

Outbreak of Conjunctivitis in South Asia: A Landscape of Current Situation and Rapid Review of Literature

Shaikh Saad Amjad^{1,*}, Hamadullah Memon¹, Shahmir Rahman Soomro¹, Mohammad Aadil Qamar^{1,2}, Muhammad Umair Anjum³, Muhammad Hasanain³, Kanza Farhan⁴, Dr. Amjad Ali Shaikh⁵ and Dr. Omar Irfan⁶

¹Ziauddin Medical College, Ziauddin University, Pakistan

²Research Associate, Research X, Pakistan

³Dow Medical College, Dow University of Health Sciences, Pakistan

⁴Jinnah Sindh Medical University, Pakistan

⁵Department of Ophthalmology, Nizwa Hospital, Sultanate of Oman, Pakistan

⁶Department of Medicine, Aga Khan University Hospital, Pakistan

***Corresponding author:** Dr. Shaikh Saad Amjad, MBBS, Institutional address and number: Ziauddin University, 4/B, Saharah-e-Ghalib, Block 6, Clifton Karachi – 75600 Sindh, Pakistan

Received: March 23 2024

Published: August 09, 2024

Abstract

Background: Conjunctivitis is an inflammatory disease of the eye that has been a global issue for many years. In August 2023, there was an outbreak of conjunctivitis not only in Pakistan but also in the neighboring South Asian countries. This article discusses the spread of conjunctivitis, its pathophysiology, symptoms, prevention, management and further highlights the strategies applied by countries worldwide.

Subject and Methods: A rapid review of databases including Google Scholar, PubMed, World Health Organization (WHO), and American Journal of Ophthalmology was conducted on October 3, 2023, using keywords; conjunctivitis, prevention, and transmission.

Results: Conjunctivitis typically presents with redness, tearing, and discomfort in the affected eye, often accompanied by a gritty sensation. Additionally, individuals may experience light sensitivity and a watery discharge. It can manifest as allergic, bacterial, or viral, with the current discussion focused on viral conjunctivitis. Viral conjunctivitis poses a unique challenge and recognizing these signs and symptoms is crucial. Evidence shows that there are no effective antiviral drugs, but there is a definite treatment present for the cure of conjunctivitis. It is endemic in low socioeconomic areas, so the best form of treatment is prevention. The article suggests the verified and approved treatment for the disease and notifies that maintaining hygiene is one of the most important factors in preventing the disease. This includes measures such as frequent hand washing and use of artificial tears, avoidance of frequent eye touching, and sharing of towels.

Conclusion: This article provides extensive information about viral conjunctivitis and recommended measures for its prevention by highlighting the strategies adopted by hospitals in different parts of the World. There is a need for more research regarding the spread and strategies to overcome it in the Asian regions including Pakistan, India, and Bangladesh.

Keywords: Conjunctivitis; Adenovirus; Prevention; Ophthalmology; Pakistan

Introduction

Conjunctivitis or pink eye, is an inflammation of the transparent mucous membrane covering the eye known as the conjunctiva. This ocular ailment primarily owes its origin to a viral source, with Adenovirus emerging as the predominant organism [1]. Its transmission occurs primarily through respiratory droplets, propagated by actions such as sneezing, coughing,

or direct contact [2]. School-going children are particularly vulnerable, owing to their close interactions in educational environments [3]. However, susceptibility to this contagious eye condition extends beyond the classroom. Workplaces, where colleagues often share common spaces and resources, present an elevated risk, as do public swimming pools, bustling gatherings, and professions involving close personal contact, such

as healthcare workers and daycare providers. These scenarios can facilitate the rapid spread of the virus, emphasizing the importance of preventive measures. Key risk factors encompass direct contact with an affected individual or contaminated surfaces, underscoring the significance of frequent hand washing and overall hygiene practices in curbing the transmission of conjunctivitis [2]. While viral conjunctivitis is generally self-limiting, there is a palpable apprehension regarding secondary bacterial infections, a concern amplified in Pakistan due to its elevated air pollution, and densely populated urban areas.

Last year, the largest province of Pakistan, Punjab, alone reported 400,000 cases diagnosed with viral conjunctivitis, with Karachi also experiencing a significant uptick in cases [4]. Such outbreaks raise concerns about public health and demand immediate attention. On 26th September 2023, 13,000 new cases were reported in 24 hours across the province of Punjab. In a report released by the provincial health department in September 2023, an alarming surge of conjunctivitis was observed across various regions of Punjab, Pakistan. Over 1 week, more than 40,000 cases of pink eye were reported, bringing the total number of cases in September to a staggering 86,133 within the province [5]. This situation required immediate attention and a coordinated response to mitigate the outbreak's impact on public health and healthcare resources in the region.

While Pakistan had witnessed a surge in the number of reported cases, similar trends also emerged in Vietnam and India. Multiple cities in Vietnam reported a notable escalation in the daily occurrence of conjunctivitis cases during September 2023 [6]. This worrisome pattern indicated that the issue was not confined to one geographical region but was a concern shared by various countries in the region.

This review is focused on identifying and exploring the underlying factors contributing to the viral conjunctivitis outbreak, raising awareness about its implications, and examining effective strategies to mitigate its impact.

Epidemiology

Given the country's situation, we know that viral keratoconjunctivitis is a highly contagious disease, spreading through direct contact with infected objects and surfaces [7]. A study carried out at the Illinois Eye and Ear Infirmary in Chicago concluded that there is an estimated 10-20% risk of infection spreading through household contacts [7, 8]. Adenovirus type 8 was initially identified as the cause of epidemic keratoconjunctivitis during a significant outbreak among shipyard workers in Hawaii and San Francisco by disease specialist Ernest Jawetz in 1941 [9,10]. In 2017, the Bahamas, Brazil, and the Dominican Republic reported outbreaks of conjunctivitis with 240, 172, and 66,626 cases respectively [11]. A keratoconjunctivitis outbreak was reported in South Korea in 2019 for which a study was conducted that included 218 samples that were suspected of the epidemic keratoconjunctivitis, out of which 128 (58.7%) were positive for the adenovirus genes by the PCR and adenovirus type 8 (HAdV-D8) being the most common of all (67.5%) [12].

Pathogenesis

Adenovirus D (AdV) is a virulent, non-enveloped double-stranded DNA virus, boasting a genome that encodes multitudes of structural and nonstructural proteins [13]. These virus-

es are categorized into serotype groups (A-G) based on various factors like hemagglutination properties, tissue tropism, serology, DNA homology, and host-receptor usage [14-16]. The presence of AdV on the ocular surface prompts ocular epithelial cells to release IL-8, eventually leading to viral internalization and replication [17-19].

Viral conjunctivitis, predominantly attributed to adenovirus infection, is a widespread issue. It can manifest sporadically or even trigger epidemics in various environments, including workplaces, schools, and swimming pools. The highly contagious nature of this ailment is well-documented [20,21]. Furthermore, studies were conducted that confirmed the virus' remarkable capacity to persist on dry surfaces for extended periods. This highlights the virus's ability to survive for weeks in a desiccated state [22,23].

According to a study by Jhanji et al. in 2015, viral shedding can initiate several days before the onset of clinical symptoms, supporting the notion that early viral shedding precedes the appearance of clinical signs and symptoms [2]. The onset of conjunctivitis occurs when a projecting fiber from the penton protein adheres to receptors in the conjunctival epithelium. Once within the cells, the virus multiplies in the nuclei, and these multiplying viral particles form inclusion bodies. These inclusion bodies within the nuclei are composed of the multiplying viruses. The release of viruses occurs when these infected cells eventually die. The immune response of lymphocytes beneath the conjunctival epithelium leads to the formation of follicles on the conjunctiva [9,24]. The primary modes of transmission encompass respiratory or ocular secretions and indirect means, such as contaminated towels [2,25].

Viral conjunctivitis comprises several distinct types, each caused by specific viruses. These include epidemic keratoconjunctivitis (EKC) and pharyngoconjunctival fever (PCF), which are primarily triggered by adenovirus. Acute hemorrhagic conjunctivitis (AHC) is commonly attributed to enterovirus and coxsackievirus, while herpetic conjunctivitis is caused by the herpes simplex virus (HSV). Conjunctivitis can also be a result of varicella-zoster virus (VZV) [26], measles virus [27], and mumps virus [28,29]. However, it's worth noting that the clinical manifestations associated with these viruses differ slightly from those seen in cases of other viral conjunctivitis.

Presentation and Transmission [25]:

- Non-specific acute follicular conjunctivitis is the most prevalent form, caused by various adenoviral serological variants. Ocular symptoms tend to be milder compared to other adenoviral infections, often accompanied by mild systemic symptoms like a sore throat and cold.
 - Pharyngoconjunctival fever, primarily caused by adenovirus serovars 3, 4, and 7, spreads through droplets in families with upper respiratory tract infections. Keratitis develops in approximately 30% of cases but is generally not severe.
 - Epidemic keratoconjunctivitis results from adenovirus serovars 8, 19, and 37 and represents the most severe form. Keratitis is associated with approximately 80% of cases.
 - Chronic/relapsing adenoviral conjunctivitis, characterized by persistent nonspecific follicular or papillary lesions, is a rare condition that can endure for years.
- The incubation period for viral conjunctivitis, primarily attributed to adenovirus infection, typically spans five to ten days

[30]. Clinical data reveals that the primary modes of transmission encompass respiratory or ocular secretions and indirect means, such as contaminated towels [2]. Adenovirus, particularly types 8 and 37, is a common culprit, spreading through contact with contaminated eye examination tools, eye solutions, or objects, as well as person-to-person transmission via eye contact. Inadequately chlorinated swimming pools can also facilitate its spread. This highly contagious nature, combined with its ability to survive on surfaces for extended periods, underscores the importance of understanding and addressing the risk factors associated with Adenovirus transmission.

Epidemic Keratoconjunctivitis (EKC) is a disease with a period of approximately 10 days. The prominent ocular feature in clinical examinations is the presence of acute follicular conjunctivitis [31]. The multiplied virus is transported to the preauricular lymph node through lymphatic channels below the conjunctival epithelium, resulting in lymph node swelling due to the proliferation of antigen-specific lymphocytes [31]. Eye discharge is often watery and accompanied by frequent tearing and conjunctival examinations reveal severe hyperemia [32]. Additionally, there are occasional findings of superficial punctate keratopathy, subconjunctival hemorrhage, pseudo membranes, and symblepharon. In untreated cases, pseudo membranes can become integrated into the host tissue, leading to the formation of scars that might restrict eye movement or cause dry eye symptoms [24]. In nearly 70% of patients, the contralateral eye is affected; however, the severity of infection is notably reduced. After a week, numerous instances of subepithelial infiltration can be observed on the cornea, and conjunctival inflammation may persist for several weeks. Notably, Freyler et al. reported that 47% of patients continued to exhibit signs of stromal keratitis even two years after the onset of infection [33]. Aoki et al. further noted that subepithelial infiltrates were present in 42.6% of early-stage infection cases, therefore, it is crucial to examine subepithelial infiltrates even in cases of mild or moderate follicular conjunctivitis [20, 34]. The surface of the corneal stroma experiences subepithelial infiltrates because of a delayed sensitivity reaction to the adenoviral antigen. While cell infiltration occurs in the cornea, it appears that adenoviral replication is not taking place.

Complications [21]:

- Punctate keratitis
- Bacterial superinfection
- Conjunctival scarring
- Corneal ulceration
- Chronic infection

Specifically related to the Pakistani population, viral conjunctivitis could have physical, emotional, and economic consequences. It may lead to psychological disturbances such as depression, insomnia, etc. There is a chance of suicide case due to unnecessary isolation and fear [35].

Diagnosis

The type of discharge is a significant sign for the diagnosis, viral conjunctivitis may present with a watery discharge, while bacterial conjunctivitis is associated with purulent discharge [7,36]. The investigations recommended for viral conjunctivitis are [7,25,37]:

- Patient's history and slit lamp examination,
- Giemsa staining is a common laboratory technique for eye infections. It differentiates between adenoviral and herpetic infections. However, it cannot reliably distinguish be-

tween the two, so PCR is needed,

- PCR is sensitive and specific for viral DNA,
- Viral culture with isolation is considered the gold standard. Its sensitivity may vary, but it is 100% specific,
- A point-of-care immunochromatography test can swiftly detect adenovirus in tears. A study based on a multi-center clinical trial consisting of 128 patients concluded that the test is 85% sensitive and 98% specific, compared to PCR.

Management and prevention:

To reduce the risk of transmission, it's crucial to practice thorough hand hygiene, avoid eye rubbing, and refrain from sharing towels [11]. Additionally, it's essential to meticulously disinfect instruments and clinical surfaces after examining an infected patient, using disinfectants like sodium hypochlorite which is recommended by the United States Centers for Disease Control and Prevention and tonometer manufacturers. Being a viral infection, there are no antiviral medications available that showed any positive results against HAdVs [8]. In cases of severe membranous or pseudomembranous adenoviral conjunctivitis, topical steroids, such as prednisolone 0.5%, may be required, to be applied four times a day. For symptomatic keratitis, mild topical steroids may be necessary, but they could develop lesions, so they should be used cautiously. If treatment is prolonged, it's essential to monitor intraocular pressure [25]. Additional measures to consider include [8,25,36,38-40]:

- Discontinuing contact lens use
- Using artificial tears four times a day for symptomatic relief, with preservative-free options for added comfort. Single-dose units can reduce the risk of transmission
- Applying cold compresses to alleviate symptoms
- Removing conjunctival membranes
- Considering topical antibiotics if a secondary bacterial infection is suspected

Exploring the effectiveness of 2% Povidone-iodine, a study concluded that its use was found to be effective when used four times a day for a week and led to significant relief from ocular discomfort

Prevention, Management, and recommendations for strategies in Pakistan:

The Outbreak of conjunctivitis in Pakistan spread rapidly across the country, which was quite alarming for the healthcare authorities. As the patient flow increased the hospitals alerted the health ministry which resulted in an immediate issuance of a public advisory. The advisory outlined the necessary precautions and urged people to enhance the use of hand sanitizer, take good care of hygiene, refrain from touching their eyes, and avoid sharing the items that came in contact with the infected individuals [35,41]. The Department of Health proposed the infected individuals use recommended eye drops and clean their eyes with tissues. It was also suggested that applying cold water would be useful to relieve the discomfort [42]. As the outbreak progressed especially among the school children, the Government of Punjab announced school closure from Thursday through Sunday as a precautionary measure [43].

Treatment of conjunctivitis is currently based on addressing the symptoms, primarily involving general measures like cold compressions and the use of artificial tears with antihistamines and mast cell stabilizers. Urging the Government of Pakistan to ensure an abundant supply of these remedies at cheaper prices for easy accessibility. According to the World Health Orga-

nization (WHO), the use of antimicrobial agents should only be conducted in patients with confirmed microbial infections. Furthermore, caution is advised against the use of steroids such as prednisolone due to their potential to boost viral replication [11,35].

Other countries' strategies:

At Johns Hopkins Hospital, a few protocols have been put in place in the ophthalmology department due to recent outbreaks. An isolation room has been added for patient screening and employee testing [8,44]. In 2011, Johns Hopkins implemented a new "red eye" policy to enhance workforce response. The aim was for healthcare workers to quickly diagnose infections and isolate affected employees [8,45,46]. A study conducted at a tertiary hospital in Brazil, where keratoconjunctivitis was prevalent, concluded that routine tests and screening were not being performed initially. However, since the inclusion of PCR testing for swift diagnosis, there has been a noticeable reduction in virus transmission [47]. Apart from the screening and PCR testing protocols, implementation of cleaning and disinfection guidelines has been a significant factor in eliminating adenovirus, a study from Hokkaido University, Japan concluded that the use of 1% potassium peroxymonosulfate in hospital and clinic settings showed positive results of the decline in adenovirus transmission [7,48]. At one of the airports in Bangladesh, passengers who had conjunctivitis were not allowed to travel unless they sought a medical checkup [49].

Recommendations that have been made by the WHO are to prevent further transmission, swift action, and surveillance. The hospitals should alert the Ministry of Health in case of an outbreak. Investigate the source of the infection and its mode of transmission. Patients are advised to promote hand washing and more importantly to take serious measures in eye hygiene, avoid rubbing and touching the eyes, and avoid sharing utensils and towels. Proper swimming pool hygiene must be made mandatory for all public swimming pools and maintaining the preventive protocols in hospital settings [11].

Conclusion

The outbreaks of conjunctivitis are common around the world, WHO has been actively monitoring the situation and therefore has issued the necessary guidelines, prevention is possible and can be achieved by following them. Delaying the treatment may result in visual complications, prompt treatment is necessary to avoid these complications. The treatment discussed in this article has been implemented by ophthalmologists all around the world and has been found to be effective in curing the disease.

Declarations:

Funding: No funding was received for conducting this study.

Conflicts of interest/Competing interests: The authors have no competing interests to declare that are relevant to the content of this article.

Ethics approval: We confirm that this study did not involve human, animal subjects or tissue.

Consent to participate: Not applicable

Consent for publication: Not applicable

Availability of data: Data will be provided by the corresponding author on reasonable request.

Code availability: Not applicable

Acknowledgements: None

Authorship contribution statement: The authors' contribu-

tions are as follows; Shaikh Saad Amjad and Mohammad Aadil Qamar came forth with the concept and designed the study. Literature review was carried out by Shaikh Saad Amjad, Hamadullah Memon and Shahmir Rahman Soomro. Hamadullah Memon worked on the introductory part and stayed up to date about the outbreak, Shahmir Rahman Soomro wrote the pathogenesis and presentation of the disease and Shaikh Saad Amjad gathered information regarding epidemiology, investigations, management and the global strategies. Shaikh Saad Amjad, Hamadullah Memon and Shahmir Rahman Soomro wrote the initial draft. Dr. Amjad Ali Shaikh provided the clinical viewpoint for the article. Dr Omar Irfan supervised and moderated the literature. Mohammad Aadil Qamar, Kanza Farhan, Muhammad Umair Anjum and Muhammad Hasnain moderated and revised the manuscript. All authors approved the final version of the manuscript.

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