

Risk Factors for Severe Adenovirus-Associated Chest Infections in Hospitalized Children in Wasit Province

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Abstract

Background: Human adenovirus (HAdV) infections are a major cause of respiratory illnesses in children, contributing to significant morbidity and mortality worldwide. These infections primarily affect mucosal surfaces, including the respiratory tract, and can range from mild upper respiratory symptoms to severe lower respiratory tract infections, particularly in young children. Severe adenoviral infections may lead to multisystem complications, making early detection and intervention crucial. However, current diagnostic methods pose challenges for early clinical differentiation. Identifying risk factors associated with severe adenoviral chest infections is essential for improving early diagnosis and guiding appropriate treatment strategies. **Objective:** This study aimed to evaluate the clinical characteristics and risk factors associated with severe adenovirus-related chest infections in hospitalized children under five years old in Wasit Governorate, Iraq. **Methods:** A case-control study was conducted from December 2023 to February 2024, involving 100 pediatric patients diagnosed with chest infections and admitted to Al-Zahraa Teaching Hospital, Al-Karama Teaching Hospital, and Al-Kut Hospital for Maternity and Children. A control group of 50 apparently healthy children was also included. Clinical characteristics, laboratory findings, and potential risk factors—including family history of atopy, family smoking, infection type, chronic disease, and premature birth—were assessed using statistical analysis. **Results:** Among the 100 hospitalized children with chest infections, 49 (26 males [53.1%] and 23 females [46.9%]) tested positive for adenovirus. The patients' ages ranged from 1 to 5 years. Statistical analysis identified significant risk factors associated with severe adenoviral infections, including family history of atopy ($p = 0.001$), type of infection ($p = 0.001$), chronic disease ($p = 0.001$), family smoking ($p = 0.003$), and premature birth ($p = 0.021$). The frequency distribution of these factors significantly differed between the adenovirus-infected patients and the healthy control group. **Conclusion:** This study highlights several clinical and social risk factors contributing to the severity of adenovirus-associated chest infections in hospitalized children. The findings emphasize the need for early detection, targeted preventive measures, and improved clinical management strategies to reduce the burden of adenoviral respiratory infections in pediatric patients. Timely identification of high-risk children and consideration of current adenovirus preventive treatments are essential for improving patient outcomes.

Keywords: Adenovirus Children Risk factor, Severity

Introduction

Human Adenoviruses (HAdV) are non-enveloped viruses with a double stranded DNA structure. They have a diameter of 70-100 nm with a distinctive icosahedral capsid [1]. Their name was coined from the term "adenoid" after being first identified in surgical human adenoid tissues in 1950 [2]. that commonly result in infections affecting the upper or lower respiratory tract, gastrointestinal (GI) tract, or conjunctiva. Adenovirus infections are more prevalent in young children, particularly in infants aged 6 months to 2 years, due to their underdeveloped humoral immunity [3]. Presently, there are around 110 genotypes of human adenovirus (HAdV) that have been identified. These genotypes are categorized into seven species (A–G) within the Mastadenovirus genus based on their morphological, chemical, and biological characteristics [4]. HAdV can be transmitted directly or indirectly through the throat, faeces, eyes, or urine, depending on the specific type of virus. Specific illnesses are primarily linked to certain forms of HAdV. For example, HAdV B,C,E is mainly connected with acute respiratory outbreaks, HAdV D is linked to epidemic keratoconjunctivitis, and HAdV F,G is related to diarrhoea and/or acute hemorrhagic cystitis [5, 6]. Adenovirus is a significant pathogen that causes upper and lower respiratory infections, particularly in children. Adenovirus is responsible for viral respiratory tract infections in around 4% to 10% of children [7]. Adenovirus infection is more common in children younger than 5 years old, and it is mostly a disease that resolves on its own. Nevertheless, a minority of children get severe viral respiratory infections, leading to acute

respiratory collapse and potentially fatal outcomes [8]. In addition, some viral respiratory infections can lead to serious complications, including bronchiolitis, obliterans, and bronchiectasis. This pathogen is commonly seen in children who have acute low respiratory tract infection (ALRTI) and is responsible for around 4–10% of all instances of young children pneumonia [9]. Adenovirus infection can result in severe pneumonia and other disseminated diseases in certain people. These complications can rapidly lead to recurrent respiratory failure, acute respiratory distress syndrome (ARDS) (10)(8), and multiple organ dysfunction syndrome (MODS). If patients do not receive prompt treatment, the fatality rate exceeds 50% [10].

Respiratory infections caused by adenovirus can result in significant rates of hospitalization and mortality among children [11]. Some serotypes have shown the ability to induce serious diseases [12]. HAdV can lead to serious respiratory infections in children and those with weakened immune systems, however there is limited knowledge on severe HAdV pneumonia in adults with a healthy immune systemized patients, but less is known about severe HAdV pneumonia in immunocompetent adults [13]. The immune systems of children of different ages cannot be treated the same, resulting in varying reactions to infections. Individuals with a compromised immune system may experience prolonged viremia [14]. Nevertheless, an excessive immune response can be detrimental to the organism since it may result in an "inflammatory storm" and then lead to more

multiorgan failure. Research has indicated that toddlers from 6 to 23 months are at a higher risk of developing severe pneumonia [15]

Risk Factors Effect of Severe Infection

Risk factors for severe adenovirus respiratory infection were identified as being under the age of 7, having a history of chronic disease [12], Multiple studies have identified numerous possible risk factors associated with the development of severe pneumonia caused by adenovirus [16]. Low birth weight and prematurity are notable risk factors for hospitalization, as are congenital and several cardiopulmonary disorders. Chronic pulmonary illness and neurodevelopmental issues. Type of infection (primary or secondary admitted). The admission to the hospital for acute respiratory infection (ARI) caused by a virus was found to be linked to an increased risk of readmission for ARI in young infant who were under 6 months old at their first admission [17]. Environmental factors that lead to a heightened vulnerability include exposure to side-stream tobacco smoke and a deficiency in breastfeeding [18]. Nevertheless, there remains a discussion over the risk factors associated with severe adenovirus respiratory infection in children. Therefore, we carried out a comprehensive review study to more accurately assess the epidemiology and risk factors associated with severe adenovirus respiratory infection in children who were admitted to hospitals in Wasit Province.

PATIENTS AND Method

The present study included a study group of 100 patients who were admitted with viral respiratory infection (VRI), 51 (51.0%) were male and 49 (49.0%) were female, and a control group of 50 individuals who were apparently healthy, Results included 49 Patients have adenovirus infection, their ages ranged from 1 to 5 years. A case-control study was conducted in the province of Wasit. The

research was carried out in Al-Zahraa Teaching Hospital, Al-Karama Teaching Hospital, and Al-Kut Hospital for maternity and children between December 2023 and February 2024. Out of the total participants, the tables (1-1) display the demographic characteristics of both the control and study groups throat swab samples were collected from 100 patients, and 50 from a control group. Data was collected through the utilization of a prearranged questionnaire, which was used to conduct interviews with Study samples families. Also the gathered information included: Age, Sex, Living area, Primary or Secondary infection, Chronic diseases, history Smoking of family, type of breast feeding, prematurity, Family history of atopy. The identification of adenovirus was detected using conventional PCR technology. the aim of study effect of risk factors (type of infection, environmental factor, chronic disease, Family history of atopy and prematurity) on severity adenovirus respiratory infection. Ethical approval for this study was obtained from the College of Medicine at the University of Al-Qadisiya. Statistical Analysis This study used a chi-square test to perform statistical analysis and assess the relationship between categorical variables. Pearson's product-moment correlation coefficient was calculated to assess the correlation between two continuous variables. A P value of ≤ 0.05 was considered statistically significant. Results and discussion.

Results and Discussion

In the current study, the presence of family history of atopy is an important contributory risk factor in viral respiratory infection. This study showed 29(59.2%) of patients with Adenovirus have positive family history of atopy and all healthy control 50 (100.0%) don't have positive family history, and there was significant difference in the frequency distribution of both group according to family history of atopy, ($P = 0.001$).

Table 1:

Characteristic	Adenovirus Patients n = 49	Control n = 50	P
	Family history of atopy		
Positive, n (%)	29 (59.2%)	0	0.001
Negative, n (%)	20 (40.8%)	50 (100.0%)	¥ S
	Family smoking		
Positive, n (%)	34 (69.4%)	20 (40.0%)	0.003
Negative, n (%)	15 (30.6%)	30 (60.0%)	¥ S
	Type of infection		
Primary infection, n (%)	17 (34.7%)	0	0.001
Secondary infection, n (%)	32 (65.3%)	50 (100.0%)	¥ S
	Chronic disease		
Positive, n (%)	16 (32.7%)	0	0.001
Negative, n (%)	33(67.3%)	50 (100.0%)	¥ S
	Premature		
Positive, n (%)	5 (32.7%)	0	0.021
Negative, n (%)	44 (67.3%)	50 (100.0%)	¥ S

A familial predisposition towards atopy may act as an indicator for a more severe development of the disease. The topic of whether familial atopy contributes to a higher risk of experiencing more frequent viral infections and more severe disease, or if it leads to immunoallergic pathways that lead to the development of bronchial asthma [19]. The present result similar the result of Simões et al., [20] who discovered

When examining patients with clinical bronchiolitis, the frequency of atopic burden was significantly higher among those who were admitted to the hospital compared to those who were not. Thus, it can be determined that having an atopic burden not only raises the likelihood of developing bronchiolitis, as evidenced by the significantly higher incidence of bronchiolitis in patients with an atopic burden

compared to those without, but it also results in a more severe progression of the disease in patients with bronchiolitis, as indicated by a higher rate of hospitalization [21]. Regarding family history of smoking in current study showed significant differences between patients with Adenovirus and healthy control according to family history of smoking, this study showed 34 of patients with Adenovirus have positive family history of smoking compared to 20 person of healthy control ($P=0.003$). this result agreement with García et al., [21] found the severity of respiratory adenovirus infections can be affected by a family history of smoking. Exposure to passive smoking has a considerable effect on the probability of newborns developing lower respiratory diseases, specifically bronchiolitis. This risk is particularly evident in relation to postpartum smoking by mothers [22]. Multiple writers have conducted comprehensive investigations and rigorous examinations in recent years to study the impact of passive smoking on children's health and immune systems. Children are disproportionately impacted by passive smoking compared to adults due to the underdevelopment of their immune and respiratory systems [23]. Type of infection (primary or secondary admitted) another risk factors effected on severity of chest infection, the present result of study show significant differences between patients with Adenovirus and healthy control according to type of infection $p=0.001$, Respiratory viruses are the primary cause of acute respiratory infection (ARI) in young children. However, the extent of their impact on future ARI admissions remains incompletely understood. Hospitalization due to viral acute respiratory infection (ARI) was observed to be associated with a higher likelihood of subsequent readmission for ARI among infants younger than 6 months old at their first hospitalization (17). The influence of viral-related acute respiratory infection (ARI) hospitalizations on ARI readmission rates differed according on the specific virus. The impact of human metapneumovirus (hMPV) was the most significant, followed by human adenovirus (HAdV) and human rhinovirus (HRV) [24]. This result similar to the current result. Chronic disease that considered one of risk factors on the severity of a viral infection [25]. The present results appeared 16 patients have chronic disease included pulmonary disease and congenital heart disease, the present result significant differences between patients with Adenovirus and healthy control ($p=0.001$). this result agreement [26] during his research, he discovered Respiratory tract infection is a common event that is often seen in children who have congenital heart disease (CHD), especially in their early years. Nevertheless, in healthy children, the mortality rate associated with respiratory tract infections in persons who had undergone heart surgery was 5.8%.

A significant number of patients presenting signs of respiratory tract infection were released from the emergency room without being hospitalized to the hospital. Therefore, this study only included patients who were significantly affected. However, these findings illustrate the essential interaction between the cardiac and pulmonary systems. Children with chronic respiratory diseases, such as chronic obstructive pulmonary disease (COPD), asthma, cystic fibrosis (CF), and interstitial lung diseases (ILD), are more susceptible to get respiratory infections. Some viral infections may exacerbate the progression of these diseases [27]. A study discovered by Flight et.al [28] that respiratory viruses increase the risk of pulmonary

exacerbation by two-fold. Additionally, it was revealed that the occurrence of pulmonary recurrence is associated with a higher rate of deterioration in forced expiratory volume in 1 second.

Prematurity is considered one of the risk factors affecting viral respiratory infections, Preterm newborns have an increased susceptibility to respiratory viral infections, including adenovirus, which can result in substantial illness and death [29]. Prematurity is associated with weak respiratory pathways, an underdeveloped and susceptible immune system, insufficient transfer of maternal antibodies, and a lack of cellular immunity required for effective viral clearance. At 30 weeks gestational age (GA), the lung development shows that lung volumes are approximately three times lower and surface area is nearly four times smaller compared to term newborns. Additionally, the air gap walls have an increased thickness that is one third of that of term infants [30]. The present result appear significant difference in the frequency distribution of both group according to prematurity ($p=0.021$) where showed 5 (32.7%) patient with Adenovirus have positive to prematurity and all healthy control 50 (100.0%) don't have positive to [31].

In this study found Adenovirus infections are frequently observed in children, with a research indicating an occurrence rate of 0.84 infections per kid year. These infections typically manifest as mild symptoms or may even be asymptomatic and these result similar the currant result of study. Moreover, viral respiratory infections in extremely low birthweight infants, particularly premature infants, can lead to significant levels of illness, as seen by a study indicating that respiratory viruses were present in 40% of cases exhibiting clinical symptoms of neonatal sepsis. Hence, it is vital to comprehend the frequency, clinical significance, and treatment of adenovirus infections in premature infants in order to enhance outcomes and minimize avoidable antibiotic administration [32].

Conclusions

In children, A severe adenoviral infection is associated with severe clinical symptoms and multiple extrapulmonary complications. Clinical management should be strengthened. Risk factors that could increase the severity of the disease must be taken into consideration, including prematurity, chronic disease such as cardiac or lung disease, family history of atopy, chronic diseases, type of infection (primary or secondary admitted), and providing rational treatment. To prevent and control the inflammatory storm caused by adenovirus, improve the recovery rate, and actively improve diagnosis, a large sample Experiments need to be performed to confirm our findings.

Some limitations that we encountered during the current study are the short time to conduct the study, non-compliance of patients during sample collection, and the small number of samples during the sample collection period.

Acknowledgements

The authors express their gratitude to the College of Medicine at Al-Qadisiyah University and the paediatric departments of the hospitals for their contribution in providing the samples. Required facilities for this study

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