

# The Impact of Human Parainfluenza Virus on Child Health: A Clinical Study

## İnsan Parainfluenza Virüsü'nün Çocuk Sağlığı Üzerindeki Etkileri: Bir Klinik Araştırma

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### ABSTRACT

**Objective:** This study aims to identify the clinical characteristics of Human Parainfluenza Virus (HPIV) infections in children, evaluate morbidity and mortality rates, and investigate the impact of chronic diseases on the course of these infections.

**Material and Methods:** The research was conducted retrospectively and cross-sectionally on children aged 0-18 who tested positive for HPIV in the respiratory viral panel at Ankara Bilkent City Hospital Children's Hospital between August 2019 and July 2023. Patients with multiple virus positivity were excluded from the study.

**Results:** The study included 160 patients, of whom 61.2% were male and 38.8% were female. The most common presenting symptoms were cough (66.3%) and fever (52.5%). Of the patients, 41.2% were treated as inpatients, and 19.6% received care in the intensive care unit. The need for invasive or noninvasive mechanical ventilation was observed in 10% of the patients. There was a statistically significant association between the presence of lung infiltration and chronic disease with hypoxia ( $p < 0.001$ ).

**Conclusion:** While HPIV infections are generally mild, they can lead to significant morbidity and the need for intensive care in children with chronic diseases. These findings highlight the necessity for careful clinical evaluation and close monitoring of children with HPIV infections. The study's results may contribute to the management and treatment strategies for HPIV infections in the pediatric population.

**Key Words:** Child, Parainfluenza virus, Pneumonia, Upper respiratory tract infection

### ÖZ

**Amaç:** Bu çalışma, İnsan Parainfluenza Virüsü (HPIV) enfeksiyonlarının çocuklarda klinik özelliklerini belirlemek, morbidite ve mortalite oranlarını değerlendirmek, ve kronik hastalıkların bu enfeksiyonların seyrine etkisini araştırmak amacıyla yapılmıştır.

**Gereç ve Yöntemler:** Araştırma, Ağustos 2019-Temmuz 2023 tarihleri arasında Ankara Bilkent Şehir Hastanesi Çocuk Hastanesi'ne başvuran, solunum yolu viral panelinde HPIV pozitifliği saptanan 0-18 yaş arası çocuklar üzerinde retrospektif ve kesitsel olarak yapılmıştır. Çoklu virüs pozitifliği gösteren hastalar çalışma dışında bırakılmıştır. İstatistiksel analizler SPSS 23.0 kullanılarak gerçekleştirilmiş ve  $p < 0.050$  anlamlı kabul edilmiştir.

**Bulgular:** Çalışmaya 160 hasta dahil edildi ve bunların %61.2'si erkek, %38.8'i kadındı. En sık başvuru şikayetleri öksürük (%66.3) ve ateş (%52.5)'di. Hastaların %41.2'si yatırılarak tedavi edilmiş, %19.6'sı yoğun bakım ünitesinde

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**Ethics Committee Approval / Etik Kurul Onayı:** This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Ankara Bilkent City Hospital, Ethics Committee No. 1 (24.04.2024/ 140).

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tedavi görmüştür. İnvaziv veya noninvaziv mekanik ventilasyon ihtiyacı %10 olarak gözlenmiştir. Akciğer infiltrasyonu ve kronik hastalık varlığının hipoksi ile istatistiksel olarak anlamlı ilişkisi bulunmuştur ( $p < 0.001$ ).

**Sonuç:** HPIV enfeksiyonları genellikle hafif seyirli olsa da, kronik hastalığı olan çocuklarda ciddi morbiditelere ve yoğun bakım ihtiyacına yol açabilmektedir. Bu bulgular, HPIV enfeksiyonu olan çocuklarda dikkatli klinik değerlendirme ve yakın takip gerekliliğini vurgulamaktadır. Çalışma, pediatrik yaş grubunda HPIV enfeksiyonlarının yönetimi ve tedavi stratejilerinin belirlenmesine katkı sağlayabilir.

**Anahtar Sözcükler:** Çocuk, Parainfluenza virüs, Pnömoni, Üst solunum yolu enfeksiyon

## INTRODUCTION

Human Parainfluenza Virus (HPIV) is an enveloped, negative-sense, single-stranded RNA virus belonging to the Paramyxoviridae family (1). It was first isolated from children with croup in the late 1950s (2). Today, it has been shown to constitute a significant portion of lower respiratory tract infections in children (3).

HPIV infections typically present with symptoms of upper respiratory tract infections, including fever, cough, runny nose, and sore throat (4). However, HPIV can cause severe respiratory diseases in young children or those with comorbid conditions (5). It is reported as the second most common cause of respiratory tract infections in children under five years of age, after RSV viruses (5–7).

This study aimed to determine the clinical features, morbidity, and mortality of HPIV infections, with a particular focus on assessing the severity of outcomes in children with chronic diseases.

## MATERIALS and METHODS

Our study was designed as a retrospective, cross-sectional analysis. It included all children aged 0-18 years who presented to Ankara Bilkent City Hospital's Children's Hospital between August 2019 and July 2023 and tested positive for HPIV on the respiratory viral panel. Patients with simultaneous positivity for other viruses were excluded from the study.

Respiratory pathogens were identified using a multiplex real-time PCR assay (Rotor-Gene Q, QIAGEN, Germantown, MD). The admission dates and seasons, presenting complaints, history of chronic diseases, laboratory values, lung infiltrations, hypoxia status, need for hospitalization, hospitalization settings (ward or intensive care), and requirements for mechanical ventilation (invasive or non-invasive) of patients who tested positive for HPIV were retrospectively reviewed. Patients with missing clinical or laboratory data were excluded.

The study population was divided into three groups based on the presence of chronic diseases. The first group comprised individuals with primary or secondary immunodeficiencies, the second included those with chronic lung diseases, and the third consisted of patients without respiratory-affecting chronic diseases or those free from any chronic conditions.

Statistical analyses were conducted using Statistical analyses were conducted using IBM Statistical Package for the Social Sciences, version 23.0 (SPSS Inc., Armonk, NY, IBM Corp., USA). The Kolmogorov-Smirnov test and histograms were used to assess the normality of numerical and continuous variables. Normally distributed numerical data were expressed as means and Standard Deviation (SD), while non-normally distributed data were presented as medians and Interquartile Range (IQR). Categorical variables were expressed as percentages (%) and counts (n). Continuous variables with normal distributions between two groups were compared using the Student's T-test, whereas the Mann-Whitney U test was employed for those not fitting a normal distribution. The Kruskal-Wallis test was used to analyze continuous variables from multiple groups without a normal distribution. Categorical variables were analyzed using Pearson's chi-square or Fisher's Exact Test. When comparing more than one group, p-values were adjusted using the Bonferroni correction. Multivariate logistic regression analysis was utilized to identify risk factors for severe illness outcomes. The significance level was set at  $p < 0.050$ .

## RESULTS

A total of 160 patients were included in the study, with 38.8% ( $n=62$ ) being female and 61.2% ( $n=98$ ) male. The median age of the participants was 3 years (IQR: 1-5). Hospital admissions peaked during the spring, accounting for 34.4% ( $n=55$ ) of the cases, with similar distributions across other seasons. The most commonly reported symptoms were cough (66.3%) and fever (52.5%). Upon admission, 22.5% ( $n=36$ ) of the patients had low oxygen saturation. Of the patients, 41.2% ( $n=66$ ) required hospitalization, with 19.6% ( $n=13$ ) of these treated in the intensive care unit. Mechanical ventilation or high-flow nasal cannula (HFNC) support was necessary for 10% ( $n=16$ ) of the patients: four required intubation, seven used non-invasive mechanical ventilation, and five received HFNC treatment.

The study participants were categorized into three groups based on the presence of chronic diseases. The first group, consisting of patients with primary or secondary immunodeficiencies, made up 15% ( $n=24$ ) of the study population; the second group, including those with chronic lung diseases, accounted for 15.6% ( $n=25$ ); the third group, comprising individuals without respiratory-affecting chronic diseases or without any chronic conditions, represented 69.4% ( $n=111$ ). Lung infiltration was

observed in 33.1% (n=53) of the patients. Statistical analysis showed significant associations between both chronic diseases and lung infiltration with hypoxia ( $p < 0.001$  for both), and with the need for mechanical ventilation ( $p < 0.001$  for both).

Factors influencing hypoxia included fever (OR=0.257, 95% CI 0.76-0.87,  $p=0.029$ ), cough (OR= 7.66, 95% CI 1.32-44.22,  $p=0.023$ ), lung infiltration (OR= 0.12, 95% CI 0.03-0.48,  $p=0.003$ ), and the presence of chronic diseases (OR= 0.27, 95% CI 0.08-0.9,  $p=0.033$ ).

Blood tests were conducted on 54% (n=87) of the patients, revealing leukopenia in 3% (n=5) and leukocytosis in 13% (n=22). C-reactive protein (CRP) levels were positive in 20% (n=18) and negative in 80% (n=69) of the cases. Three patients died from complications associated with HPIV; two of these had immunodeficiency, and one had chronic lung disease.

## DISCUSSION

HPIV infections typically present with mild symptoms in children; however, the presence of chronic diseases can significantly increase morbidity and mortality. Our study aimed to delineate the clinical features of HPIV infections and identify factors that contribute to a poorer prognosis. The insights gained provide valuable guidance for managing and treating the disease in pediatric patients.

HPIV infections are predominantly observed in the spring and late winter seasons (8,9). Our findings align with general patterns described in the literature, where PIV-3 infections often reach epidemic levels in the summer, while other subtypes peak from autumn to spring (10). PIV-4 infections are more frequent in late summer and autumn (11,12). The reasons for these seasonal variations in subtypes are not fully understood but may relate to regional rainfall patterns, possibly influencing the genetic structure of the viruses (10). Since our study did not differentiate between subtypes, we cannot comment on specific subtype-related outcomes.

In both children and adults, chronic diseases such as immunodeficiency, chronic lung disease, and heart failure are associated with more severe HPIV infections (13,14). Studies have reported severe pneumonia in children with severe combined immunodeficiency syndrome (SCID) and the progression from upper respiratory infections to pneumonia and respiratory failure in transplant patients (15,16). Our study corroborates these findings, demonstrating a significant association between chronic diseases and increased needs for hypoxia management and ventilatory support. It is crucial to rigorously assess children with chronic conditions, given their elevated risk for serious morbidity and mortality.

In a study on hospitalized patients diagnosed with HPIV infection, cough was the most common reason for admission, affecting 82.2% of cases (17). Another study reported that

fever was the most frequent cause of emergency admissions, followed by cough (18). Swamy et al. (16) noted that cough was present in all patient admissions. These findings indicate that fever and cough are the most common symptoms. Similarly, our study found that fever and cough were the most prevalent symptoms. The variation in results across different studies may be due to the differing priorities of symptoms that prompt different populations to seek hospital care. Moreover, the absence of prominent symptoms in the early stages of infection could result in a lower reported frequency of fever.

Lower respiratory tract infections are frequently associated with HPIV infections. In a study involving 743 patients, of whom 69 were diagnosed with HPIV, the incidence of lung infiltration was reported to be 15.94% (n=11) (19). Another study observed that 9.6% (n=21) of patients exhibited lung infiltration, 7.7% (n=17) required admission to the intensive care unit, and 3.2% (n=7) needed mechanical ventilation (20). Similar rates were observed in our study. It is recommended that chest radiography be performed in selected children diagnosed with HPIV, as those showing lung infiltration on chest radiographs may require intensive care admission and respiratory support.

## CONCLUSION

While HPIV infections are commonly associated with croup, they can also lead to severe lower respiratory tract infections. Hospitalized patients may necessitate intensive care and mechanical ventilation, either invasive or non-invasive. The presence of chronic diseases and lung infiltrations adversely affects patient prognosis. Therefore, careful monitoring is imperative for children with HPIV infection presenting with fever and cough, especially those with radiographic evidence of lung infiltration or a history of chronic illness, as they may develop a need for intensive care or mechanical ventilation during their illness course.

### Limitations:

The main limitations of our study include its single-center, retrospective design. Factors such as access to healthcare facilities, particularly in rural areas, and delays in seeking care due to socioeconomic reasons could significantly influence the clinical course observed. Multi-center and prospective studies are essential to obtain a more comprehensive understanding of HPIV infections and their outcomes.

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