INTRODUCTION

Human bocavirus (HBoV) is a parvovirus first identified in 2005 in nasopharyngeal aspirates of children with lower respiratory tract infection (Allander et al., 2005). Since then, it has been associated with upper and lower acute respiratory infection (ARI), a leading cause of acute illnesses worldwide and the most important cause of mortality in infants and young children and disability-adjusted life-years lost in developing countries (Simoes et al., 2006; WHO, 2009). To date, four species of HBoV have been proposed, and the name human bocavirus 1 (HBoV1) was suggested for the originally discovered virus. HBoV1 is linked to respiratory disease, while it is believed that HBoV2–4 are associated with gastroenteritis (Kapoor et al., 2010). With a ubiquitous distribution, the presence of HBoV DNA has been reported mostly in children with ARI in a variable range from 1.5 to 19% (Allander, 2008), although recently even higher prevalence (33%) has been observed in ill children (Martin et al., 2010). Although the virus is associated with ARI, the elevated rates of co-infection with other respiratory viruses with well-established pathogenic potential (Kaplan et al., 2006; Allander et al., 2007; Fry et al., 2007; Gerna et al., 2007; Kleines et al., 2007; Christensen et al., 2008, 2010; Cilla et al., 2008; Pilger et al., 2011), the detection in asymptomatic individuals (Christensen et al., 2010) and the possibility of a persistent infection (Martin et al., 2010) make it difficult to allocate a causative role for HBoV in respiratory disease. Not only is the aetiological capacity of HBoV under investigation, but the natural history of the infection is still unknown. In addition, the impact of HBoV on the global epidemiology of ARI is unclear, since most reports predominantly focus on children. A new paper also suggests that HBoV may also be a frequent virus among adults with flu-like symptoms (Guido et al., 2011). The aim of this study was to determine the rate of circulation of HBoV1 in hospitalized children and adults with lower ARI in Córdoba, Argentina, and identify associated epidemiological descriptors.

METHODS

Patients and clinical specimens. The procedures were evaluated and approved by the Ethics Committee of the Hospital Nacional de Clínicas, Universidad Nacional de Córdoba. Seventy-five clinical specimens (nasopharyngeal swabs) from patients aged 0–89 years hospitalized with a diagnosis of bronchiolitis or pneumonia were tested retrospectively. The samples were collected in the hospital room by qualified personnel and sent properly packaged to the Laboratory of Respiratory Viruses at the Institute of Virology (Laboratorio de Virus Respiratorios, Instituto de Virología) within 24 h of collection. The study involved all available samples derived for viral diagnosis of respiratory viruses [respiratory syncytial virus (RSV), parainfluenza (PIV) 1/2/3, influenza A/B (Flu) and adenovirus (AV)] during 2010.
**RESULTS AND DISCUSSION**

The mean age (±SD) of all patients included in the study was 14.1 ± 22.2 years (median 1 year). Of the 75 samples, 56 (75%) were from children younger than 15 years and 65 (86.7%) were collected during fall and winter. The prevalence of HBoV in the study population was 17/75 (22.7%). HBoV was detected in patients in the range 15 days to 64 years of age (Fig. 1), but 11/17 (64.7%) were younger than 12 months and 5/17 (29.4%) were adults older than 30 years. The bimodal age distribution among HBoV+ patients was statistically significant ($P<0.001$). The mean age (±SD) of the 17 HBoV+ patients was 14.5 ± 22.2 months (median 0.58 years). Eight out of 33 (24.4%) infants younger than 6 months, 11/38 (28.9%) infants younger than 1 year, and 5/15 (33.3%) adults older than 30 years were HBoV+ (Fig. 1). The difference in prevalence between infants younger than 1 year and adults older than 30 years was not statistically significant ($P=0.352$). HBoV was detected nearly throughout the year, although most HBoV+ cases occurred during the months corresponding to late fall and winter (Fig. 2). Of 17 HBoV+ cases, 6 (35.3%) were co-infected with another respiratory virus. All co-infections detected were single co-infections. Five out of 6 (83.3%) were HBoV-RSV co-infections (all of them occurred in infants younger than 1 year) and one was an HBoV-Flu B co-infection, which occurred in a 13-year-old child. The difference between the rate of co-infection in all HBoV+ patients (35.3%) and HBoV+ patients younger than 1 year (5 out of 10 patients, 50%) was statistically significant ($P=0.003$). No co-infections were observed among HBoV+ adult patients. HBoV was the second most frequent respiratory virus detected after RSV (20/75, 26.7%), followed by Flu B (6/75, 8%) and PIV 3 (2/75, 2.6%). HBoV was the sole virus detected in 11/75 (14.7%) patients, and the proportion at which it was found in mono-infections was 11/17 (64.7%). The median age among these patients was 1 year (25th percentile 1.5 months; 75th percentile 39.5 years).

This study shows a high prevalence of HBoV (22.7%) in 0–89-year-old patients hospitalized with lower ARI in Córdoba, Argentina, during 2010. The virus was detected across the entire age range studied (Fig. 1). Previous studies detected HBoV mainly in children less than 5 years old and mostly in infants less than 2 years old (Choi et al., 2006; Kaplan et al., 2006; Kesebir et al., 2006; Kleines et al., 2007; Brieu et al., 2008; Canducci et al., 2008; Cilla et al., 2008). However, a recent report (Guido et al., 2011) and the present work confirm that HBoV1 is also a frequent virus in adults with respiratory disease. On the other hand, since initially HBoV1 was detected in patients 5–6 months of age and older (Ma et al., 2006; Allander et al., 2007), and more than 90% of infants younger than 3 months had specific antibodies, some authors proposed that maternal antibodies could prevent neonatal infection by HBoV (Endo et al., 2007). Yet here HBoV was detected among children 0–0.5 years old at a high frequency (24.4%, Fig. 1), indicating a very early incidence of HBoV1 infection. This study and others (Weissbrich et al., 2006; Chow et al., 2008; All-Rousan et al., 2011) detected HBoV1 as early as few days after birth; thus HBoV1 infection during the first month of life may not be infrequent. HBoV+ cases occurred throughout the year but peaked during late fall and winter (Fig. 2), which is consistent with analogous findings by other authors (Allander et al., 2005; Kesebir et al., 2006; Weissbrich et al., 2006; Chow et al., 2008; Cilla et al., 2008; Martin et al., 2010). The higher frequency of detection during the cold months might partially explain the high rate of co-infection with other respiratory viruses that circulate with a similar pattern, in particular RSV. The
present work allows only an estimation of the rate of co-infection with other major respiratory viruses in lower ARI and relative frequency of detection, since we used the results of the diagnosis of RSV, PIV, Flu and AV by immuno-fluorescence assay. Due to the low sensitivity of this technique compared to PCR, the rate of co-infection in our sample is probably higher. In addition, rhinovirus, associated with the development of lower respiratory disease especially in adults (Pierangeli et al., 2011), was not diagnosed in the patients included in this study. However, considering the high frequency of HBoV1 detection in infants younger than 1 year and during the fall–winter period, plus the circulation pattern of RSV (Leung et al., 2005), a high rate of HBoV1-RSV co-infection is most likely. Elevated percentages of RSV-HBoV1 co-infections have been observed by others and RSV is commonly cited as the most frequent respiratory virus in co-infection with HBoV1 (Kaplan et al., 2006; Weissbrich et al., 2006; Gerna et al., 2007; Cilla et al., 2008; Pilger et al., 2011). Interestingly, we did not find co-infections in HBoV1+ samples from adults. Thus, an interaction between HBoV1 and RSV being at least partly responsible for the high rate of co-infections between these two viruses cannot be discarded. Taking into account the low rate of HBoV1 detection among children above 2 years old, and in teenagers and young adults, HBoV1 appears to be a respiratory virus with increased infection rate or pathogenic potential in the extremes of life.

One of the limitations of this and other studies is the lack of a control group (individuals without respiratory symptoms). Thus, several scenarios are still possible for HBoV1 (a mild respiratory agent, a respiratory pathogen with significant impact on health in children and adults, or an agent whose rate of infection and pathogenicity are facilitated by other respiratory agents). Nevertheless, the results presented suggest that HBoV1 is involved in respiratory disease.

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REFERENCES


