

Prevalence and Clinical Features of Ocular Adenoviral Infection among Patients Attended to Ibn-Alhaitham Teaching Eye Hospital in Baghdad, Iraq: A Molecular Study

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Abstract

Background: Viral conjunctivitis is commonly caused by adenoviruses, with a rate of up to 40% of all viral causes.

Objective: To show prevalence and clinical features of ocular adenoviral infection at Ibn-Alhaitham teaching eye hospital in Baghdad, Iraq.

Patients and Method: In this cross-sectional study, eye swab samples were taken from 638 patients with clinically diagnosed infectious conjunctivitis during the period from August 2019 to February 2020. Samples were processed and tested using polymerase chain reaction (PCR) to detect adenoviral infection.

Results: Of 638 patients with infectious conjunctivitis attended to the Ibn Al-Haitham teaching ophthalmic hospital in Baghdad, 113 cases (17.7%) were confirmed to having ocular adenoviral infection with the mean age 27 ± 8.4 years and The highest percentage of those affected in the age group 1-10-year-old (31.9%). Sixty-three were male (55.8%) and 50 were females (44.2%). non-statistically significant difference between unilateral & bilateral involvement. Of total 113 patients with ocular adenoviral infection, 50 (44.2%) patients experienced flu-like illness during or before their ocular complaint, 85 (75.2%), 28 (24.8%) showed conjunctival follicular reaction and conjunctival membrane formation respectively. Only four (3.5%) patients showed no corneal changes during their ocular infection, 39 (34.5%) patients showed mild punctate epithelial keratitis, 54 (47.8%) patients showed significant punctate epithelial keratitis and 16 (14.2 %) patients showed anterior stromal infiltrate. 64 (56.6%) patients developed lymphadenopathy.

During follow up, 13 (11.5%) of patients fully recovered within less than 14 days, 69 (61%) patients recovered in 2-4 weeks whereas 31 (27.4%) patients took longer than 4 weeks for a full recovery.

Conclusion: Results have demonstrated that adenoviruses are common causative agents for infectious conjunctivitis. PCR revealed to be more sensitive and accurate for detecting adenoviral ocular infection

Keywords: Ocular adenoviral infection, Prevalence, clinical features, Baghdad, Iraq.

Introduction

Adenoviral ocular contagion is mainly caused by

different strains of ocular adenovirus⁽¹⁾⁽²⁾. Conjunctivitis due to adenovirus is the world's most common cause of red eye⁽³⁾.

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One of the studies at the Wells Hospital showed that conjunctivitis due to adenovirus constitutes approximately 62% of cases of clinically diagnosed infectious conjunctiva in the emergency room and this is supported by previous studies that confirm that 15

to 70% of conjunctivitis is due to this virus^(1,3). There are approximately 50 adenovirus serotypes, distributed into six groups^(2,4,5). Certain serotypes of adenovirus are associated with certain eye diseases^(1,2). The most public types of viral conjunctivitis are "epidemic-keratoconjunctivitis" (EKC) in addition to "febrile pharyngoconjunctivitis" & non-specific "follicular conjunctivitis"^(1,6). EKC is frequently linked with "adenovirus serotypes" 8, 19 & 37^(2,4,6,7,8). EKC is considered as a more predominant form of "adenoviral-keratoconjunctivitis" owing to the adversarial magnitudes it might have on visual acuity⁽⁸⁾.

The epidemiological capacity of the adenovirus conjunctivitis has contributed to the emergence of many infections with this virus in hospitals and health care site^(9,10,11). The infection may appear in crowded places, such as schools, markets and hospitals^(1,9). The method of transmission of this virus may be through direct contact through eye secretions and the respiratory system, or by indirect means, such as dirty, contaminated tools⁽¹¹⁾. Adenovirus may remain on non-bone surfaces for a month and is ready to cause infection through surfaces such as door handles and other surfaces^(4,9). Many people infected with adenoviruses are without clinical symptoms and this represents a major problem that contributes to the spread of the virus⁽⁹⁾. Ophthalmologists may unintentionally contribute to spreading the adenovirus from infected individuals who do not show clinical signs to uninfected people⁽⁹⁾. There is no appropriate guideline treatment plan for treating viral adenoviral conjunctivitis⁽⁵⁾. The spread of the adenovirus is very fast more than expected.^(9,12)

Patients and Method

This descriptive study was conducted for a period from August 2019 to February 2020 in "Ibn Al-Haitham teaching eye hospital" in Baghdad. 638 patients with a clinical diagnosis of infectious conjunctivitis were randomly selected. Infectious conjunctivitis (conjunctival hyperemia, discharge, pain and burning) was diagnosed by an experienced ophthalmologist. Having filled the written informed consent, specimens had been scraped from "lower-palpebral conjunctiva" using cotton swab & collected by different transport media (2 ml) for PCR (distilled water). The tubes transport media had been storage at 4°C & conveyed on "cold- bag" to laboratory where they had been storage at "-70°C" till used.

Ethical approval had been obtained from Anbar medical college, Ethics Approval Committee Iraq.

Molecular study: The phenol chloroform method was used to purify the DNA from the eye sample and the following forward and reverse primers were used to amplify the gene for adenoviruses.

ADRJC1 "(5-GAC-ATG-ACT-TTC-GAG-G TC-GAT-CCC-ATG-GA-3)"

ADRJC-2 (3-ATG-G AC-GCG-TGG-GGA- AGA-GT C-G GC-C-5)"

"Thermal cycler" had been programmed for 1ST initial cycle of 94°C one min, 55°C for one min & 72°C for 1min (Repeated 40 cycles). The PCR products had been "electrophoresed on a 2% "agarose gel" that contain "Ethidium bromide stain", The PCR product of unaffected eyes scraping had been used as a negative control. The bands had been visualized through ultraviolet Trans illuminator. "PCR product " had been analyzed through comparison with positive control.

Data examination had been done through using of t-test & chi-square in SPSS software (version 24, SPSS Inc., USA).

Results

Out of 638 patients with infectious conjunctivitis, 113 (17.7%) patients were confirmed as having an ocular adenoviral infection. Sixty-three patients were male (55.8%) and 50 patients were females (44.2%) giving a male/female ratio 1:1.1.

The range of age was from 1 year to > = 41 years. The mean age was (27±8.4 years). Most of the patients with ocular adenoviral infection presented in age group 1 – 10 year old (31.9%) followed by 11 – 20-year-old (19.5%), 19.5% were also in > = 41 years old age group, & 16.8% were in 31-40-years old age group, while remaining 12.4% were in the age group 21-30-year-old as shown in Table 1.

The study showed that 50 patients (44.2%) with ocular adenoviral infection experienced flu-like illness before or during their ocular complaint and 63 patients (55.8%) with ocular adenoviral infection didn't have any systemic manifestation (Table 1).

Table 1. Socio-demographic characteristics and flu-like illness appearance of ocular adenoviral infected patients

Character	No.(%)
Age	27±8.4
Gender	
Male	63(55.8%)
Female	50(44.2%)
Age group (Years)	
1-10	36 (31.9)
11-20	22 (19.5)
> = 41	22 (19.5)
31-40	19 (16.8)
21-30	14 (12.4)
Flu-like illness	
Yes	50 (44.2%)
No	63 (55.8%)

Regarding the laterality, the study showed that 56(49.6%) patients with ocular adenoviral infection had unilateral ocular involvement while the other 57 (50.4) patients with ocular adenoviral infection had bilateral

ocular involvement. "Non-statistically significant difference" between unilateral & bilateral ocular adenoviral infection (Table 2).

Regarding the distribution of conjunctival reaction of confirmed ocular adenoviral infection, the study showed that 85 patients (75.2%) had conjunctival follicular reaction, while only 28 (24.8%) patients showed conjunctival membrane formation in addition to conjunctival follicular reaction (Table 2).

Of 113 patients having an ocular adenoviral infection, only four (3.5%) patients showed no corneal changes during their ocular infection, 39 (34.5%) patients showed mild punctate epithelial keratitis, 54 (47.8%) patients showed significant punctate epithelial keratitis and 16 (14.2 %) patients showed anterior stromal infiltrate (Table 2).

Of the total 113 patients with ocular adenoviral infection, 64 (56.6%) patients developed lymphadenopathy (mostly preauricular, less commonly retro auricular and submandibular) during their illness, while 49 (43.4%) patients did not develop any lymphadenopathy (Table 2).

Table 2. Clinical findings of ocular adenoviral infections

Character		No. of patients (%)
Laterality	Unilateral	56 (49.6%)
	Bilateral	57 (50.4%)
Associated keratopathy	None	4 (3.5%)
	Mild punctate epitheliopathy	39 (34.5%)
	Significant punctate Epitheliopathy	54 (47.8%)
	Anterior stromal infiltrate	16 (14.2%)
Conjunctival findings	Follicular reaction	85 (75.2%)
	Conjunctival membrane	28 (24.8%)
Lymphadenopathy	Present	64 (56.6%)
	Absent	49 (43.4%)

There was a statistically significant correlation between the Conjunctival reaction and corneal findings

of ocular adenoviral infected patients (P-Value 0.000) as shown in Table 3, Figure 1.

Table 3. Relationship between Conjunctival reaction and corneal findings in patients with ocular adenoviral infection

Conjunctiva	Keratopathy				Total	P-Value
	No keratopathy	Mild punctate Epitheliopathy	Significant punctate epithelial keratitis	Ant stromal infiltrate		
Follicular reaction	4 (4.7%)	36 (42.4%)	39 (45.9%)	6 (7.1%)	85(100.0%)	0.000
Membrane	0 (0.0%)	3 (10.7%)	15 (53.6%)	10 (35.7%)	28(100.0%)	
Total	4 (3.5%)	39 (34.5%)	54 (47.8%)	16 (14.2%)	113(100.0%)	

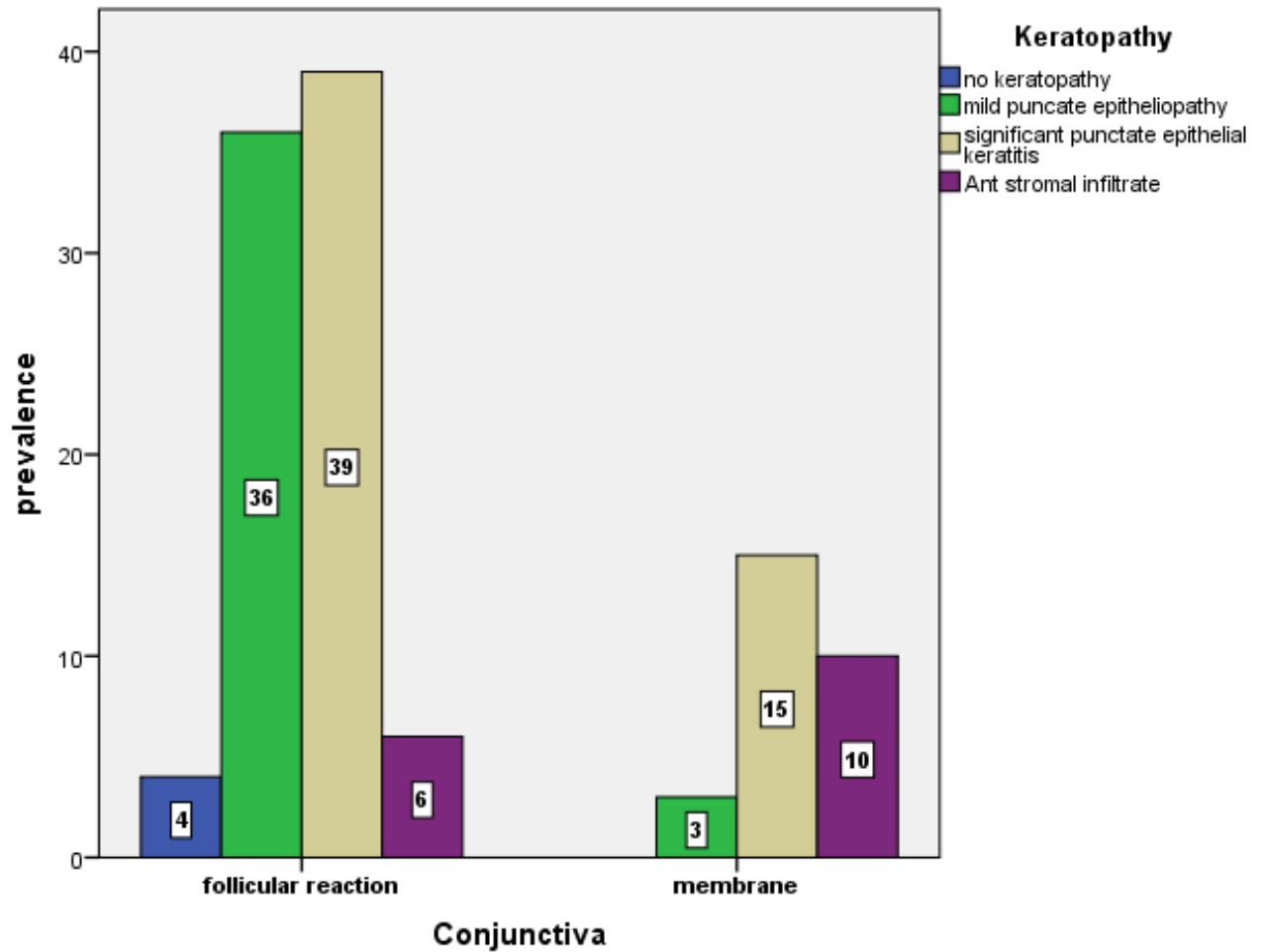


Figure 1. Relationship between Conjunctival reaction and corneal findings in patients with ocular adenoviral infection

There was no statistically significant between the Laterality andKeratopathy of ocular adenoviral infected patients (P-Value 0.742) as shown in figure 2.

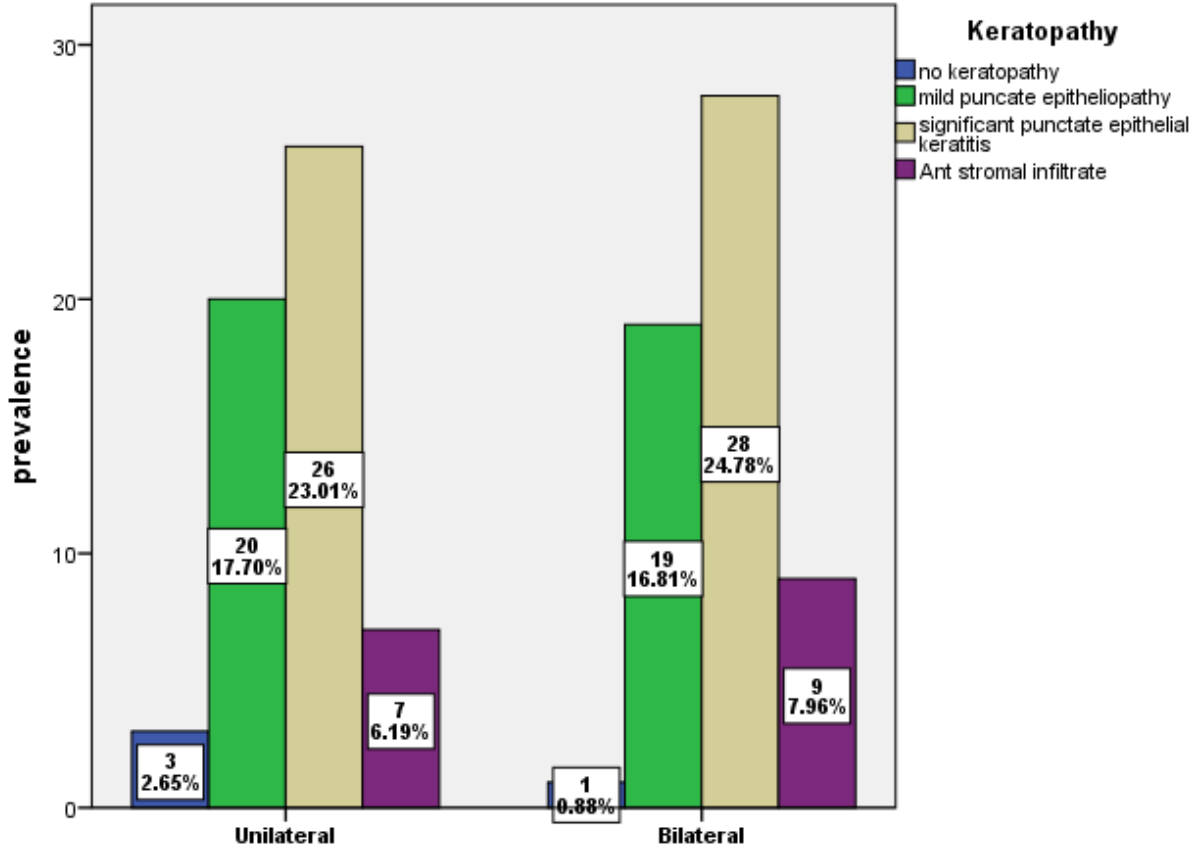


Figure 2. Correlation between Laterality and Keratopathy in patients with ocular adenoviral infection

Regarding the duration for full recovery in ocular adenoviral infection during follow up, the study showed that 13 (11.5%) patients fully recovered in less than 14

days, 69 (61%) patients recovered within 2-4 weeks whereas 31 (27.4%) patients took longer than 4 weeks for a full recovery.

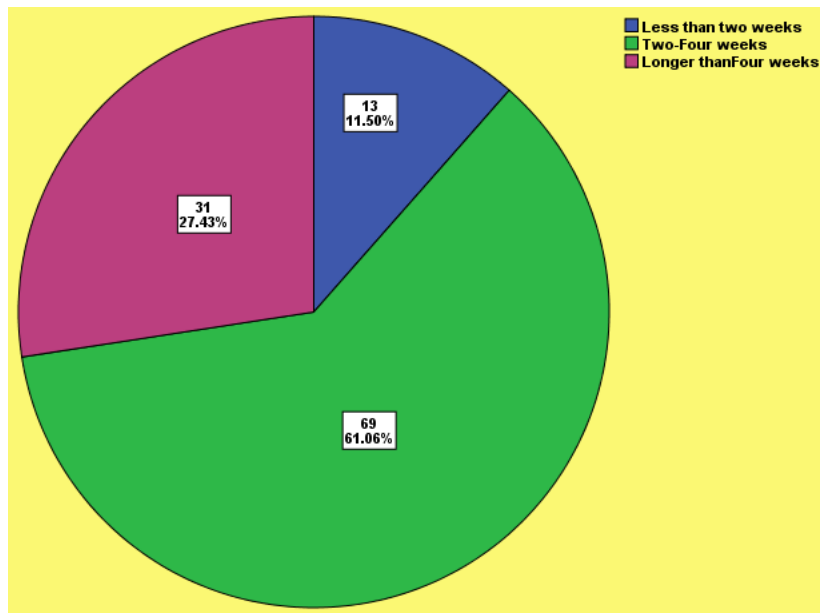


Figure 3. Duration of recovery of patients with ocular adenoviral infection

Discussions

Conjunctivitis is the most prominent eye disease where there are many viruses associated with this disease, the most important of which are (enterovirus 70 (EV70), Coxsackie A24 virus (vCA24), in addition to Denver and the last one of the most common causes of acute conjunctivitis)^(12,13).

The main symptoms of ocular adenoidal surface infection that are linked with a prominent "inflammatory reaction" are red of eye, irritation, tearfulness of the eye, edema, follicular conjunctivitis, edema of the conjunctiva, hyperemia of eye, "epithelial keratitis", & most frequently the appearance of " lympho-adenopathy" ⁽⁶⁾. The adenoviral ocular infection might be fast and clinical symptoms appear only after a week of infection, which represents the incubation period⁽¹⁴⁾. Mostly, the other eye may be affected by the infection within a days later, but to a much lesser degree⁽¹⁵⁾. Communicability time extended from the late incubation-14 days after onset disease ⁽¹⁶⁾.

Studies in Japan have shown that adenovirus constitutes almost 90% of viral conjunctivitis cases. However, conjunctivitis can be due to a virus, which is mostly adenovirus, bacteria, or allergies⁽¹⁷⁾ whereas, However, adenoviral conjunctivitis represents 15-75% of all cases in the world^(17,18). In our study, we found that the prevalence of adenoviral ocular infection is 17.7%. The infection with adenoviruses is not related to a particular season, but it is aware of an infection rate that occurs during the summer as a result of the movement of society due to social activities such as swimming and day camps⁽¹⁹⁾. Another cofactor of infection with these viruses that cause viral adenoviral conjunctivitis in urban areas is poor sanitation, in addition to overpopulation.

The discovery of a polymerase chain reaction (PCR) made it easy to use this test in the analysis of tear samples from the lower body floor in a melodramatic form, in which this test is possible to know the viral pathogen directly instead of virus isolation and this helps to reduce the prevalence of viral conjunctivitis, especially adenoviral conjunctivitis. Viral where ancient studies showed that it was 18- 45%^(20,21) of acute conjunctivitis that had no recognizable etiology. The PCR reaction, which represents the most accurate and sensitive test in diagnosing the causes of conjunctivitis, especially viral ones, has given credence to many studies.

Adenovirus induced eye infection is a self-defined

disease and yet many patients try to get treatment because of symptoms severity ⁽⁷⁾Where treatments of such infections is the use of cold compresses, artificial tears and other comfortable measures⁽⁶⁾. Very often antibiotic ointments, "topical-non-steroidal anti-inflammatory drugs" (NSAIDs) and corticosteroid ointments are used.^(4,6). Supportive therapy is necessary due to the lack of real "anti-adenoviral conjunctivitis" treatments^(5,7,8).

Conclusion:

Adenoviral ocular infection is an important cause of ocular morbidity in Iraq.

PCR is a useful test that help in diagnosis of ocular adenoviral infection, with suitable infection

control depending on speedy and precise diagnosis, we can expect a real reduction in the incidence of outbreaks of community-acquired and nosocomial contagious adenoviral conjunctivitis infections.

Ethical Clearance

The Research Ethical Committee at scientific research by ethical approval of both MOH and MOHSER in Iraq

Conflict of Interest

Non

Funding: Self-funding

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