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Serological Identification of Anti-adenovirus Antibodies in Children under Five Years with Respiratory Infection in Nasiriyah City,Iraq

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A B S T R A C T

Childhood respiratory tract infections are serious and dangerous clinical forms that occur around the world, and adenoviruses represent one of the most significant viruses that cause these respiratory infections in children. The three species B, C, and E of the adenovirus are mostly responsible for these infections. In addition, rapid identification of adenoviruses is absolutely necessary to prevent overuse of antibiotics in patients, prevent a local epidemic of adenoviruses, and treat severe infections that may cause serious and fatal disease. The current study was designed to detect the prevalence of the adenovirus antibodies in children in Nasiriyah city, Iraq. For this reason, the blood samples were collected from August 2022 to May 2023 from patients less than five years old who were hospitalized at the Muhammad Al-Musawi and Bint Al-Huda hospitals. The samples were obtained from fifty child infected with acute respiratory tract infection. Concerning the children with immunocompromised, underlying illnesses and persistent pulmonary abnormalities, they were prohibited. All individuals were investigated for the detection of Adenovirus-IgM and IgG antibodies using enzyme-linked immunosorbent assay (ELISA). The adenovirus IgM antibodies were found in 9 percent of respiratory patients, and the highest rate was found in males 24 (29.17%), compared to females 2 (7.69%), and the highest rate of IgM antibodies in the age group 1day–12 months was 58.33 percent. These results were statistically significant ($p < 0.05$). Higher rate of adenovirus IgG antibodies was found in 23 (46%) of adenovirus patients, and the highest rate was found in males (66.67%) than that in females (26.92%), and the highest rate of adenovirus IgG antibodies in the age group 37–60 months was (64.0%), while the lowest rate in the age groups 1–12 months was (8.33%). These results were statistically significant ($p < 0.05$).



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Introduction

Adenovirus is a member of the family adenoviridae and the genus Mastadenovirus. It is an uncoated icosahedron with double-strand DNA viruses, which were first discovered by Wallace and other researchers in 1953 while studying the growth of polioviruses in adenoid tissue during research on poliovirus development in adenoid tissue [1]. Adenoviruses are double-stranded structural viruses with an ordered core size of 90 to 100 nm and non-envelope the basic icosahedron shape of the human adenovirus capsid, which is composed of 240 homotrimeric hexon (hexon) proteins, has 20 faces and 30 edges. The 12 vertices of the icosahedron are covalently bonded complexes of homopentameric penton bases (penton), from which homotrimeric fiber proteins (fiber) are projected. Proteins IIIa, VI, VIII, and IX, which are minor viral proteins, interact with the capsid [2]. The main antigenic determinants are present in the viral proteins hexon, penton, and fiber[3]. Hexon is the primary target of neutralizing antibodies, although they also react with other crucial capsid proteins such penton and fiber [4]. Adenoviruses have been classified into seven groups or species according to the letters, which start from HAV-A to HAV-F more than 100 serotypes have been reported. Adenovirus infection spreads rapidly in young children, the elderly, and immunocompromised people because of their weak immunity [5].

Genus and species boundaries are established primarily using phylogenetic criteria, but they can also be based on biological traits and genomic organization [6]. Adenoviruses have been identified in numerous additional host species since they were first identified in human hosts, demonstrating that they are not just present in humans. As a result, the Adenoviridae family was divided into five genera by the International Committee on Taxonomy of Viruses: Atadenovirus, Aviadenovirus, Ichtadenoviruses, Siadenovirus, and Mastadenovirus [7].

Hospitals, daycares, military settings, schools, children 's camps and other health care centers are often breeding grounds for adenovirus outbreaks that cause a wide range of diseases such as diarrhea, gastroenteritis, pharyngoconjunctival fever, respiratory illness, keratoconjunctivitis, and fever. Throughout the stage of incubation, which normally lasts between 4 and 8 days, an individual infected by HAdV is exceedingly contagious depending on which serotype the individual will be infected with [8].The non-enveloped structure of adenovirus allows it to spread in animal-human populations , it remains outside the host for long periods of time. It can cause a local epidemic at any time without obvious seasonality, and infection is often transmitted through aerosolized droplets, tools contaminated by an infected person, touching the conjunctiva of the eye, exposure to infected blood and tissues, and fecal-loral pathogens [9]. Adenovirus infections can occur in people of any age, but they are most prevalent in children, particularly in newborns and young children. Most kids have experienced at least one adenovirus infection episode by the time they turn 10 years old. Numerous adenovirus symptoms can resemble those of the common cold [10]. A clinical assessment of the patient's symptoms is the first step of the procedure that is most frequently used to identify HAdV infection. Sometimes, medical professionals will confirm HAdV diagnosis with chest imaging, nose swabs, and blood or feces cultures. The primary purpose of laboratory diagnostics is to identify and stop major epidemics[5]. The use of amplification of DNA techniques, such as polymerase chain reaction (PCR) has been important to detect this viral infections. Serology is also used to identify HAdVs and their antibodies which result in the immune response. The IgM and IgG are increased when the HAdVs infection occurs. In addition, the immunoassays are the most frequently used serological assays [11].Adenovirus vaccination is not yet accessible to the general public. Despite the fact that adenovirus types 4 and 7 specific vaccination have been authorized for use by U.S. military personnel [12]. The present study was carried out to detect the prevalence of the adenoviruses in children under five years who had adenovirus infections in Nasiriyah city, Iraq's south.

Materials and Methods

Study design

A cross-sectional study was conducted at Muhammad Al-Musawi and Bint Al-Huda Hospital in Nasiriyah, the biggest city of Thi-qar governorate, southern Iraq. For children under five years who suffer from respiratory infections, according to clinical indications, and who have been admitted to the hospital, especially the pediatric emergency unit. The study was approved by the Department of Development and Training of Thi-Qar Health Department. Prior to starting the study, written informed consent was obtained from the children's parent or guardian. A structured questionnaire was conducted to obtain the demographic information of the patients.

Samples Collection

Fifty samples were taken from children from the end of August 2022 to May 2023. Each child was taken by drawing 5 ml of venous blood, placing the samples in test tubes (gel tubes), and leaving the blood to clot in the chamber for 10–20 minutes at room temperature. Then a centrifuge was performed at a speed and time determined by the manufacturer of the kit.

Detection of anti-adenovirus IgM and IgG by using ELISA

Serum samples were used for detection of IgM and IgG antibodies to identify infection presence according to the instructions) supplied by (Elabscience dianostics USA).

The results of the reaction were measured by using microplate reader device (DIALAB , Austria) at 450 nm within 30 min after addition of the stop Solution.

The cut-off results were calculated, which is the average absorbance value of the cut-off control decisions.

Statistical analysis

The data of the present study were analyzed statistically by SPSS statistical software version 26, based in using both Cross-tables Chi-Square, Non-parametric Chi-Square and Odds ratio at p. value < 0.05.

Results

Adenovirus Detection by IgM

The present study recorded among 50 pediatric patients with RTI 9 (18%) infected with Adenovirus, while 41 (82%) of them non-infected. the results noted a significant difference at $P < 0.05$ in prevalence of virus among RTI pediatric patients, as in figure 1:

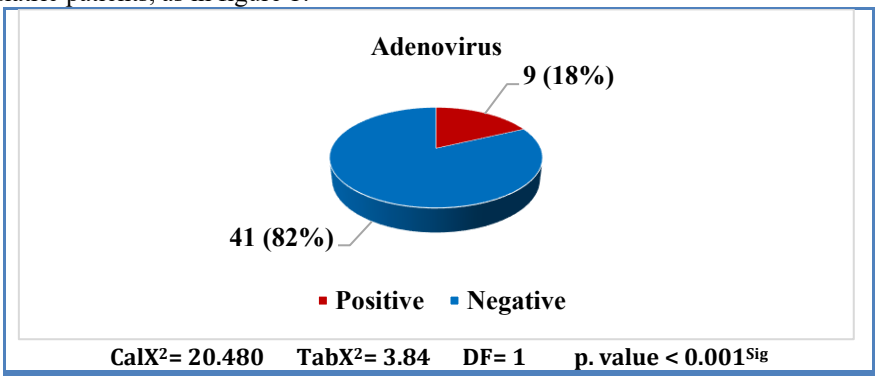


Figure 1. Adenovirus detection by IgM in pediatric with RTI

Also, the present study showed the high pediatric infected with Adenovirus was in first age group (58.33%), followed by the second age group (7.69%) while the lowest pediatric infectedwas third age group (4%). The current study showed the high pediatric infected with Adenovirus was in males (29.17%) but the lowest infected pediatric was females (7.69%). The study documented a significant difference at $P < 0.05$ according to sex and age groups, as in table 1.

Table 1. Serological detection of Adenovirus by IgM in pediatric with RTI according to sex and age.

Sex of Patients	Total No.	IgM Positive		p. value 0.048Sig
		No.	%	
Male	24	7	29.17	
Female	26	2	7.69	
Total	50	9	18.0	
Age Groups				
1 day – 12 months	12	7	58.33	p. value < 0.001Sig
13 -36 months	13	1	7.69	
37 – 60 months	25	1	4.00	
Total	**50**	**9**	**18.00**	

Adenovirus Detection by IgG

The present study recorded that among 50 pediatric patients with RTI 23 (46%) infected with Adenovirus, while 27 (54%) of them were non-infected. The results display of a non-significant difference at $P < 0.05$ in prevalence of virus among RTI pediatric patients, as in figure 2:

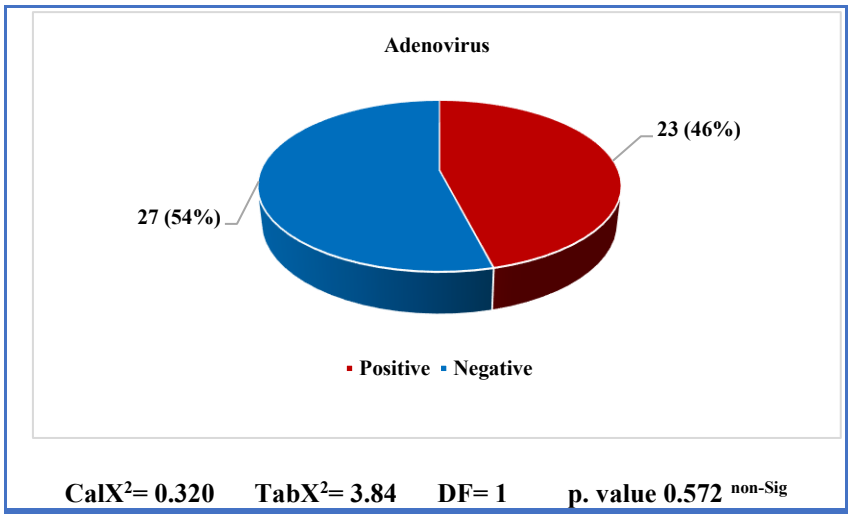


Figure 2. Adenovirus detection by IgG in pediatric with RTI

Also, the present study showed pediatrics in the third age group were infected with adenovirus at (64.0%)followed by the second age group at (46.15%) while the lowest infected pediatric was in first age group at 8.33%.

But the highest percentage of pediatric infected with Adenovirus was in males (66.67%) while the lowest percentage of pediatric infected was females (26.72%). This study also displayed a significant difference at p< 0.05 according to sex and age, as shown in table 2:

Table 2. Serological detection of Adenovirus by IgG in pediatric with RTI according to sex and age group

Sex of Patients	Total No.	IgG Positive		
		No.	%	
Male	24	16	66.67	p. value 0.005Sig
Female	26	7	26.92	
Total	50	23	46.0	
Age Groups				
1 day – 12 months	12	1	8.33	p. value 0.006Sig
13 -36 months	13	6	46.15	
37 – 60 months	25	16	64.0	
Total	50	23	46.0	

Discussion

The current results documented that HAdV IgM detected only 9 (18%) of pediatric patients with RTI. The current results were higher than those reported in the AL- anbar that located with in western of Iraq, that was revealed the presence of 3 of 90 people (3.3%) of the antibody in a study conducted on children to elderly that sufferied from acute respiratory symptoms [13]. While the study of Al-Bashar et al in Tikrit recorded the highest incidence of HAdV-IgM on children less than 10 years old (60 out of 83 patients) representing 72.2% [14]. Another study in Nigeria performed by Idris and kolawole showed the HAdV-IgM reached 91 of 200 sample (45.5%) among children with acute respiratory tract infections [15]. Also acute respiratory tract infections caused by adenoviruses in china reported that HAdV-IgM was detected in 32 of 72 sample (44.4%)[16].In the trials mentioned above, there was no set percentage for the IgM antibody response, however, IgM was thought to be an immediate marker for infection, but there are differences in the stages of infection. Specfically IgM is generated after a certain time of infection and decreases early before symptoms resolve. Also natural IgM is a crucial part of the innate immune system for recognizing microbes and acts as the first barrier to the defense against invasive pathogens before antigen-specific IgG come into play because the antigen-binding areas of natural IgM antibodies are polyreactive and interact poorly with many different antigens [17-18]. Regarding age the first group has a greater share in the number of infections compared to the other age groups. Newborns seem

to be very vulnerable to infectious diseases because of limited prenatal exposure to antigens and a lack of immune memory. Furthermore, pro-inflammatory reactions are reduced in newborns. As a result, newborns heavily rely on their innate immune system to combat illnesses. Age-dependent maturation of the immune responses, both cellular and humoral, occurs both prenatally and postnatally. The neonatal immune system is activated and this maturation process is sped up by prenatal and subsequent exposure to environmental microbes [19]. Another reason to presence IgM in children of the first age group is evidence of immunity development. IgM is the first immunoglobulin that was found in the fetus because it develops immune competence. In the second half of pregnancy, there was a viral infection inside the womb [20]. The present study showed that the high pediatric infected with Adenovirus was in males compared to females.

Current study agreed with study of (Idris and Kolawole.,2022). The infection percentage was recorded in male 64.5% compared with females were 35.5%[15]. Otherwise the present study recorded that highest incidence of HAdV-IgG . A study conducted by Sadah, and Al-Marsome in Iraq, Anbar city, reported the presence of 87 of 90 pediatric patients (96.7%) antibodies in a study of elderly and children with common acute respiratory symptoms[13]. Futhermore a study of Al-Bashar and his colleagues in Tikrit province recorded the highest incidence of Ad-IgG in children less than 10 years old 69 of 317 children (79.2%)[14].

The results of our study disagreed with a study conducted by the researcher of Trojnar and his colleagues in the Children's Clinical Hospital in Warsaw, Poland 16 of 128 patients (12.50%). The percentage recorded in their study of IgG was low than current infection percentage[21]. The present study showed more than half pediatric in the third age group were infected with adenovirus. In infants and small newborns, the immune systems are still developing, making them more vulnerable to illnesses. The trans-placental transfer of pathogen-specific antibodies and other immune mediators from the mother's system to the foetus during pregnancy, then after birth by breast milk-derived immunity, may mitigate this sensitivity throughout infancy. Neonatal immunity heavily depends on the mother concentration of respective particular antibodies throughout pregnancy because this predominantly antibody mediated passive immunity might protect the infant from infections. The protection passes to the child cannot be adequate to ward off sickness if titers are inadequate or diminish quickly after birth. This explains the lack of IgG in the first age group [22]. Also the current study did not agree with the results of Weinberg, whose study results showed that maternal antibodies faded gradually at the age of 5 to 6 months, and that more than 80% of children were infected with adenoviruses at the age of 10 months [23].

But agreed with Al-Bashar, as the result was that there was a fluctuating increase in the percentages of the age groups with age, in addition to that the older age groups were more positive for the IgM may be attributed the reason previous exposure to the virus [14].

The present study showed the high pediatric infected with Adenovirus was in male 66.67%, while the lowest infected pediatric was female 26.92%, in contrast 33.33% of male not infected with virus, compared with female 73.08%.Patients of the cases this result agreed with researcher conducting by [24] , due to the numerous reports of sex variations in the physiology and anatomy of the respiratory tract Additionally, it has been demonstrated that these inherent sex variations affect the pathogenesis, prevalence, morbidity, and mortality of a number of lung diseases over the course of a person's lifetime [25].

Conclusion

In conclusion, Adenovirus is one of the main causes of respiratory infections in children under 5 years old. Young children are highly susceptible to infection with adenovirus, and males have a higher infection rate than females.

Recommendations

This study needs to apply PCR to demonstrate adenoviruses as well as more studies of the immunology and pathology must be done.

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