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Adenovirus Genotype 7 Detection in Adults with Respiratory Infection and Elevated IL-6

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Abstract. Background (General): Human adenoviruses are widespread pathogens responsible for a significant proportion of respiratory tract infections, with genotype 7 (HAdV-7) associated with severe outcomes. Background (Specific): Despite its clinical importance, limited data exist regarding the prevalence and immunological impact of HAdV-7 among adult patients in Iraq. Knowledge Gap: The relationship between HAdV-7 infection and interleukin-6 (IL-6) levels in adults with respiratory illness has not been well characterized. Aim: This study aimed to detect HAdV-7 in adult patients with respiratory infections using RT-PCR and to evaluate its association with IL-6 levels. Results: Among 100 patients and 50 healthy controls, HAdV-7 was detected in 7% of cases, with no significant association with age, sex, or residence. Patients infected with HAdV-7 exhibited significantly elevated IL-6 levels (101.75 ± 25.17 pg/mL) compared with controls (39.26 ± 11.09 pg/mL, $p \leq 0.05$). Novelty: This is one of the first molecular investigations in Iraq to link HAdV-7 infection with heightened IL-6 responses, highlighting the virus's role in driving inflammatory pathways. Implications: Monitoring IL-6 levels may serve as a biomarker for disease severity in HAdV-7 infections and support timely therapeutic interventions to reduce complications.

Highlights:

1. HAdV-7 detection by RT-PCR shows its link with increased IL-6 levels.
2. Molecular methods enhance sensitivity for early diagnosis.
3. IL-6 monitoring can guide prognosis and therapy.

Keywords: ELISA, RT-PCR, HAdV, Respiratory Infection, IL-6

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Introduction

Adenovirus is a double-stranded, linear, without envelope virus that belongs to the Adenoviridae family and the Mastadenovirus species. The HAdV is an icosahedral, 70–90 nm double-stranded DNA virus with a genomic size of about 36 Kb [1]. Based on genome homology, HAdV's more than 100 genotypes are divided into seven species (A–G) [2]. In immunocompetent people, human adenovirus type 7, which is a member of subgenus B1, often causes mild infections that go away on their own, but outbreaks and infections that are severe and even fatal have been documented [3]. Although immunocompetent people are rarely impacted, immunocompromised hosts are vulnerable to severe or widespread AdV infections [4]. Although there is no obvious seasonality to infections, outbreaks usually take place in the spring or throughout the colder months. Infection can result from reactivation, acquisition from outside sources, or contact with infected individuals (aerosolized droplet inhalation or corneal infection) [5], [6], [7].

Understanding how IL-6 functions in viral infections can assist direct treatment plans, which may include measures to alter the immune system in extreme situations [8], [9]. The current research objective was to identify adenovirus genotype 7 among adult's patients with respiratory infection and it is effect to IL-6.

Material and Methods:

The present study enrolled 100 patients with respiratory infection (57 male and 43 female) and 50 healthy group as control. This patients attended to Kirkuk Teaching Hospital /Azadi Teaching Hospital and Gynecology , Peadritic and Women Hospital in Kirkuk state from 12/10/ 2024, until 27/2/ 2025. Each patient completed a short survey. Adenovirus DNA genotype 7 was examined in the plasma of 100 individuals with respiratory infections and 50 healthy group after five milliliters of blood were drawn ,3ml used for plasma separation in EDTA tube. The rest of blood put in gel tube and centrifugation at 5000 rpm for 3 minute for collecting the serum. The serum put in eppendorf tube in -20 °C refrigerated until the time need to detecting IL-6 level by ELISA.

Statistical Analysis: SPSS version 23 was used for the statistical analysis (SPSS, IBM Corporation, Chicago, USA). A correlation test was used, and categorical variables were presented as frequencies and percentages. Quantitative data were displayed with their 95% confidence range and mean ± standard deviation. The means of the variable values were compared using a NOVA, where a P value of less than 0.05 indicates statistical significance

Results and Discussion

The current investigation showed that 7% of patients with respiratory infection have adenovirus genotype 7 with 4% of the control group with non-significant relation ($p>0.05$) (Table 1).
Human adenovirus type 7 (HAdV-7) is known to cause severe respiratory infections in adults. Globally, adenoviruses account for approximately 5–10% of respiratory infections in children and 1–7% in adults. According to surveillance data collected in the United States between 2003 and 2016, HAdV-7 was responsible for 8.5% of the 1,497 HAdV infections that were reported [10]. This with agreement with our result. According to study, HAdV7 has been implicated in outbreaks within military settings. With a 24.8% attack rate, HAdV-

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7 caused three outbreaks of acute respiratory illness in military bases between December 2011 and March 2014 [11]. Ukuli *et al* reported the incidence of HAdV-7 in Uganda was 9.8% between the period of 2008 to 2016 from patients seeking health care at tertiary hospitals for influenza-like illness [12]. In study done in Beijing Chao-Yang Hospital for patients less than 44 years, Zhue *et al* [13] were recognized that HAdV-55 and HAdV-7 being the most predominant (50.6 %and 21.5%) causes respiratory infection that other types of adenovirus.

These results suggest that the prevalence of HAdV-7 may vary by region. Numerous additional factors, such as the type of clinical sample, the ages, occupations, increased virulence of the HAdV genome such as Ad7d, and populations with lower herd immunity to specific HAdV-7 genome, may also have an impact on these variations in HAdV-7 prevalence.

The distribution of adenovirus infection type 7 among adult with respiratory infection patients was not significant based on gender (Table 2). Despite the fact that there was no discernible variation (P>0.05), the rate of male (71.42%) was greater than that of female. (28.58%). Several studies have reported a higher prevalence of adenovirus infections among males than female. In research prepared, Ursin *et al* [14], reported that the rate of adenovirus type 7 infection more in male than female among many respiratory viral infections. In other study done in China, YangXi FY *et al* [15] also found no statistically significant differences according to gender. Rahman *et al* [16], in patients with respiratory infection that caused by adenoviral, could not find any statistically significant correlation between males and females (p value=0.61).

This difference could be due to differences in immune responses between men and women, such as hormone-related immune modulation or genetic factors. Also females often exhibit stronger immune responses to viral infections due to hormonal factors (such as estrogen), which may result in more robust antibody production.

In regard to age, patients within the 18–31 age group had the greatest adenovirus type7 rate (71.42%) (Table 3), the findings were not statistically significant (p>0.05). in study done in Japan, outbreaks of febrile respiratory disease were linked to Ad7 in high school dormitories in the mid-1990s and again in 2003[17]. Zhue *et al*, were identified that HAdV-55 and HAdV-7 being the most prevalent in age grouop ≤44 years old. These above studies with agreement with our study.

These age-group differences could be caused by the patients' immune conditions, the genetic variation of HAdV-7, and the probability that most older patients will have a lower immune response.

The research revealed that 56.50% among patients who have contracted adenovirus were from urban, while 43.50% came from the rural (Figure 1). Numerous research shed light on its epidemiology and genetic variability, despite the lack of precise data comparing its frequency in rural and urban populations. HAdV-7 infections in children were reported in a study carried out in New South Wales, Australia, underscoring the virus's influence in that area [18]. Rotavirus and adenovirus infections among children with gastroenteritis were investigated in Sulaimani Area, Iraq. According to the results, two adenovirus infection instances out of the 27 children with these viral infections came from urban areas, while one case came from a rural one. However, the study found no significant association between the type of viral infection and geographic place (p = 0.5832) [19]. These studies suggest that while there may be slight differences in adenovirus infection rates between rural and urban areas in Iraq, the variations are not statistically significant. Therefore, geographical location does not appear to be a determining factor in the prevalence of adenovirus infections in these regions.

These discrepancies in the results could be caused by inadequate health care and the

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population densities in cities and rural regions. Economic considerations may also contribute to the high rate of urban residents brought on by rural-urban migration, which would cause these cities to become more crowded and congested.

According to the effect of adenovirus type 7 to the IL-6 level, the study revealed that the mean IL-6 level in adult with respiratory infection infected by HAdV-7 was 101.75 ±25.17, compared to the mean level in healthy group was 39.26± 11.09. (Table 4). Statistical analysis revealed significant differences (P≤0.05) between the groups. Compared to other adenovirus types, research suggests that HAdV-7 infection can result in more severe clinical effects and greater viral replication rates. An intensified cytokine response, including elevated synthesis of IL-6, tumor necrosis factor-alpha (TNF-α), and other pro-inflammatory cytokines, is associated with this enhanced severity. The activation of particular signaling pathways is the mechanism underlying the production of IL-6 after HAdV-7 infection. According to research, the virus can activate the p38/NF-κB signaling pathway, which raises the expression of IL-6 [20]. IL-6 has important research significance in the development and prognosis assessment of respiratory diseases. Chen *et al* revealed that increasing of IL-6 levels in patients with respiratory infection in infected lung tissue caused by human adenovirus type 7. Arachova *et al*, noted increased level of many cytokines and chemokines including IL-6 in response to adenovirus infection.

Increasing level of IL-6 in our study may be due to severe respiratory infection by the adenovirus type 7 which triggers a strong immune response leading to increased IL-6 production, activates macrophages, dendritic cells, and epithelial cells, which release IL-6, or due to adenovirus type 7 which target the lung tissue and damaged it which stimulate IL-6 releasing.

Table 1. The rate of adenovirus genotype 7 among adult patients with respiratory infection.

Adenovirus type 7	The study groups			
	Patients with Respiratory Infection		Control group	
	No.	%	No.	%
Total positive	7	7	2	4
Negative	93	93	48	96
Total	100	100	50	100
X^2, P.Value	0.5319, 0.46 Non significant			

Table 2. Distribution of adenovirus genotype 7 among patients with respiratory infection according to sex.

Sex	The study groups			
	Patients with Respiratory Infection		Adenovirus type7 positive	
	No.	%	No.	%
Male	57	57	5	71.42
Female	43	43	2	28.58
Total	100	100	7	100
X^2, P.Value	0.55, >0.05			

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Table 3. Human adenovirus type 7 infection distribution among adult patients with respiratory infection according to age.

Age groups (Years)	The study groups			
	Patients with Respiratory Infection		Adenovirus type7 positive	
	No.	%	No.	%
18-31	48	48	5	71.42
32-72	52	52	2	28.58
Total	100	100	7	100
X^2, P.Value	1.43, >0.05			

Table 4. The mean level of IL-6 of positive patients with human adenovirus type 7 among respiratory infection adult patients compared with healthy group.

Study group	IL-6 level	P value
Adenovirus type 7 positive	101.75 ±25.17	P≤0.05
Control group	39.26± 11.09	

Conclusion

Molecular detection of HAdV Type 7 has advanced our ability to identify and monitor outbreaks of the virus. Real Time PCR has improved the sensitivity and specificity of HAdV-7 detection, enabling early diagnosis and preventing outbreak. The virus also increasing inflammatory response including elevated IL-6 levels which has role in lung inflammation and disease progression. Monitoring IL-6 levels could serve as a useful biomarker for disease severity and guide therapeutic strategies.

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