Culture performs poorly for the isolation of viruses, and variably for ocular surface bacteria.[22] One limitation of polymerase chain reaction-based laboratory testing is that clinicians must have a high degree of clinical suspicion for a particular pathogen before ordering this specific pathogen-directed test. Additionally, several etiologies of conjunctivitis are RNA viruses which are very difficult to detect. With unbiased deep sequencing, in particular RNA-sequencing analysis, viral RNA is reverse transcribed to DNA allowing for RNA pathogen detection. Because unbiased deep sequencing allows for unexpected pathogen detection, we were able to identify some uncommon pathogens in this series. In contrast to the presumption that most infectious conjunctivitis is HAdV in origin, deep sequencing was able to detect HCoV-229E and *Chlamydia trachomatis* as pathogens of conjunctivitis in this series.

There are several limitations to this study. In addition to the small sample size, samples were collected from a single urban university eye clinic in Northern California. Our regional results may have been influenced by the testing site being in a metropolitan city with a lot of foot traffic, including international travelers. Another limitation is that samples were collected during a limited period (July 2021 to December 2021), although during the Delta surge in the United States. Previous studies suggest that there may be seasonal variations in the cause of infectious conjunctivitis.[5,23] Use of topical antibiotic is not an exclusion criterion and could have limited detection of some bacterial pathogens. Another limitation may be this study's inclusion criteria of less than 14 days of ocular symptoms. Especially if an initial infectious inoculum was low, a rapid innate immune response could have promoted pathogen clearance prior to conjunctival swabbing. In an adenoviral conjunctivitis study, polymerase chain reaction was still positive in about half of the participants by day 7, and closer to a quarter of the participants on day 14.[24] Therefore, patients with a longer duration of symptoms, such as Case 3 (with 7 days of symptoms and no pathogen detected) and Case 6 (with 13 days of symptoms and *Chlamydia trachomatis* detected,) could have self-cleared an adenovirus virus prior to presentation for care. Longitudinal data regarding the timeline of infectious conjunctivitis viral clearance as determined by RNA-seq is lacking and would provide a more informative inclusion criteria for future studies. An additional limitation is that swabs from patients without infectious conjunctivitis are not included for comparison. RNA-sequencing technology, itself, has some limitations. It is not universally available or yet capable for point-of-care rapid results. Cost and bioinformatic analytic expertise limits broad utilization of this technique. However, with time, this technology is rapidly becoming less expensive and more efficient. The extreme sensitivity of RNA-sequencing allows for the detection of microbial contamination from the environment and laboratory reagents, which may lead to potential false-positive results if appropriate controls are not adequately assessed.

We are encouraged by these preliminary findings and that future reporting from the much broader SCORPIO study may confirm the variety of pathogens that underlie infectious conjunctivitis and address possible geographical and seasonal trends in the incidence and etiology of this common eye disease.

In summary, the associated pathogenic organisms found in subjects with presumed infectious conjunctivitis vary widely. This study highlights the advantages of deep sequencing as a surveillance tool for infectious conjunctivitis and emphasizes the importance of regional and local surveillance of infectious disease outbreaks. A comprehensive understanding of pathogens associated with infectious conjunctivitis allows for clinicians to better promote antibiotic stewardship and create appropriate public health strategies for decreased transmission.

ACKNOWLEDGMENTS

Research reported in this manuscript was supported by the National Eye Institute of the National Institutes of Health under Award Number R01EY032041 (TD). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Seasonal Conjunctivitis Outbreak Reporting for Prevention and Improved Outcomes (SCORPIO) Study Group

Aravind Eye Hospital, Madurai, India – Lalitha Prajna, N. Venkatesh Prajna, Ramesh Gunasekaran, Sankalp Singh Sharma, Vishnu Teja; *B.P Koirala Lions Center for Ophthalmic Studies, Kathmandu, Nepal* – Meenu Chaudhary, Sanjeeta Sitaula; *Centre de Recherche en Sante de Nouna, Nouna, Burkina Faso* – Ali Sié, Boubacar Coulibaly, Mamadou Bountogo; *Chulalongkorn University, Bangkok, Thailand* – Thanapong Somkijrungroj, Vannarut Satitpitakul; *Hai Yen Vision Institute, Ho Chi Minh City, Vietnam* – Huy Tran, Linh Hoàng Mai, Thảo Hạ Xuân, Yen Tran; *Hospital Clinico Universidad de Chile, Santiago, Chile* – Cristhian A. Urzua, Fabian Vega, Felipe Salgado, Loreto Cuitino; *Instituto Mexicano de Oftalmología, Santiago de Querétaro, Mexico* – Fernando Pérez Pérez, Jaime Macías Martínez, Van Charles Lansingh; *Khon Kaen University, Khon Kaen, Thailand* – Sukhumal Thanapaisal, Wipada Laovirojjanakul; *National Eye Institute* – George McKie (Program Officer); *Oregon Health and Science University, Portland, Oregon* – Kenia Chavez, Travis Redd, Winston Chamberlain; *Pacific Vision Institute of Hawaii, Honolulu, Hawaii* – Angel Cheng, Vivien Tham; *Phramongkutklao Hospital, Bangkok, Thailand* – Wiwan Sansanayudh; *Programme National de Santé Oculaire, Niamey, Niger* – Abba Kaka Hajia Yakoura, Abdou Amza, Abdoul Salam Youssoufou Souley, Adam Nouhou Diori, Beido Nassirou, Boubacar Kadri, Boubacar Mariama, Cissé Mamadou Ibrahim, Lamyne Aboubacar Roufaye, Ramatou Boulhassane, Saley Ali, Zakou Abdou; *Rabin Medical Center, Petah Tikva, Israel* – Lee Goren, Ruti Sella; *Sinai Hospital, Baltimore, Maryland* – Clare Kelliher, Laura Green; *Singapore Eye Research Institute, Singapore* – Hon Shing Ong, Jod Mehta, Yu-Chi Liu; *Stanford University School of Medicine* – Benjamin A. Pinsky; *Taipei Veterans General Hospital, Taipei, Taiwan* – De-Kuang Hwang, Nai-Wen Fan; *The University of Sydney, Save Sight Institute, Sydney, Australia* – Hong Sheng Chiong, Javier Lacorzana, Maria Cabrera-Aguas, Stephanie Watson; *University of California Los Angeles Stein Eye Institute, Los Angeles, California* – Edmund Tsui, Joana Ramirez, Nina M. Cherian, Rachel Feit-Leichman, Reginald E. Hughes Jr, Tania Onclinx; *University of California San Diego Shiley Eye Institute; La Jolla, California* – Carol Yu, Esmeralda McClean, Iliana Molina; *University of California San Francisco Francis I. Proctor Foundation, San Francisco, California* – Armin Hinterwirth, Cindi Chen, Danny

Yu, David Liu, Elodie Lebas, Emily Colby, Gerami Seitzman, Kevin Ruder, Lina Zhong, Michael Deiner, Thomas Abraham, Thomas Lietman, Thuy Doan (Principal Investigator), Travis Porco, Stephen McLeod; *University of California Berkeley School of Optometry, Berkeley, California* – Kuniyoshi Kanai, Meredith Whiteside; *University of Nebraska Medical Center Truhlsen Eye Institute, Omaha, Nebraska* – Steven Yeh, Tolulope Fashina; *University of New Mexico, Albuquerque, New Mexico* – James Chodosh; *University of Papua New Guinea School of Medicine and Health Sciences, Port Moresby, Papua New Guinea* – Bridgit Tarkap, Jambi N. Garap, Magdalene Mangot; *Vanuatu Eye Program, Ministry of Health, Vanuatu* – Edwin Amel, Fasihah Taleo, Johnson Kasso, Kalbule Willie, Madopule Nanu, Prudence Rymill; *World Health Organization* – Anthony W. Solomon

REFERENCES

1. Faden H, Wynn RJ, Campagna L, Ryan RM. Outbreak of Adenovirus Type 30 in a Neonatal Intensive Care Unit. J Pediatr 2005;146:523–7. [PubMed: 15812457]
2. Laibson PR, Ortolan G, Dupré-Strachan S. Community and Hospital Outbreak of Epidemic Keratoconjunctivitis. Arch Ophthalmol 1968;80:467–73. [PubMed: 4299999]
3. Cooper RJ, Hallett R, Tullo AB, Klapper PE. The Epidemiology of Adenovirus Infections in Greater Manchester, Uk 1982-96. Epidemiol Infect 2000;125:333–45. [PubMed: 11117957]
4. Sanders M GF, Forchheimer LL, Alexander RC. Epidemic Keratoconjunctivitis. Am J Public Health Nations Health 1943;33:75–6. [PubMed: 18015730]
5. Høvding G Acute Bacterial Conjunctivitis. Acta Ophthalmol 2008;86:5–17.
6. Kaur G, Seitzman GD, Lietman TM, et al. Keeping an Eye on Pink Eye: A Global Conjunctivitis Outbreak Expert Survey. Int Health 2022;14:542–4. [PubMed: 34409991]
7. Johnson SD, Harthan JS, Than T, et al. Predictive Accuracy and Densitometric Analysis of Point-of-Care Immunoassay for Adenoviral Conjunctivitis. Transl Vis Sci Technol 2021;10:30.
8. Kuo IC. Adenoviral Keratoconjunctivitis: Diagnosis, Management, and Prevention. Current Ophthalmology Reports 2019;7:118–27.
9. Udeh BL, Schneider JE, Ohsfeldt RL. Cost Effectiveness of a Point-of-Care Test for Adenoviral Conjunctivitis. Am J Med Sci 2008;336:254–64. [PubMed: 18794621]
10. Asbell PA, Sanfilippo CM, Sahm DF, DeCory HH. Trends in Antibiotic Resistance among Ocular Microorganisms in the United States from 2009 to 2018. JAMA Ophthalmol 2020;138:439–50. [PubMed: 32271355]
11. Doan T, Sahoo MK, Ruder K, et al. Comprehensive Pathogen Detection for Ocular Infections. J Clin Virol 2021;136:104759. [PubMed: 33609933]
12. Garcia-Zalisnak D, Rapuano C, Sheppard JD, Davis AR. Adenovirus Ocular Infections: Prevalence, Pathology, Pitfalls, and Practical Pointers. Eye Contact Lens 2018;44(Suppl. 1):S1–s7.
13. Lee CS, Lee AY, Akileswaran L, et al. Determinants of Outcomes of Adenoviral Keratoconjunctivitis. Ophthalmology 2018;125:1344–53. [PubMed: 29602567]
14. Vassilara F, Spyridaki A, Pothitos G, et al. A Rare Case of Human Coronavirus 229e Associated with Acute Respiratory Distress Syndrome in a Healthy Adult. Case Rep Infect Dis 2018;2018:6796839. [PubMed: 29850307]
15. AlBalawi HB. COVID-19: Precautionary Guidelines for Ophthalmologists. Cureus 2020;12:e8815. [PubMed: 32607305]
16. Alter SJ, Sanfilippo CM, Asbell PA, DeCory HH. Antibiotic Resistance among Pediatric-Sourced Ocular Pathogens: 8-Year Findings from the Antibiotic Resistance Monitoring in Ocular Microorganisms (Armor) Surveillance Study. Pediatr Infect Dis J 2019;38:138–45. [PubMed: 30281547]
17. Slack MP. A Review of the Role of Haemophilus Influenzae in Community-Acquired Pneumonia. Pneumonia (Nathan) 2015;6:26–43. [PubMed: 31641576]

18. Centers for Disease Control and Prevention (CDC). Sexual and Reproductive Health: Chlamydia. Available at https://www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/sexually-transmitted-diseases/chlamydia.html. Accessed: July 24, 2022.

19. Lalitha P, Seitzman GD, Kotecha R, et al. Unbiased Pathogen Detection and Host Gene Profiling for Conjunctivitis. Ophthalmology 2019;126:1090–4. [PubMed: 30953744]

20. Prajna NV, Lalitha P, Teja GV, et al. Outpatient Human Coronavirus Associated Conjunctivitis in India. J Clin Virol 2022;157:105300. [PubMed: 36209621]

21. Lalitha P, Prajna NV, Sikha M, et al. Evaluation of Metagenomic Deep Sequencing as a Diagnostic Test for Infectious Keratitis. Ophthalmology 2021;128:473–5. [PubMed: 32682834]

22. Thompson PP, Kowalski RP. A 13-Year Retrospective Review of Polymerase Chain Reaction Testing for Infectious Agents from Ocular Samples. Ophthalmology 2011;118:1449–53. [PubMed: 21367461]

23. Ramirez DA, Porco TC, Lietman TM, Keenan JD. Epidemiology of Conjunctivitis in Us Emergency Departments. JAMA Ophthalmol 2017;135:1119–21. [PubMed: 28910427]

24. Morettin CE, Harthan JS, Huecker JB, et al. Correlation of Adenoviral Titers with Severity of Adenoviral Conjunctivitis and Time to Viral Clearance over 21 Days. Optom Vis Sci 2023:epub February 7, 2023:doi 10.1097/OPX.0000000000001999.

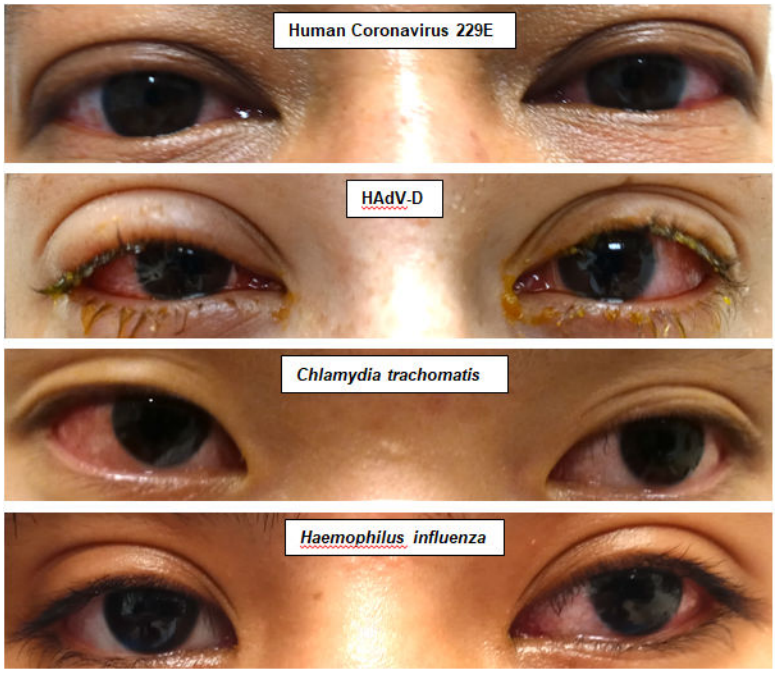

Figure 1.

Clinical presentation of four representative study subjects. Clinical presentation of four representative study subjects. Variable conjunctival injection and eyelid edema in 2 representative study subjects with viral conjunctivitis (top images) and 2 with bacterial conjunctivitis (bottom images).

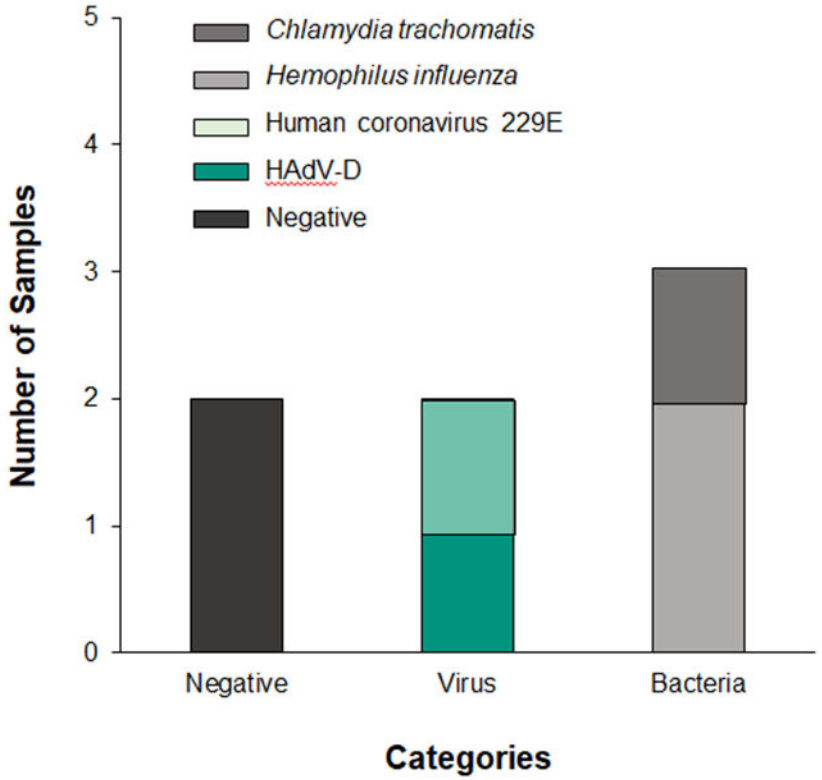

Figure 2.

Associated Pathogens Identified. Graph showing the category and frequency of pathogens found in swabs taken from subjects presenting with acute conjunctivitis. “Negative” indicates that no virus or bacteria were found in the samples.

Table 1:

Demographics, systemic symptoms, medication use, ocular symptoms and identified associated pathogens.

Case #	Age	Gender	Eye affected	Sore throat	Runny nose	Coughing	Vomiting	Diarrhea	Topical drops	Days of Symptoms	Itching	Tearing	Purulent discharge	Pathogen Identified
1	20	Female	Both	No	No	No	No	No	Moxifloxacin	7	No	Yes	Yes	*HAdV-D*
2	18	Female	Left	Yes	Yes	Yes	No	No	No	2	No	Yes	Yes	*Haemophilus influenza*
3	37	Female	Right	No	No	No	No	No	No	7	Unknown	Yes	Yes	*None*
4	21	Female	Both	Yes	Yes	No	No	No	No	3	No	Yes	No	*Haemophilus influenza*
5	38	Male	Both	No	No	No	No	No	Unknown antibiotics from Japan	3	No	Yes	Yes	*Human coronavirus 229E*
6	19	Male	Both	No	No	No	No	No	Artificial tear	13	Yes	No	No	*Chlamydia trachomatis*
7	19	Male	Both	No	No	No	No	No	Polymyxin/ Trimethoprim	3	Yes	Yes	Yes	*None*

HAdV-D = human adenovirus D.