**Review article**

# A REVIEW ON HUMAN METAPNEUMOVIRUS AND HUMAN BOCAVIRUS ASSOCIATED WITH ACUTE RESPIRATORY TRACT INFECTIONS



## Abstract

Acute respiratory tract infections (ARTIs) are among the most significant causes of morbidity and mortality among young children in developing countries. Human metapneumovirus (hMPV) and human bocavirus (HBoV) infections are uncommon, especially among rural children. Acute respiratory infections are infectious and can also spread from one person to another, and the disease is quite widespread. It is hazardous for children, older adults, and people with immune system disorders. According to the World Health Organization (WHO), acute respiratory infections are estimated at 2.6 million deaths in children annually worldwide [1]. Based on published literature, only a few studies have identified ARTIs or shown the importance of early diagnosis and treatment of ARTIs. This review article aims to comprehensively describe the aetiology, epidemiology, clinical features, diagnostic methods, and treatment in managing hMPV and HBoV.

**Keywords:** communicable diseases, emerging, human metapneumovirus, human bocavirus, acute respiratory tract infections.

## Introduction

There is a significant prevalence of ARTIs of viral and bacterial origin, such as the common cold, pharyngitis, laryngitis, tracheitis, bronchitis, bronchiolitis, pneumonia, and bronchopneumonia. These ARTIs are associated with high mortality rates and high economic costs [2]. ARTIs are infections of body parts involved in breathing, such as the sinuses, throat, airways or lungs. Viral pathogens are the most common cause of respiratory disease in children. The causative agents include rhinoviruses, respiratory syncytial virus, influenza virus, parainfluenza virus, hMPV, HBoV, measles, mumps, adenovirus, and coronaviruses [3, 4]. HBoV and hMPV are two important viruses for children with ARTIs. HBoV was initially identified in the airway of children with high rates of mixed infection with other viral pathogens. Detecting the virus in the stool has raised questions about the proper role of HBoV as a cause of respiratory diseases [5]. The hMPV has been established as a common cause of upper and lower respiratory tract infections in children, compared second only to the respiratory syncytial virus as a cause of bronchiolitis in infants. These viruses are also important causes of ARTI in the elderly and immunocompromised patients. The hMPV belongs to the Paramyxoviridae family and has a negative-sense single-stranded RNA genome, which includes eight genes coding for nine different proteins [6]. HBoV belongs to the Parvoviridae family and has single-stranded DNA [7]. The hMPV and HBoV are now considered critical viral pathogens that cause undiagnosed LRTI and URTI in children less than five years of age. Diagnostic tools have been developed for the clinician, and effective treatment and prevention strategies are being investigated. This review focuses on epidemiology, pathogenesis, clinical features, and diagnostic techniques for HBoV and hMPV.



**Acute Respiratory Tract Infection**

ARTIs include infections in any area of the respiratory tract, including paranasal sinuses, the middle ear, and the pleural cavity lasting less than 30 days [8]. Respiratory infections can be bacterial or viral in origin, the latter being more common and are mostly limited to the upper respiratory tract. ARTIs can be classified as upper respiratory tract infections (URIs) or lower respiratory tract infections (LRIs) based on the organs affected. Based on the clinical severity, ARTIs can be classified into mild, moderate, and severe types [9]. Children are especially at risk because of their constant contact with other kids who could be virus carriers. Children often do not wash their hands regularly, rub their eyes, and put their fingers in their mouths, resulting in the spread of viruses. People with heart diseases or other lung problems are more likely to contract an acute respiratory infection. Anyone whose immune system might be weakened by another disease is at risk. Smokers are also at high risk and have more trouble recovering from it [10].

URI can be defined as an acute febrile illness with cough, coryza, sore throat, or hoarseness, which are very common in the community and are one of the primary reasons for hospitalization, particularly during the winter and wet season. The frequency of URI can be six to eight episodes per year and even more in children attending daycare centres and schools. Most of these URIs are mild, self-limiting, and not often life-threatening. URI in infants can cause lethargy and poor feeding. It can also lead to clinical conditions like acute otitis media, asthma exacerbations, and LRI, such as bronchitis, bronchiolitis, and pneumonia [11].

LRI is an acute illness (present for 21 days or less), usually with cough as the primary symptom, and secondarily sputum production, dyspnoea, wheezing or chest discomfort/pain with no other complications (e.g., sinusitis or asthma). Tachypnea, fever, cough, hypoxia, bronchitis, bronchiolitis, and pneumonia are the clinical symptoms of LRI. Chest radiograph changes include infiltrated hyperinflation and peribronchial cuffing. LRI, particularly pneumonia, causes the most severe illnesses and deaths in ARTIs. The disease's severity is very high in children under five years of age and the immunocompromised [12].

**Prevalence of ARTIs**

Globally, ARTIs (predominantly pneumonia) have a 20% of mortality among children <5 years old. If neonatal pneumonia is also considered, the mortality increases to 35–40% among under-five children, accounting for 2.04 million deaths/per year. Southeast Asia has the highest incidence of ARI, followed by the sub-Saharan African countries; they contribute to more than 80% of the total global cases [13]. Multiple social and environmental factors affect the morbidity and mortality of ARI in childhood. Factors include poverty, poor nutrition, poor housing conditions, indoor air pollution (including parental smoking), poor ventilation, overcrowding, industrialization, sociocultural values, overuse and misuse of antibiotics, lack of basic health services, and lack of awareness [14]. It is also important to note that a quarter of ARI deaths in children are attributable to passive smoking. The National Family Health Survey, conducted in 2019–2020, reported a 2.4% prevalence of ARI in the preceding two weeks in the urban areas and a 3.8% in the rural areas in Maharashtra state. In the Indian slum areas, ARI constitutes more than two-thirds of all childhood illnesses [15]. Globally, in 2010, nearly 2, 65,000 hospital deaths of young children were attributed to ARI, 99% of which were reported in developing countries. In urban slum areas, ARI constitutes over two-thirds of all childhood illnesses. In India, 14.3% of the deaths among infants and 15.9% among children between 1 and 5 years of age are due to ARTIs, and most of these deaths are preventable. Because of the high morbidity and mortality rates associated with ARTIs, their control continues as a major challenge to the healthcare system [16].

**Aetiology of ARTIs**

A wide range of microorganisms, including bacteria, viruses, fungi, and protozoa, can cause respiratory tract infections, the standard being bacteria and viruses. Viruses are responsible for most upper respiratory tract infections, while bacterial infections can be primary or secondary to measles, influenza, or RSV infections [17]. The common bacteria known to cause acute respiratory tract infections are *Streptococcus pneumoniae*, *Haemophilus influenzae* (type B), *Streptococcus pyogenes* and *Staphylococcus aureus*. Other pathogens are *Mycoplasma pneumoniae and Chlamydia pneumoniae* which causes atypical pneumonia [18]. ARTIs in viruses are a significant cause of morbidity and mortality. The primary viral etiological agents of ARTIs in all age groups include respiratory syncytial virus (RSV), influenza viruses, parainfluenza viruses (PIV), adenoviruses, human rhinovirus (hRV), hMPV, HBoV, coronaviruses and picornaviruses [19, 20]. Among these, RSV, hMPV, hRV and PIV predominate as the cause of ARTIs in children under five years of age and have a seasonal occurrence with or without co-infection [21].

**Diagnosis of viral respiratory tract infections**

The differentiation of the etiological agent for respiratory tract infection based on clinical conditions is practically impossible. Rapid and precise diagnosis of the etiological agent is essential in treating and controlling the spread of viral respiratory infections [22]. Laboratory diagnosis can significantly improve care based on the appropriate diagnostic method chosen by the health care personnel in performing the test. There are various methods for detecting respiratory tract infections: rapid antigen testing, immunofluorescence tests for antibody detection, conventional and rapid cell culture methods, and molecular-based nucleic acid amplification assays [23]. The various specimen types for detecting respiratory viruses include nasopharyngeal aspirates, nasopharyngeal washes, nasopharyngeal swabs and oropharyngeal swabs in viral transport media. Sputum, endotracheal aspirates, and bronchioalveolar lavages are collected in tubes. The sensitivity of each method depends on factors such as sample type, time of sample collection, the onset of the symptoms, patient age, antigen target, and the properties of the virus [24, 25]. Immunocompromised patients shed low titters of the virus over an extended period, making it difficult to detect it by nonmolecular methods. Hence nucleic acid amplification by molecular-based methods has become more popular for identifying respiratory viruses as they are rapid and most sensitive assays [26, 27]. The various methods for identifying respiratory viruses have their advantages and drawbacks.

The traditional tube culture method is advantageous for growing a wide variety of viruses, including novel or unknown viruses, but it takes days and often weeks to provide results. Over the years, modified cell culture methods such as the centrifugation-enhanced shell-vial method have reduced the turnaround time from 10 days to 24 hours [28]. Shell-vial culture using combination cell lines allows simultaneous detection of multiple respiratory viruses and, as compared to conventional culture, has similar sensitivity for parainfluenza 1-3 (87% vs 83%) and influenza A/B (78% vs 75%) and significantly higher sensitivity for RSV (73% vs 42%) [29].

Rapid immunoassays (RIAs) can deliver test results in less than 30 minutes and are usually performed in the point of care testing (POCT), thus allowing the test results to be incorporated into the clinical decision-making algorithm. In the pediatric population, commercially available immunoassays have demonstrated high sensitivity (93%) for the detection of RSV, and a systematic review of published studies has further revealed that the sensitivity of RSV RIAs is relatively higher for children (81%) than adults (29%). The higher sensitivity can be attributed to the fact that pediatric patients often shed higher titers of respiratory viruses for a longer time than adults [30, 31].

Pathogen-specific antibodies typically appear about two weeks after the initial infection and can be detected by serological tests. Serological tests can successfully identify antibodies to most respiratory pathogens such as RSV, adenovirus, influenza A and B, parainfluenza 1-3 virus, etc., and can detect mixed infections from hospitalized children suffering from acute respiratory infections, except infants for whom an antibody response is usually undetected [32]. However, it has been reported that serological assays are significantly less sensitive for the detection of parainfluenza virus and adenovirus when compared to molecular methods, such as RT-PCR [33]. RT-PCR can detect 40% more specimens from pediatric patients that were positive for at least one respiratory virus than were detected by fluorescent antibody assay (FA). FA testing, in addition to RT-PCR, is useful for epidemiological studies as it increases the probability of identifying acute viral infections and has been used to accurately assess respiratory viruses other than influenza in children [34, 35, 36].

## HUMAN METAPNEUMOVIRUS

### Discovery and classification of hMPV

The hMPV was initially isolated in the Netherlands from 28 nasopharyngeal aspirates (NPA) collected from children younger than five years of age presenting with respiratory tract infections over 20 years [37, 38]. The virus replicated very slowly in tertiary monkey kidney cells, and the cytopathic effect produced was similar to that of RSV. Electron microscopy of the supernatant from the infected cells showed the presence of paramyxovirus-like pleomorphic particles with a diameter of 150 to 600nm with short projections of 13 to 17 nm length was observed. The nucleocapsid was not visible as in the case of other Paramyxoviruses like RSV and parainfluenza. It was inactivated by chloroform and did not agglutinate erythrocytes. Reverse transcriptase reaction using primers specific to other respiratory viruses did not produce positive results. The genomic pattern and morphological features classified it under the *Paramyxoviridae*, subfamily Pneumovirinae, and genus Metapneumovirus [39, 40].

### Genotypes of hMPV

The genomic organization of hMPV is similar to RSV; however, hMPV lacks the non-structural genes NS1 and NS2, and the hMPV antisense RNA genome contains eight open reading frames in slightly different gene order than RSV (viz. 3'-N-P-M-F-M2-SH-G-L-5') [41]. The hMPV is genetically similar to the avian metapneumoviruses A, B, and, in particular, type C. Phylogenetic analysis of hMPV has demonstrated the existence of two main genetic lineages termed subtype A and B containing within them the subgroups A1/A2 and B1/B2 respectively. Genotyping based on sequences of the F and G genes showed that subtype B was associated with increased cough duration and general respiratory systems compared to hMPV-A [42]. The hMPV infects airway epithelial cells in the nose and lungs. In addition to interacting with heparan sulfate and other glycosaminoglycans, hMPV attaches to the target cell via its glycoprotein (G) protein. The hMPV fusion (F) protein encodes an RGD (Arg-Gly-Asp) motif that engages RGD-binding integrins as cellular receptors [43, 44, and 45] and then mediates fusion of the cell membrane and viral envelope in a pH-independent fashion, likely within endosomes.

**Prevalence of hMPV**

The hMPV is more commonly found in the pediatric population, predominately in children less than two years of age with an average age of 22 months. Approximately 90 to 100% of children are infected by hMPV by the age of 5 to 10 years old, according to seroprevalence studies [46]. About 5 to 10% of pediatric hospitalizations result from hMPV causing acute lower respiratory tract infections. On average, children under six months of age with hMPV infection were three times as likely to be hospitalized compared to children between the ages of 6 months to 5 years [47, 48]. Re-infection may occur due to different viral genotypes or insufficient immunity from the initial infection. Although adults typically only experience mild flu-like symptoms, complications can be seen in the elderly, immunocompromised, or those individuals with chronic lung diseases [49, 50].

**Clinical manifestations of hMPV**

The hMPV infects the cells of the respiratory tract, including the mouth, nose, and throat, when it enters the body. Whenever these cells are infected, the immune system reacts and causes symptoms like pain, low-grade fever, cough, runny nose, headache, and sore throat. In some people, the disease can affect the bronchi or main airways. The spread of this virus can cause coughing and wheezing. Children under one year can experience decreased fever and weight loss [51, 52]. There is a possibility that hMPV can cause severe illness requiring hospitalization in certain patient populations. These include immunocompromised patients and those with preexisting cardiac or respiratory conditions. These patients are more susceptible to developing acute respiratory failure requiring high-flow oxygen support, with some patients even deteriorating enough to require mechanical ventilation. Patients need to be admitted to the intensive care unit for close monitoring [53].

## Diagnosis of hMPV

The diagnosis of hMPV infection can be approached using techniques like cell culture, nucleic acid amplification tests, antigen detection and serological methods. The hMPV replicates poorly in conventional cell cultures and reveals mild cytopathic effects [54]. Also, the technique is laborious and expensive and requires special procedures like trypsin addition. The various cell lines in which hMPV can be cultivated are tertiary monkey kidney cells, Vero cells, LLC-MK2-cells, BEAS-2B cells, A549 cells, and HepG2 [55]. The cytopathic effects are seen in tertiary monkey kidney, LLC-MK2 and Vero cell lines but only after 10 to 21 days of incubation. The shell vial culture technique, which includes centrifugation, short incubation and fluorescent staining, is a rapid method for identifying hMPV [56]. Direct immunofluorescence assay is a rapid method for identifying hMPV in which labelled antibodies are used to identify hMPV antigens in respiratory specimens. ELISA and microarray methods are also used but are not available commercially. Reverse transcriptase PCR assays amplifying the viral RNA is the most widely used and sensitive method employed to identify hMPV. Various regions viz F, N, G, L, and M are commonly used as targets. The F and N genes are considered more specific and conserved, suitable for identifying hMPV [57, 58].

## Treatment for hMPV

No specific FDA-approved antiviral therapy is currently available for hMPV infection. Routine treatment includes symptomatic care, with respiratory support when required [59]. The primary mainstays of treatment are supportive measures. Anti-pyretic medications such as acetaminophen and ibuprofen are given to those patients with fever. Intravenous fluid hydration is indicated if the patient appears dehydrated and cannot tolerate oral hydration [60]. Additionally, patients with hMPV may require supplemental oxygen support such as high flow nasal cannula or even mechanical ventilation in severe cases causing acute respiratory failure, especially in patients with preexisting respiratory or cardiac illness and those with immunocompromised. Most patients do undergo a full recovery. However, every patient with hMPV should be placed on droplet precautions to limit and prevent spread. There is no current vaccine available for hMPV [61, 62]. However, various vaccines against different structures of hMPV have been tested on non-human primates and rodents that appear promising. Still, none have been tested on human volunteers.

**Prevention of hMPV**

Control measures used for other respiratory illnesses should be emphasized: covering the mouth and nose with a tissue when coughing or sneezing, or coughing or sneezing into the upper sleeve rather than the hands, prompt disposal of used tissues and proper hand washing. Wash their hands often with soap and water for at least 20 seconds. Avoid touching eyes, nose, or mouth with unwashed hands. Avoid close contact with people who are sick [63].

**HUMAN BOCAVIRUS**

**Discovery and classification of HBoV**

HBoV was discovered in Sweden in 2005 from the pooled cell-free filtrates of the NPA from children with ARTIs by molecular screening methods. HBoV belongs to the family Parvoviridae, subfamily parvovirinae and genus Bocavirus. The name Bocavirus was derived from the combination of the terms bovine parvovirus (BPV) and canine minute virus (CMV) and was based on the sequence similarities and genomic organization of these two close relatives [64]. The parvoviruses associated with human infections are parvovirus B19 (B19V), within the genus Erythroparvovirus, the apathogenic adeno-associated virus, belonging to the genus Dependoparvovirus, and the recently discovered parvoviruses 4 (PARV4) and 5 (PARV5), affiliated with the new genus Tetraparvovirus [65, 66]. The latter has not yet been associated with any clinical significance; based on similarity, however, it has been allocated to the new genus Hokovirus [67, 68].

**Genotypes of HBoV**

The genus Bocavirus consists of bovine parvovirus (BPV), canine minute virus (CMV) and HBoV [69]. At present, there are four subtypes of HBoV (1 to 4) have been identified. HBoV 1 is the common subtype found in respiratory specimens, whereas the other three are commonly identified in gastrointestinal specimens. HBoV genotypes belong to Parvoviridae, subfamily Parvovirinae, and genus Bocavirus and cause infection in vertebrates exclusively [70, 71]. Parvoviridae also comprises the subfamily Densovirinae, which infects arthropods and shares no sequence homology with the other subfamily. The current classification of the International Committee on Taxonomy of Viruses database recognizes eight genera of the subfamily Parvovirinae: Amdoparvovirus, Aveparvovirus, Bocaparvovirus, Copiparvovirus, Dependoparvovirus, Erythroparvovirus, Protoparvovirus and Tetraparvovirus [72, 73].

**Etiology of HBoV**

The exact mode of transmission of HBoV infection is unknown. HBoV1 is presumed to be transmitted through inhalation of aerosols contaminated by the virus, similar to the mode of transmission of other parvoviruses. HBoV has been detected in urine and faeces and is also known to cause viraemia in the active stage of replication in the host. Nosocomial acquirement of HBoV infection has also been reported [74].

The pathogenesis of HBoV needs to be better established due to the need for standardized in vitro culture methods and animal models. There are studies across the world which suggest that HBoV is a respiratory pathogen. It is known to cause lower respiratory tract infection, and the symptoms associated are acute wheezing, bronchiolitis, fever and pneumonia. The occurrence of HBoV infection in immunocompromised (transplant) individuals has also been established [75]. HBoV DNA has been detected in the serum of patients with acute primary and severe infections [76]. Several studies indicate the role of HBoV (especially subtypes 2, 3 and 4) as a gastrointestinal pathogen [77]. HBoV was also identified from urine specimens. The pathogenicity of HBoV can be assumed to be analogous to that of minute virus of canines (MVC). The virus enters the body through the respiratory tract, multiplies, and enters the bloodstream and, finally, the gastrointestinal tract through blood or ingestion. Viral shedding occurs either by coughing or defecation [78]. Reports suggest latent infection or the persistence of HBoV in patients. There is a high rate of co-infection of HBoV with other viruses [79, 80].

**Prevalence of HBoV**

In three studies, HBoV was detected via PCR in respiratory secretions from 1 of 126 (0.8%), [19] 3 of 202 (1.5%), [20], and 3.1% [21] of adults with respiratory tract infection [81, 82, 83].

Five cases were included in a case study of five adults with bocavirus-associated pneumonia [84]. Another series included one hospitalized and four outpatient cases of bocavirus-associated pneumonia in adults. The first report of HBoV and adenovirus co-infection in immunosuppressed and nonimmunosuppressed children in Mexico was published in [85]. [84] Serologic responses to HBoV infection have also been documented. A 2008 study by Lindner found an immunoglobulin G (IgG) response in 280 of 299 (94%) adults, while immunoglobulin M (IgM) results were positive in 2 of 299 cases (1%) [85].

**Clinical manifestations of HBoV**

The clinical manifestations of HBoV infections are indistinguishable from that of other respiratory pathogens [86]. The common respiratory symptoms in HBoV-infected individuals are wheezing, respiratory distress, fever, cough, rhinorrhea, bronchiolitis and pneumonia. HBoV 1 has been identified in the NPA and middle ear fluid in children with acute otitis media [87]. Several studies have detected HBoV in stool samples of children with an acute gastrointestinal disorder, but its pathogenicity is uncertain [88, 89]. The risk factors associated with HBoV infection are similar to those for other respiratory viruses like congenital heart diseases, asthma, chronic obstructive pulmonary disease, immunosuppression, maternal smoking, premature birth, and winter birth. Daycare centres and sewage or river water drinking may also be a factor for HBoV infection [90].

**Diagnosis of HBoV**

Currently, there needs to be an adequate culture method developed for the identification of HBoV. Hence the identification of the virus is commonly carried out from NPAs using conventional and real-time PCR assays, mostly targeting the NS1, NP1 and VP1/2 genes [91]. Other molecular methods are also used for detecting HBoV [92]. Real-time PCR is more sensitive, specific and time-saving when compared to conventional PCR assay methods. A wide range of commercial multiplex assay methods is also available to detect HBoV [93]. The EIA of IgG avidity has been developed to diagnose primary HBoV infection and immune activation accurately [94]. Antibodies against HBoV in serum can be detected using ELISA methods with virus-like particles (VLPs) of VP1 and VP2 [95, 96]. Immunofluorescence assays for detecting IgG antibodies and assays based on biomarkers are encouraging methods for identifying HBoV infections [97, 98, 99]. Initial screening of clinical samples (respiratory or stool) followed by the subsequent serum sample will help in the accurate diagnosis of HBoV infection as the virus will be present in the blood during the active infective stage.

**Treatment of HBoV**

No specific in vivo or in vitro antiviral therapy or prevention by immunization is available for HBoV. There are only supportive measures present. The transmission of the virus through contaminated aerosols should be prevented using standard precautions [100, 101].

**Prevention of HBoV**

The preventive and infection control measures for HBoV1 are the same as for other respiratory viruses [102]. As these viruses infect the respiratory tract, the viruses are disseminated into the air by coughing. Although the major mode of transmission of respiratory viruses is through large droplets, transmission through contact and infectious respiratory aerosols of various sizes may also occur [103]. However, adequate hand hygiene, medical masks and gloves, and isolation precautions are general infection control measures for all respiratory viral infections.

## Conclusion

ARTIs contribute to significant morbidity and mortality in children and adults worldwide. Over the last two decades, novel viral infections have dramatically emerged. A cautious thought of clinical features, diagnosis and epidemiology survey is necessary to direct the clinicians in decision-making on diagnosis and treatment. This review can help to understand the clinical presentations, diagnostic methods, available treatments and prevention of ARTIs.

## References


1. Merera A, Asena T, Senbeta M. Bayesian multilevel analysis of determinants of acute respiratory infection in children under the age of five years in Ethiopia. BMC Pediatr. 2022 Mar 10; 22(1):123. doi: 10.1186/s12887-022-03187-4. PMID: 35272658; PMCID: PMC8908561.

2. Hassen S, Getachew M, Eneyew B, Keleb A, Ademas A, Berihun G, Berhanu L, Yenuss M, Natnael T, Kebede AB, Sisay T. Determinants of acute respiratory infection (ARI) among under-five children in rural areas of Legambo District, South Wollo Zone, Ethiopia: A matched case-control study. Int J Infect Dis. 2020 Jul; 96:688-695. doi: 10.1016/j.ijid.2020.05.012. Epub 2020 May 12. PMID: 32413607.
3. Kumar P, Srivastava M. Prophylactic and therapeutic approaches for human metapneumovirus. Virusdisease. 2018 Dec; 29(4):434-444. doi: 10.1007/s13337-018-0498-5. Epub 2018 Oct 20. PMID: 30539045; PMCID: PMC6261883.
4. Murgia V, Manti S, Licari A, De Filippo M, Ciprandi G, Marseglia GL. Upper Respiratory Tract Infection-Associated Acute Cough and the Urge to Cough: New Insights for Clinical Practice. Pediatr Allergy Immunol Pulmonol. 2020 Mar; 33(1):3-11. doi: 10.1089/ped.2019.1135. PMID: 33406022; PMCID: PMC7875114.
5. Carroll KC, Adams LL. Lower Respiratory Tract Infections. Microbiol Spectr. 2016 Aug;4(4). doi: 10.1128/microbiolspec.DMIH2-0029-2016. PMID: 27726814.
6. Thapa P, Pandey AR. Risk of ARI among non-exclusively breastfed under-five passive smoker children: a hospital-based cross-sectional study of Nepal. Front Public Health. (2016) 4:23. doi: 10.3389/fpubh.2016.00023
7. NFHS-5 Factsheet (2019-2020). Available online at: http://rchiips.org/nfhs/ NFHS-5_FCTS/FactSheet_MH.pdf (accessed December 23, 2020).
8. Islam F, Sarma R, Debroy A, Kar S, Pal R. Profiling acute respiratory tract infections in children from Assam, India. J Glob Infect Dis. (2013) 5:8–14. doi: 10.4103/0974-777X.107167
9. Geberetsadik A, Worku A, Berhane Y. Factors associated with acute respiratory infection in children under the age of 5 years: evidence from the 2011. Ethiopia demographic and health survey. Pediatr Health Med Therap. (2015) 6:9–13. doi: 10.2147/PHMT.S77915.
10. Lu D. Children's immunity at risk. New Sci. 2021 May 1; 250(3332):8-9. doi: 10.1016/S0262-4079(21)00716-8. Epub 2021 Apr 30. PMID: 33967369; PMCID: PMC8087417.
11. Kumar SG, Majumdar A, Kumar V, Naik BN, Selvaraj K, Balajee K. Prevalence of acute respiratory infection among under-five children in urban and rural areas of Puducherry, India. J Nat Sci Biol Med. (2015) 6:3–6. doi: 10.4103/0976-9668.149069.

12. Assane D, Makhtar C, Abdoulaye D, Amary F, Djibril B, Amadou D, Niokhor DJB, Amadou D, Cheikh L, Ndongo D, Mbayame N, Lamine F, Bouh BCS. Viral and Bacterial Etiologies of Acute Respiratory Infections among Children Under 5 Years in Senegal. Microbiol Insights. 2018 Feb 13; 11:1178636118758651. doi: 10.1177/1178636118758651. PMID: 29467579; PMCID: PMC5815418.
13. Selvaraj K, Chinnakali P, Majumdar A, Krishnan IS. Acute respiratory infections among under-5 children in India: A situational analysis. J Nat Sci Biol Med. 2014 Jan;5(1):15-20. doi: 10.4103/0976-9668.127275. PMID: 24678190; PMCID: PMC3961922.
14. Murarkar S, Gothankar J, Doke P, Dhumale G, Pore PD, Lalwani S, Quraishi S, Patil RS, Waghachavare V, Dhobale R, Rasote K, Palkar S, Malshe N, Deshmukh R. Prevalence of the Acute Respiratory Infections and Associated Factors in the Rural Areas and Urban Slum Areas of Western Maharashtra, India: A Community-Based Cross-Sectional Study. Front Public Health. 2021 Oct 26; 9:723807. doi: 10.3389/fpubh.2021.723807. PMID: 34765581; PMCID: PMC8576147.
15. Islam F, Sarma R, Debroy A, Kar S, Pal R. Profiling acute respiratory tract infections in children from assam, India. J Glob Infect Dis. 2013 Jan; 5(1):8-14. doi: 10.4103/0974-777X.107167. PMID: 23599611; PMCID: PMC3628235.
16. Radó MK, Mölenberg FJM, Westenberg LEH, Sheikh A, Millett C, Burdorf A, van Lenthe FJ, Been JV. Effect of smoke-free policies in outdoor areas and private places on children's tobacco smoke exposure and respiratory health: a systematic review and meta-analysis. Lancet Public Health. 2021 Aug; 6(8):e566-e578. doi: 10.1016/S2468-2667(21)00097-9. Epub 2021 Jul 16. PMID: 34274050.
17. Griffiths C, Drews SJ, Marchant DJ. Respiratory Syncytial Virus: Infection, Detection, and New Options for Prevention and Treatment. Clin Microbiol Rev. 2017 Jan; 30(1):277-319. doi: 10.1128/CMR.00010-16. PMID: 27903593; PMCID: PMC5217795.
18. Pahal P, Rajasurya V, Sharma S. Typical Bacterial Pneumonia. 2022 Aug 1. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 30485000.
19. Al-Ayed MS, Asaad AM, Qureshi MA, Ameen MS. Viral etiology of respiratory infections in children in southwestern Saudi Arabia using multiplex reverse-transcriptase

polymerase chain reaction. Saudi Med J. 2014 Nov;35(11):1348-53. PMID: 25399211; PMCID: PMC4362149.

20. Esposito S, Mastrolia MV. Metapneumovirus Infections and Respiratory Complications. Semin Respir Crit Care Med. 2016 Aug;37(4):512-21. doi: 10.1055/s-0036-1584800. Epub 2016 Aug 3. PMID: 27486733; PMCID: PMC7171707.
21. Chu FL, Li C, Chen L, Dong B, Qiu Y, Liu Y. Respiratory viruses among pediatric in patients with acute lower respiratory tract infections in Jinan, China, 2016-2019. J Med Virol. 2022 Sep; 94(9):4319-4328. doi: 10.1002/jmv.27875. Epub 2022 May 28. PMID: 35593042.
22. Basile K, Kok J, Dwyer DE. Point-of-care diagnostics for respiratory viral infections. Expert Rev Mol Diagn. 2018 Jan;18(1):75-83. doi: 10.1080/14737159.2018.1419065. Epub 2017 Dec 26. PMID: 29251007; PMCID: PMC7103700.
23. Nabeya D, Kinjo T, Ueno S, Setoguchi M, Nishiyama N, Kami W, Arakaki W, Haranaga S, Fujita J. Characteristics of patients with viral infections of the lower respiratory tract: A retrospective study. Medicine (Baltimore). 2022 Sep 23;101(38):e30819. doi: 10.1097/MD.0000000000030819. PMID: 36197196; PMCID: PMC9509109.
24. Zhang N, Wang L, Deng X, Liang R, Su M, He C, Hu L, Su Y, Ren J, Yu F, Du L, Jiang S. Recent advances in the detection of respiratory virus infection in humans. J Med Virol. 2020 Apr;92(4):408-417. doi: 10.1002/jmv.25674. Epub 2020 Feb 4. PMID: 31944312; PMCID: PMC7166954.
25. Babaei A, Rafiee N, Taheri B, Sohrabi H, Mokhtarzadeh A. Recent Advances in Early Diagnosis of Viruses Associated with Gastroenteritis by Biosensors. Biosensors (Basel). 2022 Jul 8; 12(7):499. doi: 10.3390/bios12070499. PMID: 35884302; PMCID: PMC9313180.
26. Dolskiy AA, Grishchenko IV, Yudkin DV. Cell Cultures for Virology: Usability, Advantages, and Prospects. Int J Mol Sci. 2020 Oct 27; 21(21):7978. doi: 10.3390/ijms21217978. PMID: 33121109; PMCID: PMC7662242.
27. Loeffelholz M, Chonmaitree T. Advances in diagnosis of respiratory virus infections. Int J Microbiol. 2010;2010:126049. doi: 10.1155/2010/126049. Epub 2010 Oct 19. PMID: 20981303; PMCID: PMC2958490.

28. Dilnessa, T., & Zeleke, H. (2017). Cell culture, cytopathic effect and immunofluorescence diagnosis of viral infection. J. Microbiol. Mod. Tech, 2, 102-110.
29. LaSala PR, Bufton KK, Ismail N, Smith MB. Prospective comparison of R-mix shell vial system with direct antigen tests and conventional cell culture for respiratory virus detection. J Clin Virol. 2007 Mar;38(3):210-6. doi: 10.1016/j.jcv.2006.12.015. Epub 2007 Jan 16. PMID: 17229589; PMCID: PMC7108409.
30. Chartrand C, Tremblay N, Renaud C, Papenburg J. Diagnostic Accuracy of Rapid Antigen Detection Tests for Respiratory Syncytial Virus Infection: Systematic Review and Meta-analysis. J Clin Microbiol. 2015 Dec;53(12):3738-49. doi: 10.1128/JCM.01816-15. Epub 2015 Sep 9. PMID: 26354816; PMCID: PMC4652120.
31. Benirschke RC, McElvania E, Thomson RB Jr, Kaul KL, Das S. Clinical Impact of Rapid Point-of-Care PCR Influenza Testing in an Urgent Care Setting: a Single-Center Study. J Clin Microbiol. 2019 Feb 27;57(3):e01281-18. doi: 10.1128/JCM.01281-18. PMID: 30602445; PMCID: PMC6425177.
32. Chkhaidze I, Manjavidze N, Nemsadze K. Serodiagnosis of acute respiratory infections in children in Georgia. Indian J Pediatr. 2006 Jul;73(7):569-72. doi: 10.1007/BF02759919. PMID: 16877849.
33. Kuypers J, Wright N, Ferrenberg J, Huang ML, Cent A, Corey L, Morrow R. Comparison of real-time PCR assays with fluorescent-antibody assays for diagnosis of respiratory virus infections in children. J Clin Microbiol. 2006 Jul;44(7):2382-8. doi: 10.1128/JCM.00216-06. PMID: 16825353; PMCID: PMC1489473.
34. Sawatwong P, Chittaganpitch M, Hall H, Peruski LF, Xu X, Baggett HC, Fry AM, Erdman DD, Olsen SJ. Serology as an adjunct to polymerase chain reaction assays for surveillance of acute respiratory virus infections. Clin Infect Dis. 2012 Feb 1;54(3):445-6. doi: 10.1093/cid/cir710. Epub 2011 Nov 4. PMID: 22057703.
35. Feikin DR, Njenga MK, Bigogo G, Aura B, Gikunju S, Balish A, Katz MA, Erdman D, Breiman RF. Additional diagnostic yield of adding serology to PCR in diagnosing viral acute respiratory infections in Kenyan patients 5 years of age and older. Clin Vaccine Immunol. 2013 Jan;20(1):113-4. doi: 10.1128/CVI.00325-12. Epub 2012 Oct 31. PMID: 23114699; PMCID: PMC3535781.

36. Zhang Y, Sakthivel SK, Bramley A, Jain S, Haynes A, Chappell JD, Hymas W, Lenny N, Patel A, Qi C, Ampofo K, Arnold SR, Self WH, Williams DJ, Hillyard D, Anderson EJ, Grijalva CG, Zhu Y, Wunderink RG, Edwards KM, Pavia AT, McCullers JA, Erdman DD. Serology Enhances Molecular Diagnosis of Respiratory Virus Infections Other than Influenza in Children and Adults Hospitalized with Community-Acquired Pneumonia. J Clin Microbiol. 2016 Dec 28;55(1):79-89. doi: 10.1128/JCM.01701-16. PMID: 27795341; PMCID: PMC5228265.
37. Zhao H, Feng Q, Feng Z, Zhu Y, Ai J, Xu B, Deng L, Sun Y, Li C, Jin R, Shang Y, Chen X, Xu L, Xie Z. Clinical characteristics and molecular epidemiology of human metapneumovirus in children with acute lower respiratory tract infections in China, 2017 to 2019: A multicentre prospective observational study. Virol Sin. 2022 Dec;37(6):874-882. doi: 10.1016/j.virs.2022.08.007. Epub 2022 Aug 22. PMID: 36007839; PMCID: PMC9797368.
38. Liu WK, Chen DH, Tan WP, Qiu SY, Xu D, Zhang L, Gu SJ, Zhou R, Liu Q. Paramyxoviruses respiratory syncytial virus, parainfluenza virus, and human metapneumovirus infection in pediatric hospitalized patients and climate correlation in a subtropical region of southern China: a 7-year survey. Eur J Clin Microbiol Infect Dis. 2019 Dec;38(12):2355-2364. doi: 10.1007/s10096-019-03693-x. Epub 2019 Sep 5. PMID: 31489496; PMCID: PMC6858468.
39. El Najjar F, Schmitt AP, Dutch RE. Paramyxovirus glycoprotein incorporation, assembly and budding: a three way dance for infectious particle production. Viruses. 2014 Aug 7;6(8):3019-54. doi: 10.3390/v6083019. PMID: 25105277; PMCID: PMC4147685.
40. Kenmoe S, Vernet MA, Penlap Beng V, Vabret A, Njouom R. Phylogenetic variability of Human Metapneumovirus in patients with acute respiratory infections in Cameroon, 2011-2014. J Infect Public Health. 2020 Apr; 13(4):606-612. doi: 10.1016/j.jiph.2019.08.018. Epub 2019 Sep 14. PMID: 31530440.
41. Uche IK, Guerrero-Plata A. Interferon-Mediated Response to Human Metapneumovirus Infection. Viruses. 2018 Sep 18;10(9):505. doi: 10.3390/v10090505. PMID: 30231515; PMCID: PMC6163993.

42. Jesse ST, Ludlow M, Osterhaus ADME. Zoonotic Origins of Human Metapneumovirus: A Journey from Birds to Humans. Viruses. 2022 Mar 25;14(4):677. doi: 10.3390/v14040677. PMID: 35458407; PMCID: PMC9028271.
43. Nao N, Saikusa M, Sato K, Sekizuka T, Usuku S, Tanaka N, Nishimura H, Takeda M. Recent Molecular Evolution of Human Metapneumovirus (HMPV): Subdivision of HMPV A2b Strains. Microorganisms. 2020 Aug 21; 8(9):1280. doi: 10.3390/microorganisms8091280. PMID: 32839394; PMCID: PMC7564156.
44. Li J, Ren L, Guo L, Xiang Z, Paranhos-Baccalà G, Vernet G, Wang J. Evolutionary dynamics analysis of human metapneumovirus subtype A2: genetic evidence for its dominant epidemic. PLoS One. 2012;7(3):e34544. doi: 10.1371/journal.pone.0034544. Epub 2012 Mar 30. PMID: 22479641; PMCID: PMC3316673.
45. Cox RG, Livesay SB, Johnson M, Ohi MD, Williams JV. The human metapneumovirus fusion protein mediates entry via an interaction with RGD-binding integrins. J Virol. 2012 Nov;86(22):12148-60. doi: 10.1128/JVI.01133-12. Epub 2012 Aug 29. PMID: 22933271; PMCID: PMC3486500.
46. Malekshahi SS, Yavarian J, Shafiei-Jandaghi NZ, Mokhtari-Azad T, Farahmand M. Prevalence of Human Metapneumovirus Infections in Iran: A Systematic Review and Meta-Analysis. Fetal Pediatr Pathol. 2021 Dec; 40(6):663-673. doi: 10.1080/15513815.2020.1725939. Epub 2020 Feb 21. PMID: 32081050.
47. Jallow MM, Fall A, Kiori D, Sy S, Goudiaby D, Barry MA, Fall M, Niang MN, Dia N. Epidemiological, clinical and genotypic features of human Metapneumovirus in patients with influenza-like illness in Senegal, 2012 to 2016. BMC Infect Dis. 2019 May 22;19(1):457. doi: 10.1186/s12879-019-4096-y. PMID: 31117983; PMCID: PMC6532257.
48. Vinci A, Lee PJ, Krilov LR. Human Metapneumovirus Infection. Pediatr Rev. 2018 Dec;39(12):623-624. doi: 10.1542/pir.2017-0213. PMID: 30504257.
49. Uche IK, Guerrero-Plata A. Interferon-Mediated Response to Human Metapneumovirus Infection. Viruses. 2018 Sep 18;10(9):505. doi: 10.3390/v10090505. PMID: 30231515; PMCID: PMC6163993.
50. Panda S, Mohakud NK, Pena L, Kumar S. Human metapneumovirus: review of an important respiratory pathogen. Int J Infect Dis. 2014 Aug;25:45-52. doi:

10.1016/j.ijid.2014.03.1394. Epub 2014 May 17. PMID: 24841931; PMCID: PMC7110553.

51. Hermos CR, Vargas SO, McAdam AJ. Human metapneumovirus. Clin Lab Med. 2010 Mar; 30(1):131-48. doi: 10.1016/j.cll.2009.10.002. PMID: 20513544; PMCID: PMC7115734.
52. Wang C, Wei T, Ma F, Wang H, Guo J, Chen A, Huang Y, Xie Z, Zheng L. Epidemiology and genotypic diversity of human metapneumovirus in paediatric patients with acute respiratory infection in Beijing, China. Virol J. 2021 Feb 18;18(1):40. doi: 10.1186/s12985-021-01508-0. PMID: 33602245; PMCID: PMC7890387.
53. Haas LE, Thijsen SF, van Elden L, Heemstra KA. Human metapneumovirus in adults. Viruses. 2013 Jan 8;5(1):87-110. doi: 10.3390/v5010087. PMID: 23299785; PMCID: PMC3564111.
54. Jeong S, Park MJ, Song W, Kim HS. Advances in laboratory assays for detecting human metapneumovirus. Ann Transl Med. 2020 May;8(9):608. doi: 10.21037/atm.2019.12.42. PMID: 32566634; PMCID: PMC7290561.
55. Feng ZS, Zhao L, Wang J, Qiu FZ, Zhao MC, Wang L, Duan SX, Zhang RQ, Chen C, Qi JJ, Fan T, Li GX, Ma XJ. A multiplex one-tube nested real time RT-PCR assay for simultaneous detection of respiratory syncytial virus, human rhinovirus and human metapneumovirus. Virol J. 2018 Oct 30;15(1):167. doi: 10.1186/s12985-018-1061-0. PMID: 30376870; PMCID: PMC6208169.
56. Nao N, Sato K, Yamagishi J, Tahara M, Nakatsu Y, Seki F, Katoh H, Ohnuma A, Shirogane Y, Hayashi M, Suzuki T, Kikuta H, Nishimura H, Takeda M. Consensus and variations in cell line specificity among human metapneumovirus strains. PLoS One. 2019 Apr 23;14(4):e0215822. doi: 10.1371/journal.pone.0215822. PMID: 31013314; PMCID: PMC6478314.
57. Aslanzadeh J, Zheng X, Li H, Tetreault J, Ratkiewicz I, Meng S, Hamilton P, Tang YW. Prospective evaluation of rapid antigen tests for diagnosis of respiratory syncytial virus and human metapneumovirus infections. J Clin Microbiol. 2008 May;46(5):1682-5. doi: 10.1128/JCM.00008-08. Epub 2008 Mar 12. PMID: 18337386; PMCID: PMC2395112.
58. You HL, Chang SJ, Yu HR, Li CC, Chen CH, Liao WT. Simultaneous detection of respiratory syncytial virus and human metapneumovirus by one-step multiplex real-time

RT-PCR in patients with respiratory symptoms. BMC Pediatr. 2017 Mar 27;17(1):89. doi: 10.1186/s12887-017-0843-7. PMID: 28347279; PMCID: PMC5368990.

59. Cong S, Wang C, Wei T, Xie Z, Huang Y, Tan J, Chen A, Ma F, Zheng L. Human metapneumovirus in hospitalized children with acute respiratory tract infections in Beijing, China. Infect Genet Evol. 2022 Dec;106:105386. doi: 10.1016/j.meegid.2022.105386. Epub 2022 Nov 11. PMID: 36372116.
60. Wyde PR, Chetty SN, Jewell AM, Boivin G, Piedra PA. Comparison of the inhibition of human metapneumovirus and respiratory syncytial virus by ribavirin and immune serum globulin in vitro. Antiviral Res. 2003 Sep;60(1):51-9. doi: 10.1016/s0166-3542(03)00153-0. PMID: 14516921.
61. Hamelin ME, Prince GA, Boivin G. Effect of ribavirin and glucocorticoid treatment in a mouse model of human metapneumovirus infection. Antimicrob Agents Chemother. 2006 Feb;50(2):774-7. doi: 10.1128/AAC.50.2.774-777.2006. PMID: 16436743; PMCID: PMC1366914.
62. Hamelin ME, Prince GA, Gomez AM, Kinkead R, Boivin G. Human metapneumovirus infection induces long-term pulmonary inflammation associated with airway obstruction and hyperresponsiveness in mice. J Infect Dis. 2006 Jun 15;193(12):1634-42. doi: 10.1086/504262. Epub 2006 May 11. PMID: 16703506.
63. Schuster JE, Williams JV. Human Metapneumovirus. Microbiol Spectr. 2014 Oct;2(5). doi: 10.1128/microbiolspec.AID-0020-2014. PMID: 26104361.
64. Guido M, Tumolo MR, Verri T, Romano A, Serio F, De Giorgi M, De Donno A, Bagordo F, Zizza A. Human bocavirus: Current knowledge and future challenges. World J Gastroenterol. 2016 Oct 21;22(39):8684-8697. doi: 10.3748/wjg.v22.i39.8684. PMID: 27818586; PMCID: PMC5075545.
65. Lasure N, Gopalkrishna V. Molecular epidemiology and clinical severity of Human Bocavirus (HBoV) 1-4 in children with acute gastroenteritis from Pune, Western India. J Med Virol. 2017 Jan; 89(1):17-23. doi: 10.1002/jmv.24593. Epub 2016 Jul 11. PMID: 27272684.
66. Vicente D, Cilla G, Montes M, Pérez-Yarza EG, Pérez-Trallero E. Human bocavirus, a respiratory and enteric virus. Emerg Infect Dis. 2007 Apr; 13(4):636-7. doi: 10.3201/eid1304.061501. PMID: 17553287; PMCID: PMC2725986.

67. Lau SK, Yip CC, Que TL, Lee RA, Au-Yeung RK, Zhou B, So LY, Lau YL, Chan KH, Woo PC, Yuen KY. Clinical and molecular epidemiology of human bocavirus in respiratory and fecal samples from children in Hong Kong. J Infect Dis. 2007 Oct 1; 196(7):986-93. doi: 10.1086/521310. Epub 2007 Aug 29. PMID: 17763318; PMCID: PMC7111856.
68. Kapoor A, Simmonds P, Slikas E, Li L, Bodhidatta L, Sethabutr O, Triki H, Bahri O, Oderinde BS, Baba MM, Bukbuk DN, Besser J, Bartkus J, Delwart E. Human bocaviruses are highly diverse, dispersed, recombination prone, and prevalent in enteric infections. J Infect Dis. 2010 Jun 1; 201(11):1633-43. doi: 10.1086/652416. PMID: 20415538; PMCID: PMC2902747.
69. Allander T, Tammi MT, Eriksson M, Bjerkner A, Tiveljung-Lindell A, Andersson B. Cloning of a human parvovirus by molecular screening of respiratory tract samples. Proc Natl Acad Sci U S A. 2005 Sep 6;102(36):12891-6. doi: 10.1073/pnas.0504666102. Epub 2005 Aug 23. Erratum in: Proc Natl Acad Sci U S A. 2005 Oct 25;102(43):15712. PMID: 16118271; PMCID: PMC1200281.
70. Guido M, Tumolo MR, Verri T, Romano A, Serio F, De Giorgi M, De Donno A, Bagordo F, Zizza A. Human bocavirus: Current knowledge and future challenges. World J Gastroenterol. 2016 Oct 21; 22(39):8684-8697. doi: 10.3748/wjg.v22.i39.8684. PMID: 27818586; PMCID: PMC5075545.
71. Abozahra R, Abdelhamid SM, Khairy K, Baraka K. Detection and phylogenetic analysis of Human bocavirus in children diagnosed with acute respiratory tract infection. J Med Microbiol. 2020 Sep; 69(9):1197-1202. doi: 10.1099/jmm.0.001243. Epub 2020 Aug 19. PMID: 32812862.
72. Mohammadi M, Yavarian J, Karbasizade V, Moghim S, Esfahani BN, Hosseini NS. Phylogenetic analysis of human bocavirus in children with acute respiratory infections in Iran. Acta Microbiol Immunol Hung. 2019 Dec 1;66(4):485-497. doi: 10.1556/030.66.2019.017. Epub 2019 May 31. PMID: 31146533.
73. Cotmore SF, Agbandje-McKenna M, Canuti M, Chiorini JA, Eis-Hubinger AM, Hughes J, Mietzsch M, Modha S, Ogliastro M, Pénzes JJ, Pintel DJ, Qiu J, Soderlund-Venermo M, Tattersall P, Tijssen P, Ictv Report Consortium. ICTV Virus Taxonomy Profile:

Parvoviridae. J Gen Virol. 2019 Mar;100(3):367-368. doi: 10.1099/jgv.0.001212. Epub 2019 Jan 23. PMID: 30672729; PMCID: PMC6537627.

74. Qiu J, Söderlund-Venermo M, Young NS. Human Parvoviruses. Clin Microbiol Rev. 2017 Jan;30(1):43-113. doi: 10.1128/CMR.00040-16. PMID: 27806994; PMCID: PMC5217800.
75. Petrarca L, Nenna R, Frassanito A, Pierangeli A, Di Mattia G, Scagnolari C, Midulla F. Human bocavirus in children hospitalized for acute respiratory tract infection in Rome. World J Pediatr. 2020 Jun;16(3):293-298. doi: 10.1007/s12519-019-00324-5. Epub 2019 Nov 27. PMID: 31776891; PMCID: PMC7091143.
76. Sun H, Sun J, Ji W, Hao C, Yan Y, Chen Z, Wang Y. Impact of RSV Coinfection on Human Bocavirus in Children with Acute Respiratory Infections. J Trop Pediatr. 2019 Aug 1;65(4):342-351. doi: 10.1093/tropej/fmy057. PMID: 30202992; PMCID: PMC7107312.
77. Szomor KN, Kapusinszky B, Rigó Z, Kis Z, Rózsa M, Farkas A, Szilágyi A, Berencsi G, Takács M. Detection of human bocavirus from fecal samples of Hungarian children with acute gastroenteritis. Intervirology. 2009;52(1):17-21. doi: 10.1159/000210834. Epub 2009 Apr 7. PMID: 19349714.
78. Longtin J, Bastien M, Gilca R, Leblanc E, de Serres G, Bergeron MG, Boivin G. Human bocavirus infections in hospitalized children and adults. Emerg Infect Dis. 2008 Feb;14(2):217-21. doi: 10.3201/eid1402.070851. PMID: 18258113; PMCID: PMC2600186.
79. Calvo C, García-García ML, Pozo F, Carballo D, Martínez-Monteserín E, Casas I. Infections and coinfections by respiratory human bocavirus during eight seasons in hospitalized children. J Med Virol. 2016 Dec;88(12):2052-2058. doi: 10.1002/jmv.24562. Epub 2016 May 6. PMID: 27124519; PMCID: PMC7166349.
80. Lüsebrink J, Wittleben F, Schildgen V, Schildgen O. Human bocavirus - insights into a newly identified respiratory virus. Viruses. 2009 Jun;1(1):3-12. doi: 10.3390/v1010003. Epub 2009 Apr 21. PMID: 21994534; PMCID: PMC3185462.
81. Lindner J, Karalar L, Zehentmeier S, Plentz A, Pfister H, Struff W, Kertai M, Segerer H, Modrow S. Humoral immune response against human bocavirus VP2 virus-like particles. Viral Immunol. 2008 Dec;21(4):443-9. doi: 10.1089/vim.2008.0045. PMID: 19115933.

82. Garcia-Garcia ML, Calvo Rey C, Del Rosal Rabes T. Pediatric Asthma and Viral Infection. Arch Bronconeumol. 2016 May;52(5):269-73. doi: 10.1016/j.arbres.2015.11.008. Epub 2016 Jan 4. PMID: 26766408; PMCID: PMC7105201.
83. Ringshausen FC, Tan AY, Allander T, Borg I, Arinir U, Kronsbein J, Hauptmeier BM, Schultze-Werninghaus G, Rohde G. Frequency and clinical relevance of human bocavirus infection in acute exacerbations of chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis. 2009;4:111-7. doi: 10.2147/copd.s4801. Epub 2009 Apr 15. PMID: 19436697; PMCID: PMC2672801.
84. von Mollendorf C, Berger D, Gwee A, Duke T, Graham SM, Russell FM, Mulholland EK; ARI review group. Aetiology of childhood pneumonia in low- and middle-income countries in the era of vaccination: a systematic review. J Glob Health. 2022 Jul 23;12:10009. doi: 10.7189/jogh.12.10009. PMID: 35866332; PMCID: PMC9305023.
85. Uribe-Gutiérrez G, Hernández-Santos H, Manjarrez-Zavala ME, Rosete-Olvera DP, Nava-Frías M, Moreno-Espinosa S, Velázquez-Guadarrama N, Gómez R, González-Márquez H, Fierro R, Mejía-Arangure JM, Zavala-Vega S, Hernández-Fernández M, Arellano-Galindo J. Prevalence and genotypes of the adenovirus infection as well detection of co-infection with bocavirus in Mexican immunosuppressed and non-immunosuppressed children with pneumonia. Clin Lab. 2014;60(8):1277-85. doi: 10.7754/clin.lab.2013.130449. PMID: 25185412.
86. Lu QB, Wo Y, Wang HY, Huang DD, Zhao J, Zhang XA, Zhang YY, Liu EM, Liu W, Cao WC. Epidemic and molecular evolution of human bocavirus in hospitalized children with acute respiratory tract infection. Eur J Clin Microbiol Infect Dis. 2015 Jan;34(1):75-81. doi: 10.1007/s10096-014-2215-7. Epub 2014 Jul 29. PMID: 25070494; PMCID: PMC7087953.
87. Pavia AT. Viral infections of the lower respiratory tract: old viruses, new viruses, and the role of diagnosis. Clin Infect Dis. 2011 May;52 Suppl 4(Suppl 4):S284-9. doi: 10.1093/cid/cir043. PMID: 21460286; PMCID: PMC3106235.
88. Peltola V, Söderlund-Venermo M, Jartti T. Human bocavirus infections. Pediatr Infect Dis J. 2013 Feb;32(2):178-9. doi: 10.1097/INF.0b013e31827fef67. PMID: 23328822.

89. Guido M, Quattrocchi M, Campa A, Zizza A, Grima P, Romano A, De Donno A. Human metapneumovirus and human bocavirus associated with respiratory infection in Apulian population. Virology. 2011 Aug 15;417(1):64-70. doi: 10.1016/j.virol.2011.04.016. Epub 2011 Jun 1. PMID: 21636105; PMCID: PMC7173056.
90. Jartti T, Hedman K, Jartti L, Ruuskanen O, Allander T, Söderlund-Venermo M. Human bocavirus-the first 5 years. Rev Med Virol. 2012 Jan;22(1):46-64. doi: 10.1002/rmv.720. Epub 2011 Oct 28. PMID: 22038931.
91. Petrarca L, Nenna R, Frassanito A, Pierangeli A, Di Mattia G, Scagnolari C, Midulla F. Human bocavirus in children hospitalized for acute respiratory tract infection in Rome. World J Pediatr. 2020 Jun;16(3):293-298. doi: 10.1007/s12519-019-00324-5. Epub 2019 Nov 27. PMID: 31776891; PMCID: PMC7091143.
92. Colazo Salbetti MB, Boggio GA, Abbiatti G, Montañez Sandoz A, Villarreal V, Torres E, Pedranti M, Zalazar JA, Moreno L, Adamo MP. Diagnosis and clinical significance of Human bocavirus 1 in children hospitalized for lower acute respiratory infection: molecular detection in respiratory secretions and serum. J Med Microbiol. 2022 Oct;71(10). doi: 10.1099/jmm.0.001595. PMID: 36301612.
93. Zhou L, Zheng S, Xiao Q, Ren L, Xie X, Luo J, Wang L, Huang A, Liu W, Liu E. Single detection of human bocavirus 1 with a high viral load in severe respiratory tract infections in previously healthy children. BMC Infect Dis. 2014 Jul 30;14:424. doi: 10.1186/1471-2334-14-424. PMID: 25078257; PMCID: PMC4125703.
94. Xu M, Arku B, Jartti T, Koskinen J, Peltola V, Hedman K, Söderlund-Venermo M. Comparative Diagnosis of Human Bocavirus 1 Respiratory Infection With Messenger RNA Reverse-Transcription Polymerase Chain Reaction (PCR), DNA Quantitative PCR, and Serology. J Infect Dis. 2017 May 15;215(10):1551-1557. doi: 10.1093/infdis/jix169. PMID: 28379530.
95. Meriluoto M, Hedman L, Tanner L, Simell V, Mäkinen M, Simell S, Mykkänen J, Korpelainen J, Ruuskanen O, Ilonen J, Knip M, Simell O, Hedman K, Söderlund-Venermo M. Association of human bocavirus 1 infection with respiratory disease in childhood follow-up study, Finland. Emerg Infect Dis. 2012 Feb;18(2):264-71. doi: 10.3201/eid1802.111293. Erratum in: Emerg Infect Dis. 2016 Sep;22(9):1695. PMID: 22305021; PMCID: PMC3310460.

96. Wang K, Wang W, Yan H, Ren P, Zhang J, Shen J, Deubel V. Correlation between bocavirus infection and humoral response, and co-infection with other respiratory viruses in children with acute respiratory infection. J Clin Virol. 2010 Feb;47(2):148-55. doi: 10.1016/j.jcv.2009.11.015. PMID: 20022295; PMCID: PMC7172221.
97. Shirkoohi R, Endo R, Ishiguro N, Teramoto S, Kikuta H, Ariga T. Antibodies against structural and nonstructural proteins of human bocavirus in human sera. Clin Vaccine Immunol. 2010 Jan;17(1):190-3. doi: 10.1128/CVI.00355-09. Epub 2009 Dec 2. PMID: 19955324; PMCID: PMC2812099.
98. Tamošiūnas PL, Petraitytė-Burneikienė R, Bulavaitė A, Marcinkevičiūtė K, Simutis K, Lasickienė R, Firantienė R, Ėmužytė R, Žvirblienė A, Sasnauskas K. Yeast-generated virus-like particles as antigens for detection of human bocavirus 1-4 specific antibodies in human serum. Appl Microbiol Biotechnol. 2016 Jun;100(11):4935-46. doi: 10.1007/s00253-016-7336-8. Epub 2016 Feb 4. PMID: 26846623.
99. Guido M, Zizza A, Bredl S, Lindner J, De Donno A, Quattrocchi M, Grima P, Modrow S; Seroepidemiology Group. Seroepidemiology of human bocavirus in Apulia, Italy. Clin Microbiol Infect. 2012 Apr;18(4):E74-6. doi: 10.1111/j.1469-0691.2011.03756.x. Epub 2012 Feb 6. PMID: 22309610.
100. Wong SS, Yuen KY. Antiviral therapy for respiratory tract infections. Respirology. 2008 Nov;13(7):950-71. doi: 10.1111/j.1440-1843.2008.01404.x. PMID: 18922142; PMCID: PMC7192202.
101. Bhat R, Almajhdi FN. Induction of Immune Responses and Immune Evasion by Human Bocavirus. Int Arch Allergy Immunol. 2021;182(8):728-735. doi: 10.1159/000514688. Epub 2021 Apr 19. PMID: 33873181.
102. Gerna G, Piralla A, Campanini G, Marchi A, Stronati M, Rovida F. The human bocavirus role in acute respiratory tract infections of pediatric patients as defined by viral load quantification. New Microbiol. 2007 Oct;30(4):383-92. PMID: 18080673.
103. Wang W, Guan R, Liu Z, Zhang F, Sun R, Liu S, Shi X, Su Z, Liang R, Hao K, Wang Z, Liu X. Epidemiologic and clinical characteristics of human bocavirus infection in children hospitalized for acute respiratory tract infection in Qingdao, China. Front Microbiol. 2022 Aug 10;13:935688. doi: 10.3389/fmicb.2022.935688. PMID: 36033842; PMCID: PMC9399728.