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## Clinical and epidemiological study of acute lower respiratory tract infections caused by adenovirus in hospitalized children. Nineteen years of active epidemiological surveillance

Acute respiratory tract infections are the main cause of morbidity in the pediatric population. Although the burden of disease is higher in low-resource areas, those with greater resource availability face the challenge of antibiotic resistance in bacterial infections and the identification of new pathogens.<sup>1,2</sup>

In recent years, the identification of respiratory viruses and their role in pneumonia in the pediatric population have increasingly progressed. Molecular techniques used for viral diagnosis help to detect up to 92 % of respiratory viruses in children with pneumonia. Viruses associated with community-acquired pneumonia include human adenovirus (HAdV), human bocavirus (HBoV), human coronavirus (HCoV), enterovirus (EV), influenza virus (Flu), human metapneumovirus (hMPV), parainfluenza virus (PIV), and respiratory syncytial virus (RSV).<sup>3,4</sup>

The case-control study conducted by Rhedin et al., in Stockholm analyzed the association between respiratory viruses and pneumonia in children younger than 5 years and detected viruses in 98/121 children with pneumonia (81 %) and in 134/240 controls (56 %). The univariate analysis showed that the viruses significantly associated with community-acquired pneumonia were hMPV ( $p < 0.001$ ), RSV ( $p < 0.001$ ), Flu ( $p = 0.03$ ), and HAdV ( $p = 0.05$ ), whereas in the multivariate analysis HAdV did not show a significant relation to pneumonia

and was quite common among controls.<sup>3</sup> This may be due to the fact that, although adenovirus causes community-acquired pneumonia, it has been observed that it may remain in the lymphatic tissue in the tonsils for weeks. On the other side, there have also been reports of adenovirus latency in the lungs and reactivation in immunosuppressed hosts.<sup>5</sup>

Nascimento-Carvalho et al., found viruses in 708 children younger than 5 years old with pneumonia (91.5 %; 95 % confidence interval [CI]: 89.3-93.3); of them, 491 (69.4 %; 95 % CI: 65.9-72.7) were identified as having a viral co-infection. Rhinovirus (46.1 %; 95 % CI: 42.6-49.6), adenovirus (38.4 %; 95 % CI: 35.0-41.8), and enterovirus (26.5 %; 95 % CI: 23.5-29.7) were the most common viruses, and the most frequent co-infection corresponded to rhinovirus and adenovirus.<sup>4</sup>

Although adenovirus was the less commonly respiratory virus identified through the entire period in the study of Bakir et al.,<sup>6</sup> published in this issue of *Archivos*, 4.4 % (265/6047) of all positive cases, this may be due to the lower sensitivity and specificity of indirect immunofluorescence (IIF). On the other side, having included children with bronchiolitis may also have contributed to the lower detection ratio. As mentioned in the article, the most common clinical presentation was pneumonia.

The study by Yu Lin et al., reported a higher

frequency of respiratory viruses in the pediatric population by means of reverse transcription polymerase chain reaction (RT-PCR) (75.3 %) than with traditional testing techniques (49.3 %). The main pathogens detected were RSV (23.8 %), rhinovirus (15.2 %), PIV3 (11.2 %), FluA (10.8 %), and HAdV (10.1 %). RSV and rhinovirus were the most frequent pathogens among children younger than 5 years old, whereas FluA and HAdV, among those older than 5 years.<sup>7</sup>

On the other side in Bakir's study,<sup>6</sup> it is worth nothing that among associated factors a high percentage of children with comorbidities was observed, possibly related to the characteristics of the institution. This may also be observed in relation to fatality, given that out of the 20 children who died, 55 % had a comorbidity.

The following were identified as independent predictors of adenovirus infection: male sex, age 12 months or older, rehospitalization, prior hospitalization due to respiratory causes, and clinical presentation of pneumonia; this is relevant information in the case of suspicion of adenovirus.

In addition, considering that one of the predictors was pneumonia as an admission diagnosis, it is important to reinforce the significance of detecting respiratory viruses in lower respiratory tract infections to establish an adequate management and the need for isolation. As mentioned in Bakir's study, molecular biology techniques allow for a greater frequency of respiratory virus identification and the IIF is an appropriate screening technique.

It is important to continue with epidemiological surveillance and data analysis so as to identify any changes that may occur over time with the introduction of the pneumococcal vaccine and an adequate coverage. This way,

an adequate antibiotic use and prevention measures to reduce nosocomial transmission can be facilitated. ■

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<http://dx.doi.org/10.5546/aap.2020.eng.158>

**To cite:** Bruno M. Clinical and epidemiological study of acute lower respiratory tract infections caused by adenovirus in hospitalized children. Nineteen years of active epidemiological surveillance [Commentary]. *Arch Argent Pediatr* 2020;118(3):158-159.

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