Original Investigation / *Özgün Araştırma*

**DOI:** 10.5578/ced.20260103 • *J Pediatr Inf 2026;20(1):e19-e27*

# The Frequency and Clinical Findings of Human Bocavirus in Hospitalized Children: A Tertiary Hospital Experience in İstanbul

## Yatan Çocuklarda İnsan Bocavirüs Sıklığı ve Klinik Bulguları: İstanbul'da Üçüncü Basamak Bir Hastane Deneyimi

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**Cite this article as:** Kılıçaslan Ö, Karbuz A, Kızmaz İşançlı D, Emre I, Beşel L, Kırmacı Ç, et al. The frequency and clinical findings of human bocavirus in hospitalized children: A tertiary hospital experience in İstanbul. J Pediatr Inf 2026;20(1):e19-e27.

**Abstract**

**Objective:** Human bocavirus (HBoV), the predominant viral contributor to respiratory tract infections (RTIs) in children, remains a global health challenge. This study aimed to delineate the frequency and clinical manifestations of HBoV in pediatric patients admitted to a tertiary healthcare hospital's pediatric infectious diseases clinic in İstanbul, thereby contributing to a broader understanding of its impact.

**Material and Methods:** A retrospective review of children under 18 years of age hospitalized for RTIs was conducted from June 2021 to February 2023. The demographic, clinical, and laboratory data were evaluated using descriptive statistics and comparative tests.

**Results:** A total of 48 hospitalized children tested positive for HBoV. Median age was 18.5 months [interquartile range (QR): 9.0-30.0], and 58.3% of the patients were male. Most patients (85.4%) had no chronic diseases and 66.7% were born via cesarean section. Autumn was the most frequent admission season (64.6%). The predominant symptoms were coughing (77.1%) and fever (75.0%). Respiratory distress was observed in 47.9% of the patients, and 75.0% required oxygen supplementation, primarily via masks (41.7%). Chest radiographs showed infiltration in 41.7%

**Öz**

**Giriş:** Çocuklarda solunum yolu enfeksiyonlarına (RTI) neden olan başlıca viral etkenlerden biri olan insan bocavirüsü (HBoV) küresel bir sağlık sorunu olmaya devam etmektedir. Bu çalışmanın amacı, İstanbul'da üçüncü basamak bir hastanenin pediyatrik enfeksiyon hastalıkları kliniğine başvuran çocuk hastalarda HBoV'nin sıklığını ve klinik belirtilerini tanımlamak ve böylece hastalığın etkisinin daha geniş bir şekilde anlaşılmasına katkıda bulunmaktır.

**Gereç ve Yöntemler:** Haziran 2021-Şubat 2023 tarihleri arasında RTI nedeniyle hastaneye yatırılan 18 yaş altı çocukların retrospektif bir incelemesi yapılmıştır. Demografik, klinik ve laboratuvar verileri tanımlayıcı istatistikler ve karşılaştırmalı testler kullanılarak değerlendirilmiştir.

**Bulgular:** Toplamda hastaneye yatırılmış 48 çocukta HBoV pozitifliği saptandı. Medyan yaş 18.5 ay [çeyreklikler arası açıklık (IQR): 9.0-30.0] olup hastaların %58.3'ü erkekti. Hastaların büyük çoğunluğunun (%85.4) altta yatan kronik hastalığı yoktu ve %66.7'si sezaryen ile doğmuştu. Başvuru mevsimi en sık sonbahardı (%64.6). En yaygın semptomlar öksürük (%77.1) ve ateş (%75.0) idi. Solunum sıkıntısı %47.9 oranında gözlendi; hastaların %75'i oksijen desteğine ihtiyaç duydu ve en yaygın uygula-

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**Received:** 06.02.2025 **Accepted:** 27.05.2025
**Available Online Date:** 17.03.2026

of the cases. Inhaler use was reported in 62.5% of patients, whereas antibiotics were initiated in 85.4% the of patients. Oseltamivir was administered only to patients with co-infection (20.0%, p= 0.043), and steroid use was more frequent in this group (46.7% vs. 22.2%, p= 0.090). Among all patients, 22.9% required intensive care unit admission. Co-infection with at least one other respiratory virus, most commonly respiratory syncytial virus (20.8%), was observed in 62.5% of the cases. No significant differences were found between the HBoV-only and HBoV-co-infected groups in terms of demographic variables, symptoms, laboratory parameters, or hospitalization duration.

**Conclusion:** This study elucidated the pivotal role of HBoV in pediatric RTIs. HBoV is associated with a high rate of coinfection with other respiratory viruses. This study contributes to a broader understanding of HBoV infections and can guide clinicians in implementing appropriate treatment strategies.

**Keywords:** Human bocavirus (HBoV), pediatric respiratory tract infections (RTIs), co-infections, viral etiology

ma yöntemi maske ile sağlandı (%41.7). Göğüs radyografisinde olguların %41.7'sinde infiltrasyon saptandı. İnhaler kullanım oranı %62.5, antibiyotik başlama oranı ise %85.4 idi. Oseltamivir sadece ek viral enfeksiyonu olan hastalara uygulandı (%20.0; p= 0.043) ve steroid kullanımı bu grupta daha yüksekti (%46.7'ye karşı %22.2; p= 0.090). Tüm hastaların %22.9'u yoğun bakım ünitesine yatırıldı. Hastaların %62.5'inde en az bir ek solunum yolu virüsü ile ko-enfeksiyon mevcuttu; en sık saptanan etken respiratuvar sinsityal virüstü (%20.8). İnsan bocavirüsü ile tek enfekte olanlar ve ko-enfekte olan gruplar arasında demografik özellikler, semptomlar, laboratuvar parametreleri veya hastanede yatış süresi açısından anlamlı fark bulunmadı.

**Sonuç:** Bu çalışma, HBoV'nin pediyatrik RTI'lardaki önemli rolünü aydınlatmaktadır. İnsan bocavirüsü, diğer solunum yolu virüsleri ile yüksek oranda ko-enfeksiyon göstermektedir. Bu araştırma, HBoV enfeksiyonlarının daha iyi anlaşılmasına katkıda bulunmakta ve uygun tedavi stratejilerinin uygulanmasında klinisyenlere yol gösterebilir.

**Anahtar Kelimeler:** İnsan bocavirüsü (HBoV), pediyatrik solunum yolu enfeksiyonları (RTIs), ko-enfeksiyonlar, viral etiyoloji

## Introduction

Respiratory tract infections (RTIs) continue to pose substantial health challenges among pediatric populations globally given their contribution to morbidity and mortality rates. Viruses are predominantly responsible for these infections, with human bocavirus (HBoV) emerging as a critical pathogen after its identification in 2005 (1). HBoV, a linear single-stranded DNA virus belonging to the Parvoviridae family, is typically associated with acute RTIs, particularly in children below five years of age (2-4).

Several studies have investigated the role of HBoV in pediatric RTIs and their frequency across diverse geographic locations. A study conducted in Egypt identified HBoV as a significant viral contributor to pediatric RTIs, as evidenced by findings at Benha University Hospital (5). Correspondingly, research in India has underscored the prevalence of HBoV in children with acute RTIs (4). Italian research has outlined the clinical and serological attributes of pediatric RTIs associated with HBoV (2).

Observations indicate a variation in the frequency of HBoV infections in pediatric patients depending on regional factors. For instance, an investigation conducted in Singapore revealed that the frequency of HBoV infection among 1024 hospitalized children was 8% (6). Similarly, Iranian research has confirmed the presence of HBoV in 8% of 261 Iranian children aged <5 years experiencing acute respiratory infections (7). Nevertheless, the precise frequency of HBoV infections and their contribution to the overall pediatric RTI burden remain somewhat nebulous, warranting further comprehensive research.

This study contributes to the growing body of knowledge by examining the frequency and clinical manifestations of HBoV in children hospitalized at the pediatric infectious diseases clinic of a tertiary healthcare hospital in Istanbul. A thorough understanding of the burden of HBoV in this region will be instrumental in crafting suitable management strategies and contribute to a more comprehensive global understanding of HBoV in pediatric RTIs.

## Materials and Methods

This study was retrospectively conducted by scanning the files of children under 18 years of age who were hospitalized for upper and lower RTIs in the pediatric infectious diseases clinic between June 2021 and February 2023. Demographic, clinical, and laboratory data were evaluated. This study was approved by the local ethics committee of Prof. Dr. Cemil Taşçıoğlu City Hospital (13.01.2025/05).

Nasopharyngeal swab samples were collected from viral transport media (Copan Diagnostics, Italy). RTI pathogens were detected using the Bio-Speedy Respiratory Tract real-time polymerase chain reaction (PCR) MX -24S multiplex PCR Panel (Bioeksen, Türkiye).

Inclusion criterion was children under 18 years of age hospitalized for RTIs with a confirmed HBoV detection via multiplex PCR. Exclusion criteria included incomplete clinical records, hospitalization for non-respiratory causes, or unrelated immunosuppressive conditions. From an initial pool of 61 eligible patients, 13 were excluded, resulting in a final cohort of 48 patients.

### Statistical analysis

The mean, standard deviation (SD), median lowest, highest, frequency, and ratio values were used in the descriptive statistics of the data. The distribution of variables was tested using the Kolmogorov-Smirnov test. For non-normally distributed variables, medians and interquartile ranges (IQR) were calculated and analyzed using the Mann-Whitney U test. The chi-square test was used to analyze independent qualitative data, and the Fischer test was used when the chi-square test conditions were not met. SPSS 28.0 program was used for the analysis.

## Results

Our study population consisted of 48 children with HBoV infection, ranging in age from 1.5 to 102.0 months, with a median age of 18.5 months (IQR: 9.0-30.0). Sex distribution showed a slight male predominance, with 41.7% female patients and 58.3% male patients.

Most of the children (85.4%) had no chronic diseases. However, among those with preexisting chronic conditions (14.6%), the most common was Down syndrome (6.3%). Hospital admission period ranged from June to December, with November accounting for the highest percentage of admissions (52.1%). When categorized by season, most admissions occurred in the autumn (64.6%). Regarding birth-related variables, most children were born via cesarean section (66.7%), in the term period (75.0%), and with an average birth weight for gestational age (85.4%). The results of the evaluation of the demographic, clinical, and laboratory data are presented in Table 1.

**Table 1.** The demographic, clinical, and laboratory data of the patients

| | | n | % |
|---|---|---|---|
| Sex | Female | 20 | 41.7 |
| | Male | 28 | 58.3 |
| Chronic disease | None | 41 | 85.4 |
| | Yes | 7 | 14.6 |
| Down syndrome | | 3 | 6.3 |
| Epilepsy | | 2 | 4.2 |
| Hypothyroidism | | 1 | 2.1 |
| Hypotonicity | | 1 | 2.1 |
| Admission (month) | November | 25 | 52.1 |
| | December | 12 | 25.0 |
| | October | 4 | 8.3 |
| | June | 3 | 6.3 |
| | September | 2 | 4.2 |
| | January | 1 | 2.1 |
| | February | 1 | 2.1 |
| | Autumn | 31 | 64.6 |
| Admission (season) | Winter | 14 | 29.2 |
| | Summer | 3 | 6.3 |
| | Cesarean section | 32 | 66.7 |
| Type of birth | NSD | 16 | 33.3 |
| | Term | 36 | 75.0 |
| Birth week | Preterm | 12 | 25.0 |
| | AGA | 41 | 85.4 |
| Birth weight | SGA | 6 | 12.5 |
| | LGA | 1 | 2.1 |

NSD: Normal spontaneous delivery, AGA: Appropriate for gestational age, SGA: Small for gestational age, LGA: Large for gestational age.

The most common symptoms observed in the children were cough (77.1%) and fever (75.0%). Respiratory distress was observed in 47.9% of the patients, and gastrointestinal symptoms such as diarrhea and vomiting were reported in 18.8% of the patients. Upon physical examination, 89.6% of the children showed pathological findings, with the most common being a coarse breathing voice (75.0%). Chest radiograms showed normal findings in 35.4% of the patients, whereas infiltration was detected in 41.7% of the cases. Regarding treatment, inhaler usage was reported in 62.5% of the patients. Most children (85.4%) received antibiotics until the virus was detected, and ampicillin-sulbactam was the most commonly used antibiotic (45.8%). A significant proportion of the patients (75.0%) required oxygen supplementation, with the most common method being via mask (41.7%). Mean number of febrile days was 2.85 (± 2.19 SD), with a median of 3.0 days. Mean hospital stay was 6.65 days (± 2.38) days. Among these patients, 22.9% required admission to the intensive care unit. Data related to the symptoms, physical examination findings, chest X-ray findings, and treatment approaches of the study population are presented in Table 2.

Of the patients, 41.7% had one additional virus detected, 16.7% had two, and 4.2% had three. A sizable proportion (37.5%) of the patients showed no viruses other than HBoV. Regarding the specific viruses identified, respiratory syncytial virus was detected in 20.8% of the children. Human rhino/enterovirus and coronavirus OC43 were detected in 16.7% and 14.6% of the samples, respectively. Table 3 illustrates the co-infection profile of the patients, detailing the number of additional viruses detected along with HBoV.

In the group with no additional virus to HBoV, 72.2% were male and 27.8% were female, while the group with additional viruses had an equal distribution of sex (50.0% each; p= 0.131). In these groups, chronic disease was present in 5.6% and 20.0% of the patients, respectively (p= 0.170). The patients' laboratory parameters were also compared, and no significant differences were found. In terms of birth characteristics, there were no significant differences in birth type, birth week, or birth weight. The length of hospital stay and requirement for intensive care unit (ICU) admission did not differ significantly between the two groups. ICU admission was required for 11.1% of the HBoV-only patients and 30.0% of those with co-infections (p= 0.302). High-flow nasal cannula (HNFC) was used more frequently in patients with co-infection (40.0% vs. 11.1%, p= 0.029) (Table 4).

Cough was present in 77.8% and 76.7% of the patients, respectively (p= 0.929). The two groups showed no significant differences in the incidence of fever, respiratory distress, diarrhea/vomiting, rash, or other symptoms. Physical examination findings were similar between the groups. However, retraction was more frequent in patients infected

**Table 2.** The symptoms, physical examination findings, chest X-ray findings, and treatment approaches

| | | n | % |
|---|---|---|---|
| **Symptom** | | | |
| Cough | | 37 | 77.1 |
| Fever | | 36 | 75.0 |
| Respiratory distress | | 23 | 47.9 |
| Diarrhea/Vomiting | | 9 | 18.8 |
| Other | | 6 | 12.5 |
| | Rash | 2 | 4.2 |
| | Convulsion | 3 | 6.3 |
| | Lymphadenopathy | 1 | 2.1 |
| Physical Examination | Pathological | 43 | 89.6 |
| | Normal | 5 | 10.4 |
| **Respiratory-Lung** | | | |
| Coarseness in respiratory sounds | | 36 | 75.0 |
| Expiratory elongation/Rhonchus | | 33 | 68.8 |
| Ral | | 25 | 52.1 |
| Retraction | | 19 | 39.6 |
| Other | | 6 | 12.5 |
| | Dehydrated | 1 | 2.1 |
| | Rash | 2 | 4.2 |
| | Lymphadenopathy | 1 | 2.1 |
| | Oropharynx hyperemic | 2 | 4.2 |
| Chest radiogram | Normal | 17 | 35.4 |
| | Infiltration | 20 | 41.7 |
| | Ventilation increase | 4 | 8.3 |
| | Lobar pneumonia | 3 | 6.3 |
| | Fissures | 3 | 6.3 |
| | Infiltration+atelectasis | 1 | 2.1 |
| $O_2$ supplementation | (-) | 12 | 25.0 |
| | (+) | 36 | 75.0 |
| $O_2$ application way | Mask | 20 | 41.7 |
| | HNFC | 14 | 29.2 |
| | MV | 2 | 4.2 |
| **Medication** | | | |
| Inhaler | | 30 | 62.5 |
| Antibiotic | | 41 | 85.4 |
| Ampicillin-sulbactam | | 22 | 45.8 |
| Ampicillin-cefotaxime | | 4 | 8.3 |
| Ceftriaxone | | 13 | 27.1 |
| Azithromycin/clarithromycin | | 18 | 37.5 |
| Teicoplanin | | 8 | 16.7 |
| Piperacillin-tazobactam | | 3 | 6.3 |
| Oseltamivir | | 6 | 12.5 |
| **Steroid** | | 18 | 37.5 |

HNFC: High flow nasal cannula, MV: Mechanical ventilation.

**Table 3.** The distribution of additional viruses detected alongside HBoV in pediatric patients with respiratory tract infections

| | | n | % |
|---|---|---|---|
| Number of Additional Viruses Detected with HBoV | Only HBoV | 18 | 37.5 |
| | I | 20 | 41.7 |
| | II | 8 | 16.7 |
| | III | 2 | 4.2 |
| Respiratory syncytial virus | | 10 | 20.8 |
| Human rhino/Enterovirus | | 8 | 16.7 |
| Corona OC43 | | 7 | 14.6 |
| Influenza A | | 4 | 8.3 |
| Parainfluenza type 3 | | 3 | 6.3 |
| Adenovirus | | 3 | 6.3 |
| SARS-CoV-2 | | 3 | 6.3 |
| Corona 229E | | 2 | 4.2 |
| Human metapneumovirus | | 1 | 2.1 |
| Corona NL63 | | 1 | 2.1 |

OC43/NL63/229E: Human coronavirus subtypes.

with additional viruses (50.0% vs. 22.2%, p= 0.057). There were no significant differences in radiological findings between the two groups. Normal findings were reported in 27.8% of the patients without additional viruses and in 40.0% of those with additional viruses (p= 0.681). Table 5 compares the symptoms, physical examination findings, and radiological findings between patients with only HBoV and those with additional viral infections.

Regarding oxygen supplementation, 72.2% of the patients without additional viruses and 76.7% of patients with additional viruses required oxygen supplementation (p= 0.731). HNFC was used more frequently in the group with additional viruses (40.0% vs. 11.1%). Mechanical ventilation was only required in the group with additional viruses (6.7%). There were no significant differences in the use of inhalers (p= 0.441) or antibiotics (p= 0.751). Finally, steroids were more common in the group with additional viruses, although the difference was not statistically significant (46.7% vs. 22.2%, p= 0.090). Table 6 compares the treatment and management strategies between the groups with and without additional viruses.

## Discussion

Our study contributes to the understanding of HBoV infections in pediatric patients, particularly in the context of lower RTIs. We revisit, validate, and extend various aspects of the existing literature to further enhance the comprehension

**Table 4.** Comparison of demographic and clinical characteristics between the groups with and without an additional virus to HBoV

| | No Additional Virus to HBoV | | | HBoV+Additional Virus | | | | |
|---|---|---|---|---|---|---|---|---|
| | Mean ± SD | | | Mean ± SD | | | | p |
| Age (month) | 26.8 | ± | 18.3 | 22.0 | ± | 23.5 | 0.150 | M |
| CRP | 21.8 | ± | 26.5 | 18.6 | ± | 25.8 | 0.602 | M |
| PCT | 2.2 | ± | 4.1 | 1.3 | ± | 1.5 | 1,000 | M |
| WBC (x$10^3$) | 11.4 | ± | 4.3 | 12.1 | ± | 5.8 | 0.662 | T |
| Neutrophil (x$10^3$) | 13.2 | ± | 25.5 | 7.3 | ± | 4.5 | 0.717 | M |
| Lymphocyte (x$10^3$) | 2.8 | ± | 1.4 | 3.9 | ± | 3.3 | 0.565 | M |
| Eosinophil | 195.0 | ± | 396.5 | 142.3 | ± | 190.5 | 0.822 | M |
| Monocyte | 871.1 | ± | 478.3 | 672.7 | ± | 543.2 | 0.207 | T |
| Platelet (x$10^3$) | 388.9 | ± | 133.9 | 348.3 | ± | 160.6 | 0.373 | T |
| MPV | 8.8 | ± | 1.0 | 9.4 | ± | 1.1 | 0.156 | M |
| HB | 11.9 | ± | 2.1 | 11.2 | ± | 3.3 | 0.741 | M |
| ALT | 14.9 | ± | 4.1 | 23.0 | ± | 22.1 | 0.315 | M |
| AST | 34.3 | ± | 11.3 | 39.0 | ± | 31.6 | 0.966 | M |
| Urea | 19.7 | ± | 8.1 | 17.0 | ± | 10.5 | 0.346 | T |
| Creatine | 0.3 | ± | 0.1 | 0.3 | ± | 0.1 | 0.224 | M |
| Number of days with fever | 2.94 | ± | 1.92 | 2.80 | ± | 2.37 | 0.429 | M |
| Number of hospitalization days | 6.33 | ± | 2.52 | 6.83 | ± | 2.32 | 0.371 | M |

**Table 4.** Comparison of demographic and clinical characteristics between the groups with and without an additional virus to HBoV (continue)

| | | No Additional Virus to HBoV | | HBoV+Additional Virus | | | p |
|---|---|---|---|---|---|---|---|
| | | n | % | n | % | | |
| Sex | Female | 5 | 27.8 | 15 | 50.0 | 0.131 | $X^2$ |
| | Male | 13 | 72.2 | 15 | 50.0 | | |
| Chronic disease | None | 17 | 94.4 | 24 | 80.0 | 0.170 | $X^2$ |
| | Yes | 1 | 5.6 | 6 | 20.0 | | |
| Admission (season) | Autumn | 13 | 72.2 | 18 | 60.0 | 0.071 | $X^2$ |
| | Summer | 3 | 16.7 | 0 | 0.0 | | |
| | Winter | 2 | 11.1 | 12 | 40.0 | | |
| Type of birth | CS | 13 | 72.2 | 19 | 63.3 | 0.527 | $X^2$ |
| | NSD | 5 | 27.8 | 11 | 36.7 | | |
| Birth week | Term | 12 | 66.7 | 24 | 80.0 | 0.302 | $X^2$ |
| | Preterm | 6 | 33.3 | 6 | 20.0 | | |
| Birth weight | AGA | 16 | 88.9 | 25 | 83.3 | 0.915 | $X^2$ |
| | SGA | 2 | 11.1 | 4 | 13.3 | | |
| | LGA | 0 | 0.0 | 1 | 3.3 | | |
| ICU admission | (-) | 16 | 88.9 | 21 | 70.0 | 0.302 | $X^2$ |
| | (+) | 2 | 11.1 | 9 | 30.0 | | |

[M]Mann-Whitney U test, [t]Independent sample t test, $X^2$Chi-square test (Fischer's exact test).
HBoV: Human bocavirus, SD: Standard deviation, CS: Cesarean section, NSD: Normal spontaneous birth, AGA: Average for gestational age, SGA: Small for gestational age, LGA: Large for gestational age.

of this infection. In concordance with previous findings, such as those by Kesebir et al., our study's demographics indicated a marginal male predominance, with a mean age of 23.8 months among HBoV infections (8). This finding suggests a potential sex-related disparity in susceptibility that warrants further exploration.

The peak incidence of HBoV infections during autumn noted in our study is consistent with studies by Calvo et al. and Silva et al., suggesting a plausible relationship between environmental conditions and HBoV transmission (9,10). The seasonal pattern of HBoV infection, with a peak in autumn, is consistent with a body of research pointing to a higher frequency of HBoV infections during colder months (9,11). Liu et al. observed dual peaks in the prevalence of HBoV in the summer (from June to September) and winter (from November to December) months. They reported a notable positive association between the incidence of HBoV and average temperature, in contrast to a negative relationship with mean relative humidity. Interestingly, the mean temperature of the previous month provided a more robust explanation for prevalence than the temperature of the current month (12). This pattern suggests a possible relationship between environmental conditions and HBoV transmission, an area that requires further exploration.

Our study found fever and cough to be the most common symptoms of HBoV infection, consistent with numerous previous studies, confirming the typical clinical profile of HBoV infection (3,9,10). The prevalence of these symptoms underscores the need for heightened diagnostic suspicion in pediatric patients presenting with such a clinical picture. The results of our study reaffirmed that fever and cough are the predominant symptoms associated with HBoV infection, a finding that corresponds with a number of previous studies, including those conducted by Bakir et al. and Kesebir et al. (1,8). This pattern of symptoms effectively consolidates the established clinical profile of HBoV infection. In light of these findings, it is evident that the prominence of these symptoms (fever and cough) calls for an elevated level of alertness and suspicion in the diagnostic process, particularly when dealing with pediatric patients exhibiting such symptoms. This is crucial, as early identification and appropriate management of HBoV infections can significantly impact the course of the disease, especially in this vulnerable population. However, it is noteworthy that while fever and cough are common symptoms, the presentation of HBoV infections can vary, and other symptoms or complications should not be dismissed. Here, we analyzed patients with a commonly lower RTI; however, HBoV infection may present with diarrhea, vomiting, rash, encephalitis, or eye symptoms (3,9,10). Furthermore, it is important to consider co-infections that may complicate or amplify symptomatology.

**Table 5.** Comparison of symptoms, physical examination findings, and other clinical features between the groups with and without an additional virus to HBoV

| | | No Additional Viruses to HBoV | | HBoV+Additional Virus | | p | |
|---|---|---|---|---|---|---|---|
| | | n | % | n | % | | |
| **Symptom** | | | | | | | |
| Fever | | 13 | 72.2 | 23 | 76.7 | 0.731 | $X^2$ |
| Cough | | 14 | 77.8 | 23 | 76.7 | 0.929 | $X^2$ |
| Respiratory distress | | 7 | 38.9 | 16 | 53.3 | 0.332 | $X^2$ |
| Diarrhea/Vomiting | | 2 | 11.1 | 7 | 23.3 | 0.294 | $X^2$ |
| Other | | 2 | 11.1 | 4 | 13.3 | 0.822 | $X^2$ |
| Rash | | 2 | 11.1 | 0 | 0.0 | | |
| Convulsion | | 0 | 0.0 | 3 | 10.0 | | |
| Lymphadenopathy | | 0 | 0.0 | 1 | 3.3 | | |
| Physical Examination | Pathological | 16 | 88.9 | 27 | 90.0 | 1.000 | $X^2$ |
| | Normal | 2 | 11.1 | 3 | 10.0 | | |
| **Respiratory-Lung** | | | | | | | |
| Coarseness in respiratory sounds | | 13 | 72.2 | 23 | 76.7 | 0.731 | $X^2$ |
| In expiration/Rhonchus | | 12 | 66.7 | 21 | 70.0 | 0.809 | $X^2$ |
| Ral | | 9 | 50.0 | 16 | 53.3 | 0.823 | $X^2$ |
| Paravertebral retraction | | 4 | 22.2 | 15 | 50.0 | 0.057 | $X^2$ |
| Other | | 3 | 16.7 | 3 | 10.0 | 0.499 | $X^2$ |
| Dehydrated | | 0 | 0.0 | 1 | 3.3 | | |
| Rash | | 2 | 11.1 | 0 | 0.0 | | |
| Lymphadenopathy | | 0 | 0.0 | 1 | 3.3 | | |
| Oropharynx hyperemic | | 1 | 5.6 | 1 | 3.3 | | |
| **Chest X-ray** | | | | | | | |
| Normal | | 5 | 27.8 | 12 | 40.0 | 0.681 | $X^2$ |
| Infiltration | | 7 | 38.9 | 13 | 43.3 | | |
| Fissures | | 3 | 16.7 | 0 | 0.0 | | |
| Lobar pneumonia | | 3 | 16.7 | 0 | 0.0 | | |
| Ventilation increase | | 0 | 0.0 | 4 | 13.3 | | |
| Infiltration+atelectasis | | 0 | 0.0 | 1 | 3.3 | | |

$X^2$Chi-square test (Fischer's exact).
HBoV: Human bocavirus.

A key finding of our study was the prevalence of co-infections with HBoV and other respiratory viruses. This aligns with the results of Allander et al., Foulongne et al., and others have reported co-infections as a recurring theme in HBoV infection (13,14). Given the frequency of co-infection, future studies must dissect the interactions between HBoV and other respiratory viruses to elucidate the effects of co-infection on disease trajectory. Investigating respiratory tract illnesses can be challenging, given the wide array of pathogens that can produce similar symptoms. Moreover, respiratory tract samples from healthy individuals or patients without respiratory symptoms are seldom accessible, which complicates the study. Allender et al. addressed this problem by comparing 258 cases of lower RTIs with a confirmed cause to 282 instances in which the cause remained unknown (13). They primarily found HBoV in the segment of patients with lower RTI with unresolved etiology, and this uneven distribution indicated that HBoV is a probable pathogenic agent of lower RTI. The three instances of co-infection involving HBoV and another virus did not negate this conclusion. Co-infections are often encountered in studies with lower RTI, likely because of the high prevalence of viral infections among infants and young children.

**Table 6.** Comparison of the treatments and medications administered to patients with and without an additional virus to HBoV

| | | No Additional Viruses to HBoV | | HBoV+Additional Virus | | p | |
|---|---|---|---|---|---|---|---|
| | | n | % | n | % | | |
| $O_2$ supplementation | (-) | 5 | 27.8 | 7 | 23.3 | 0.731 | $X^2$ |
| | (+) | 13 | 72.2 | 23 | 76.7 | | |
| $O_2$ application way | Mask | 11 | 61.1 | 9 | 30.0 | | |
| | HNFC | 2 | 11.1 | 12 | 40.0 | | |
| | MV | 0 | 0.0 | 2 | 6.7 | | |
| **Medication** | | | | | | | |
| **Inhaler** | | 10 | 55.6 | 20 | 66.7 | 0.441 | $X^2$ |
| **Antibiotic** | | 15 | 83.3 | 26 | 86.7 | 0.751 | $X^2$ |
| Ampicillin-sulbactam | | 11 | 61.1 | 11 | 36.7 | 0.100 | $X^2$ |
| Ampicillin-cefotaxime | | 0 | 0.0 | 4 | 13.3 | 0.282 | $X^2$ |
| Ceftriaxone | | 4 | 22.2 | 9 | 30.0 | 0.557 | $X^2$ |
| Azithromycin/clarithromycin | | 7 | 38.9 | 11 | 36.7 | 0.878 | $X^2$ |
| Teicoplanin | | 4 | 22.2 | 4 | 13.3 | 0.424 | $X^2$ |
| Piperacillin-tazobactam | | 1 | 5.6 | 2 | 6.7 | 1.000 | $X^2$ |
| Oseltamivir | | 0 | 0.0 | 6 | 20.0 | **0.043** | $X^2$ |
| Steroid | | 4 | 22.2 | 14 | 46.7 | 0.090 | $X^2$ |

$X^2$Chi-square test (Fischer's exact test).
HBoV: Human bocavirus, HNFC: High flow nasal cannula, MV: Mechanical ventilation.

Aligning with the works of Pierangelli et al. and Calvo et al. our study confirmed the frequent occurrence of coinfections with HBoV and other respiratory viruses (15,16). However, our comparative analysis revealed intriguing trends. Despite the lack of significant disparities in demographic, laboratory, and birth characteristics between the co-infected patients and those with HBoV monoinfection, the co-infected group exhibited a higher frequency of retraction and greater demand for HNFC and mechanical ventilation, echoing the findings of Franz et al. (17). Furthermore, we found that treatment strategies for the co-infected group diverged, marked by increased use of oseltamivir (only influenza) and steroids, underlining the potential need for personalized treatment plans for co-infected patients, an aspect underscored by Yen et al. (18). Nevertheless, our study did not find any significant differences in symptomatology, physical examination findings, radiological findings, or duration of hospital stay between the two groups. This is partially inconsistent with the findings of Schildgen et al., who reported a more severe clinical course in co-infected patients (19). In addition, our findings are consistent with those of Kim et al., who reported that co-infection with numerous viruses does not correlate with increased disease severity in pediatric patients with bronchiolitis (20).

This study has several limitations. Its retrospective and cross-sectional design precludes causal inference. The limited sample size reduces statistical power and generalizability. Additionally, being a single-center study may introduce referral bias. These limitations should be addressed in future multicenter and prospective studies.

## Conclusion

Although our findings add valuable insights to the existing literature, some limitations must be noted. The study's small sample size may constrain the generalizability of the results, and its cross-sectional nature limits our ability to infer causality. Our results highlight the complex nature of HBoV infections in pediatric patients and the possible role of co-infections in shaping clinical presentations and treatment approaches.

**Acknowledgments**

We thank the virology and molecular diagnostics laboratory team for their technical assistance. We also express our sincere appreciation to Assoc. Prof. Feruza Turan Sönmez for her valuable supervision and contribution to the conceptualization and planning of this study.

**Ethics Committe Approval:** This study has been approved by the Non-Interventional Clinical Research Ethics Committee of Prof. Dr. Cemil Taşcıoğlu City Hospital (Decision no: 05, Date: 14.01.2025).
**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - ÖK, AK, DKİ; Design - All of authors; Supervision - All of authors; Resource - All of authors; Data Collection and/or processing - ÖK, ÇK, AB; Analysis and/or interpretation - ÖK, AK, IE, LB; Literature search - All of authors; Writing - All of authors; Critical review - All of authors.

**Conflict of Interest:** All authors declare that they have no conflict of interest.

**Financial Disclosure:** The authors declared that this study has received no financial support.

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