

# Human Bocavirus-1 infection: a closer look into its clinical and virological features

Sandra Rajme-López

Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

Human Bocavirus 1 (HBoV1), described in 2005, is being increasingly identified as a cause of respiratory illness in both children and adults.<sup>1</sup> However, lack of animal experimental models limits the current knowledge on the pathogenesis of HBoV1 infections.<sup>2</sup> Therefore, research focussing on its epidemiological, clinical, and virological characteristics is of the utmost importance.

In *The Lancet Regional Health—Americas*, Gamino-Arroyo et al. describe the clinical characteristics, virological features, and seasonality of HBoV-1 infection in children and adults from a prospective observational cohort of influenza-like illness (ILI) in Mexico. In children, the prevalence of HBoV-1 infection was 4.5%, with fever being the most common symptom, significantly associated with a higher viral load. In adults, the prevalence of HBoV-1 infection was 1.8%, with fatigue being the most common symptom, and sore throat was significantly associated with a higher viral load. Using the information from two weather stations, the authors predicted the seasonal frequency of HBoV-1 infections. However, no seasonality was observed. Co-infections with other pathogens were observed in 59% of children and 54% of adults in whom HBoV-1 was detected. Interestingly, the frequency of severe disease was similar between HBoV-1 single infections and HBoV-1 co-infections, both for children and adults. As reported by other authors, severe disease appeared to be more frequent in children.<sup>3</sup>

The prevalence of HBoV-1 infections varies according to age but appears to be higher in very young children.<sup>4</sup> Seroepidemiological data has suggested that by age six, all children might have been exposed to HBoV-1.<sup>5</sup> However, cross reactivity between HBoV-1 and HBoV-2, 3 & 4 antibodies has been demonstrated, challenging the estimates of HBoV-1 disease frequency.<sup>6</sup> Compared to other HBoV-1 epidemiological studies, the observations made by Gamino-Arroyo et al. are nested in a prospective cohort. Thus, their reported prevalences of HBoV-1 infection in children and adults are expected to be more accurate. Interestingly, the frequency of cases needing intensive care was much higher in children than in adults. Protective immunity acquired

through repeated exposures may be related to this observation, but further studies are needed.

The relationship between higher viral loads and the severity of HBoV-1 infection was initially described by Zhao et al. in children.<sup>7</sup> In the study by Gamino-Arroyo et al., this was not replicated. However, there was an association of high viral load with systemic inflammatory response in children, mainly fever. Notably, this was not seen in adults, in whom systemic inflammatory symptoms were overall less frequent. This apparent milder disease in adults may also be related to immunity generated by exposures to the virus during early childhood.

The pathogenic relevance of HBoV-1 has long been questioned for two main reasons. First, the most frequently used diagnostic tools are polymerase chain reaction (PCR)-based techniques, limiting the ability of clinicians to establish causality. Second, HBoV-1 is frequently identified simultaneously with other well-known respiratory pathogenic viruses, making it difficult to identify which symptoms are related to one or the other virus.<sup>8</sup> Moreover, it has been hypothesized that HBoV-1 might have a synergistic or antagonistic role with other viruses, especially rhinovirus and respiratory syncytial virus (RSV).<sup>9</sup> More studies supporting these hypotheses are needed. The findings reported by Gamino-Arroyo et al. support the pathogenic role of HBoV-1. All samples were tested for at least 19 respiratory viral and bacterial pathogens other than HBoV-1. By comparing signs and symptoms between HBoV-1 single infections and HBoV-1 co-infections, its pathogenic role becomes clearer, especially in young infants with critical respiratory illness.

One of the most major lessons learned from the COVID-19 pandemic is the importance of accurate and timely diagnoses. The first step for any diagnostic test relies on clinical suspicion, and studies that generate awareness of new or relatively infrequent diseases help clinicians consider them in their differential diagnoses. The results from Gamino-Arroyo et al. indicate that 1) HBoV-1 is a cause of respiratory disease on its own, 2) adults remain susceptible to severe HBoV-1 infection, 3) a higher viral load is associated with more symptomatic disease in children, and 4) the surveillance of infrequent respiratory pathogens helps understand their clinical characteristics and their relationship with other pathogens. This information is valuable not only to Mexico but to all Latin American region, where HBoV-1 may not be considered an important cause of respiratory disease.



The Lancet Regional Health - Americas  
2024;29: 100672  
Published Online xxx  
<https://doi.org/10.1016/j.lana.2023.100672>

DOI of original article: <https://doi.org/10.1016/j.lana.2023.100672>

E-mail address: [sandra.rajmel@incmnsz.mx](mailto:sandra.rajmel@incmnsz.mx).

© 2023 The Author. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Contributors

Sandra Rajme-López: conceptualisation, investigation, writing.

## Declaration of interests

This manuscript did not receive funding and there are no conflicts of interest to disclose.

## References

- 1 Polo D, Lema A, Gándara E, Romalde JL. Prevalence of human bocavirus infections in Europe. A systematic review and meta-analysis. *Transbound Emerg Dis*. 2022;69(5):2451–2461.
- 2 Mohammadi M. HBoV-1: virus structure, genomic features, life cycle, pathogenesis, epidemiology, diagnosis, and clinical manifestations. *Front Cell Infect Microbiol*. 2023;13:1198127.
- 3 Bagasi AA, Howson-Wells HC, Clark G, et al. Human bocavirus infection and respiratory tract disease identified in a UK patient cohort. *J Clin Virol*. 2020;129:104453.
- 4 Christensen A, Kesti O, Elenius V, et al. Human bocaviruses and paediatric infections. *Lancet Child Adolesc Health*. 2019;3(6):418–426.
- 5 Endo R, Ishiguro N, Kikuta H, et al. Seroepidemiology of human bocavirus in Hokkaido prefecture, Japan. *J Clin Microbiol*. 2007;45(10):3218–3223.
- 6 Kantola K, Hedman L, Arthur J, et al. Seroepidemiology of human bocaviruses 1-4. *J Infect Dis*. 2011;204(9):1403–1412.
- 7 Zhao B, Yu X, Wang C, et al. High human bocavirus viral load is associated with disease severity in children under five years of age. *PLoS One*. 2013;8(4):e62318.
- 8 Calvo C, García-García ML, Pozo F, Carballo D, Martínez-Monteserin E, Casas I. Infections and coinfections by respiratory human bocavirus during eight seasons in hospitalized children. *J Med Virol*. 2016;88(12):2052–2058.
- 9 Lukkarinen H, Söderlund-Venermo M, Vuorinen T, et al. Human bocavirus 1 may suppress rhinovirus-associated immune response in wheezing children. *J Allergy Clin Immunol*. 2014;133(1):256–258.e4.